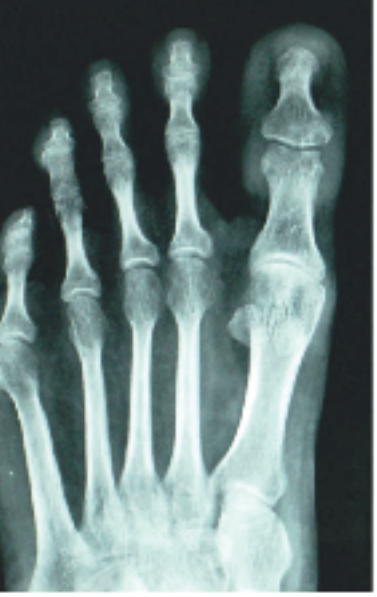

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CONTENTS

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Systemic lupus erythematosus: not a rare disease among black Africans

Systemic Lupus Erythematosus (SLE) is a multi – systemic, auto immune and often severe disease. Its aetiology is still poorly understood. Factors such as genetic, environmental, hormonal and immunological have been implicated in its pathogenesis. It occurs worldwide but is more prevalent among black Americans and Hispanics. It also runs a more severe and fatal course among this group[1]. While it occurs more commonly in black females, the mean age at onset is lower than among Caucasians[2].

Lupus had always been said to be rare among black Africans[3-5]. Symmons[3] has proposed a prevalent gradient hypothesis which describes an increasing prevalence of SLE as one moves from Africa to North America and Europe. Butcher[6] has suggested that the presence of malaria prevents auto – immune disease such as lupus and sarcoidosis among West Africans by inhibiting macrophage function. McGill and Oyoo[7] have suggested that rheumatoid arthritis and SLE while increasing in frequency in the indigenous population of East, Central and Southern Africa remain rare in West Africa. Case reports predominantly and small case studies seen over many years had been reported in Ghana, Guinea, Cote d' Ivoire, Senegal, Zimbabwe, Kenya and Congo Republic[4]. In spite of the foregoing there have been increasing reportage of SLE among black Africans since 1988 – Dessein *et al*[8] - South Africa, Tikly *et al*[9] - South Africa, Adelowo *et al*[11] – Nigeria, Ekwom[12] – Kenya. There have also been reports of SLE among migrants of West African origin residing in United Kingdom[13]. This reported frequency was comparable to Afro - Caribbeans, but more than in Caucasians.

The demographic characteristics in these reports are similar in some studies but differ in others. Female preponderance is seen in all reports, as expected. The mean ages at presentation are also identical, 33 years in Nigerians[11]; 35 years in South Africans[9]; 34 years in Kenyans[12]. The largest reported series is from South Africa with 111 patients[9]; 95 patients in Nigeria[14]; but 13 patients in Kenya[12].

Malar rash and arthritis were reported in 69.2% of Kenyan patients, Discoid rashes were frequently seen in South Africans patients, while arthritis was seen in 70.4% of South African[15,16]. In contrast, Adelowo *et al*[11] reported arthritis in 87% of their patients but had a lower frequency of malar rashes (21.2%); photosensitivity (9%); discoid rashes (43.9%). In another report from South Africa, there was low frequency of malar rash and photosensitivity in black lupus patients[10]. Of particular interest concerning clinical presentation among Nigerian patients is the presentation with recurrent fever, seen in 50% of patients. This was usually being diagnosed by doctors as malaria or typhoid fever. It is not surprising that the other features of lupus may be masked since these patients are treated with anti malarials. However, other common features of lupus are often seen in Nigerian patients. These include fatigue, seizures, pleuritic chest pain, hair loss, weight loss, mouth and pharyngeal ulcers and cognitive impairment[11]. Associations with Anti – phospholipid syndrome have also been reported among black Africans[16,17].

Mortality and morbidity among SLE patients are usually high, particularly so among black Americans and Hispanics. Various factors have been attributed such as genetic, socioeconomic, high incidence of hypertension, poor drug compliance. Mortality and morbidity have been mostly associated with renal damage, infections, atherosclerosis. Wadee *et al*[18] have looked at this in the South African population including blacks. Of the 270 cases studied, there were 55 deaths during the course of a mean follow up of 54.9 months. The estimated 5 year survival rate was estimated at between 57% and 72%. Infections and renal failure were reported as the commonest causes of mortality. Renal involvement may even be the presenting feature of patients with SLE, even when they do not yet fulfil the ACR criteria. We are presently following up twelve of such cases in our unit; of which there have already been four fatalities. As elsewhere, many SLE patients are often lost to follow-up.

Lupus is such a chameleonic disease that is capable of showing up in unexpected places. We have reported two patients presenting with digital gangrene even before other SLE features appeared[19]. We have also reported a case of neonatal lupus in the daughter of a patient being managed for SLE[20].

Serologic abnormalities are characteristics of SLE. Not much work has been done among black Africans. In the few reported series, there are some similarities as well as dissimilarities. In a study from Nigeria among 95 lupus patients, the following frequency of auto antibodies was reported ANA – 95.7%; dsDNA-54.4%; Anti Sm – 75.7%; Anti RNP – 81.8%; Ro/SSA – 69.7%; La/SSA – 15.2% anti chromatin – 66.7%; Rheumatoid factor – 42.1%14. The titre of ANA is mostly on the high side among Nigerians with titres of 1:320 and above constituting 57.8% of the cases, and a patient having a titre of above 1:5120. The dominant staining pattern on immune fluorescence is speckled (77.5%). Tikly *et al*[9] in contrast have reported frequencies of auto antibodies as follows – ANA (98.2%); ds DNA (66.2%); Anti Sm (44.2 %); Anti RNP (65.5%); Anti Ro/SSA (60.5%); anti La/SSB (10.1%), Rheumatoid factors (10.1%).

Management in all cases were with the standard drugs of corticosteroids, anti malarials, immuno suppressive. B lymphocyte cell depletors have been used in a few cases from Nigeria most especially patients with lupus nephritis[21].

SLE is not a rare disease in black Africans. An increased awareness may be the key to diagnosing this often severe

disease among the population. The new SLICC criteria offer hopes of early diagnosis and effective management. In a recent unpublished audit of 3000 patients with rheumatological diseases seen in a private clinic in Lagos' Nigeria, 170 (5.7%) were diagnosed as SLE using the ACR criteria while rheumatoid arthritis constituted 12.6% of all the cases seen by us[22]. It may not be surprising therefore that many more are undiagnosed in Nigeria with a population of 140 million.

We have in our unit screened patients with recurrent fever; loss of weight associated with polyarthralgia and markedly elevated ESR for SLE. Of course, the usual suspects of HIV and tuberculosis would have been excluded. Such background helps us to select patients for serology investigations. Of course, as with all chronic illnesses among black Africans, laboratory investigations and drug treatment are mostly unaffordable. We may therefore have to rely on clinical acumen to initiate management.

It is hoped that community based studies will be able to elucidate some of the issues concerning this chameleonic hydra – headed disease. Such may decrease mortality and morbidity in these patients.

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Rheumatologic manifestations associated with Hepatitis C virus infection: A cross sectional multicentric study in Cameroon

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Abstract

Background: Hepatitis C Virus (HCV) infection is a worldwide burden whose seroprevalence is higher in developing countries with Cameroon being the third most affected country in Africa. HCV both a hepatotropic and lymphotropic infection is responsible for a great number of hepatic and extra hepatic disorders some of which are rheumatic in nature. These rheumatologic manifestations though extensively studied in western countries; there is little or no data in sub-Saharan Africa.

Objective: The study was conducted with the aim to describe the musculoskeletal manifestations associated to HCV infection in a hospital setting in Cameroon.

Design: A cross-sectional study.

Setting: Three hospitals in Cameroon: the Douala General Hospital, a tertiary referral hospital with a capacity of 320 beds in Douala, the largest city and economic capital of Cameroon; the University Teaching Hospital of the Faculty of Medicine and Biomedical Sciences of the university of Yaoundé 1, a 240 beds hospital in Yaoundé the political capital of Cameroon and the "Centre Médical de la Cathédrale", a private acceptable standard Gastroenterology clinic also found in Yaoundé.

Patients and methods: From February to June 2009, we did a multicentric cross-sectional study of patients from the Gastroenterology, Rheumatology and Internal medicine outpatient clinics of three hospitals in Cameroon. Patients with HIV or HBV infection and those on antiviral treatment were excluded.

Results: Among 148 patients with HCV infection identified during the study period, only 62 fulfilled eligibility, 15 (24.2%) of whom had musculoskeletal manifestations related to HCV, the commonest of which were myalgia 9/62 (14.5%) , arthritis 6/62 (9.7%), bone pain 6.4% (4/62), sicca syndrome 3/62 (4.8%), and Raynaud's phenomenon 6/62 (9.7%). Among patients with rheumatologic manifestations, 9/15 (60%), had rheumatologic symptoms at HCV diagnosis and in 6/15 (40%). HCV infection was discovered during routine medical check-up. Musculoskeletal manifestations were neither associated with the genotype (*p=0.17*) nor with the viral load (*p>0.98*).

Conclusion: Arthralgia is the most common presenting feature of the symptomatic disease. Musculoskeletal manifestations may be confused with symptoms of common tropical infections, leading to delayed diagnosis and treatment of HCV infection.

Key words: Hepatitis C Virus, Arthralgia, Extra hepatic manifestations; Africa

Introduction

Hepatitis C Virus (HCV) infection which occurs worldwide has a higher seroprevalence in Africa, estimated at 5.3% compared to about 1.03% in Europe[1,2]. Cameroon, the third most affected country in Africa, has a seroprevalence which varies from as low as 0.6% to 4.8% in Pygmy groups and blood donors, to as high as 13% in hospital based studies[4,5]. Hepatitis C virus (HCV) which is a single-stranded, spherical RNA enveloped flavivirus, measuring 38 to 50 nm in diameter has multiple genotypes and quasispecies classified in six major clades. This genetic diversity confers to this virus a difference in pathogenicity, disease severity, and response to treatment with interferon[3]. Though considered a hepatotropic virus, HCV's lymphotropic nature is responsible for a great number of extra hepatic immune system disorders[1]. About 40 to 70% of affected patients will develop an extra hepatic manifestation that can have a rheumatic nature. These

rheumatologic manifestations include arthralgia, arthritis, myalgia, Sicca syndrome, vasculitis, and high prevalence of auto antibodies[6,7]. In western countries with relatively low burden of HCV infection, these syndromes have been extensive[6-9] but in sub-Saharan Africa with the higher burden of HCV, little or no data is available and some of the rheumatologic manifestations may be considered as symptoms of common tropical parasitic infections, thus retarding diagnosis and appropriate medical care. In this light, we opted to carry out this study with the aim of describing the musculoskeletal manifestations in HCV infection in a hospital based setting in Cameroon (Central Africa).

Study setting and patients: From February to June 2009, after prior institutional ethical clearance, we carried out a cross-sectional study in three hospitals in Cameroon: the Douala General Hospital, a tertiary referral hospital with a capacity of 320 beds in Douala, the largest city and economic capital of Cameroon; the University Teaching Hospital of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé 1, a 240 beds hospital in Yaoundé the political capital of Cameroon and the "Centre Médical de la Cathédrale", a private acceptable standard Gastroenterology clinic also found in Yaoundé. Our study population comprised of consenting adult patients diagnosed to be HCV infected diagnosed either through a routine medical check-up or those who presented with symptoms suspicious of HCV infection. Our study units were the Gastroenterology, Rheumatology and Internal medicine units of these hospitals. HCV infection was defined by positive serum antibodies against HCV detected by Enzyme linked Immunosorbent Assay (Abbot Architect i1000SR immunology analyser, Abbott, France), followed by positive RNA plasma detection of viral particles, quantified by Polymerase Chain Reaction (Cobas Tagman, Roche). Genotype specification was done using Immunoblot Genolipa, Bayer. Patients with Human Immunodeficiency Virus (HIV) or Hepatitis B Virus (HBV) infection and patients on antiviral treatment were not included in this study. For each eligible patient, socio-demographic, clinical and biological data relevant to the study comprising age, sex, past medical history of rheumatologic disease, symptoms relevant to musculoskeletal disease, as well as hepatic tests (transaminases), HCV RNA viral load and genotype, Antinuclear Antibodies (ANA), Rheumatoid Factor (RF), and Anti-Citrullinated Peptide Antibodies (ACPA). HCV RNA viral loads were later stratified: below 800,000 IU/ml were considered low and above 800,000 IU/ml were considered high. Categorical variables were presented as percentages of the total study population and continuous variables presented as mean and standard deviation. Statistical significance was considered at p values < 0.05.

Results

Out of 148 patients with HCV infection seen during the study period, 62 were eligible for the study (Figure 1). Among the studied patients, 37/62 (59.7%) were female (Table 1).

Figure 1: Flow chart of patient selection

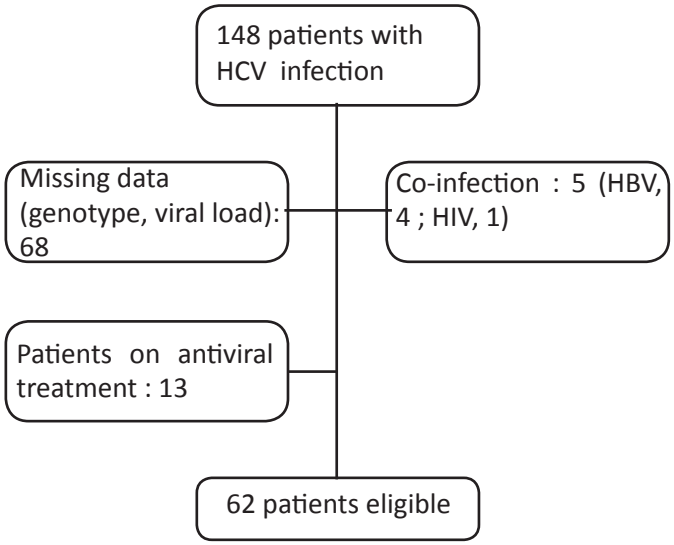

Table 1: Baseline characteristics of patients included in this study

Characteristics	No. (%)
Age, median [Interquartile range]	54 (28 – 76)
Female/male, n (sex ratio)	37/25 (1.7:1)
Viral genotype(n=62)	
Genotype 1,	31(50%)
Genotype 2,	9 (14.6%)
Genotype 3,	1 (1.6%)
Genotype 4,	20 (32.2%)
Genotype 5,	1 (1.6%)
Viral load (n=57)	
< 800,000 IU/mL	34 (59.6%)
≥ 800,000 IU/mL	23 (40.4%)

Fifteen patients (24.2%) had rheumatologic manifestations related to HCV infection all of whom had arthralgia 15/62 (24.2%). The diagnosis of HCV infection in these patients with rheumatologic manifestations was made during routine medical check-up in 6/15 (40%) of patients and in 9/15 (60%) of patients because of symptoms and/or signs that motivated testing for HCV. In the study population, arthritis was 6/62 (9.7%), myalgia was 9/62 (14.5%), bone pain was 4/62 (6.4%), sicca syndrome was 3/62 (4.8%), and Raynaud's phenomenon 6/62 (9.7%) (Figure 2).

Figure 2: Presenting complaints of HVC

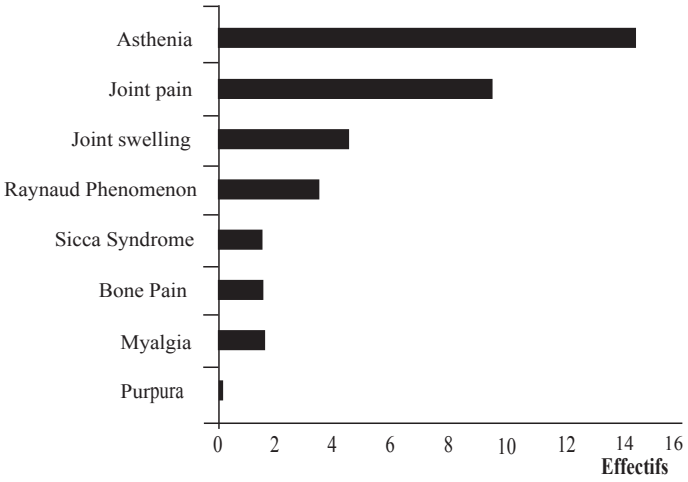

Table 2: Rheumatologic manifestations according to genotype

	Genotype 1 (n=8)	Genotype 2 (n=2)	Genotype 3 (n=2)	Genotype 4(n=3)
Arthralgia	8	1	1	2
Arthritis	3	1	0	0
Myalgia	4	2	0	2
Bone pain	2	0	0	2
Sicca syndrome	1	0	0	1
Raynaud's phenomenon	2	1	0	1

One genotype could present one or more rheumatologic manifestations

Among patients with arthralgia, the joint areas affected included: hands 12/15 (80%), knees 11/15 (73.3%), spine 8/15 (53.3%) and shoulder 7/15 (46.7%). RF, ANA and ACPA were done in some patients among whom RF was found in 4/8 (50%), ANA in 2/4 (50%) and ACPA in 1/3 (33.3%) tested patients respectively. One patient fulfilled the 1987 American College of Rheumatology (ACR) criteria for rheumatoid arthritis and another one the 1997 ACR criteria for systemic lupus erythematous. HCV genotype 1 was the most common in the study population (Table 1). Genotype and viral loads were not statistically significantly associated to presence of rheumatologic manifestations and were not associated with the genotype (p=0.17 and 0.98 respectively).

Discussion

To the best of our knowledge, our study is the first to describe prevalence and characteristics of rheumatologic manifestations in HCV-infected patients in sub-Saharan Africa. Our finding of a prevalence of rheumatologic manifestations in our HCV-infected patients to be 24.2% is not different to those reported in Western countries where it ranges from 19% to 31% [6-9]. In Egypt, a country with the highest burden of HCV infection in Africa, the overall estimated prevalence of rheumatologic manifestations of HCV infection was 16.39%[10]. In our study population, the diagnosis of HCV was made in the presence of nonspecific symptoms in 60% of patients with asthenia and musculoskeletal complains being the leading symptoms which is higher than 25% found in patients with extra-hepatic symptoms described as initial manifestations of HCV infection[9]. Though we found many patients to have symptoms that could be related to HCV, arthralgia, myalgia, arthritis, and Raynaud's phenomenon were the most common musculoskeletal manifestations as described in other studies[6-8]. Inflammatory arthralgia and arthritis were almost exclusively found in small joints of the hand. Two of our patients fulfilled classification criteria of RA and SLE. Rheumatologic manifestations of HCV infection can mimic some chronic inflammatory rheumatic diseases as RA, SLE, polymyositis, and Sjögren syndrome[6,11,12]. More so, the onset of arthritis has been reported in about 2 to 3% of HCV infected patients making the distinction from classical RA difficult. However, the presence of cyclic citrullinated peptide antibody is considered a discriminatory marker between RA and chronic HCV related arthritis[13]. Though patients in our study population were not tested for the presence of cryoglobulins, none was found to have clinical signs of small-vessel vasculitis amongst which purpura, livedo reticularis, distal ulcers and glomerulonephritis which are commonly associated with cryoglobulinemia. Two patients had Raynaud's phenomenon and one a Sicca syndrome.

Genotype 1 was the most common in our patients with rheumatologic manifestations. This could simply be reflecting the prevalence of this genotype in the general population in Cameroon[14]. Though common, this genotype was not statistically associated with rheumatic disorders. Contrary to expectation, this could suggest that rheumatologic manifestations could not be due to the direct effect of the virus; else we should have expected to see more in genotype 1 patients. Though viral load was not associated with an increase in rheumatologic manifestations, more manifestations were found in patients with low viral loads. Our finding is in favour of previous evidence that suggested that viral load or viral replication is not involved in the occurrence of rheumatologic manifestations[15]. Also, interferon reduces the prevalence of rheumatologic manifestations independently to viral response[16].

Our study had some limitations. Being a hospital based hospital study with few patients precludes generalization. Secondly, financial and laboratory limitations rendered it difficult to detect autoantibody profile in all patients (ANA, RF, and ACPA) and these were done only in patients with high suspicion of autoimmune disease, meaning that some patients with autoimmune diseases in our study population might have been missed.

Conclusion

Rheumatologic manifestations are frequent in HCV infection and may even be a diagnostic lead to HCV infection and therefore patients presenting with nonspecific rheumatologic manifestations should also be screened for HCV. HCV infected patients with rheumatologic manifestations should also be worked up for autoimmune antibodies because they could be associated.

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Research article

Antiphospholipid antibodies in patients with venous thrombosis at Kenyatta National Hospital

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Abstract

Objective: To determine the presence and types of antiphospholipid antibodies in patients with venous thrombosis at Kenyatta National Hospital.

Design: A cross-sectional descriptive study.

Setting: This study was conducted at Kenyatta National Hospital (KNH), a major referral and teaching hospital in Nairobi, Kenya, between January and November 2011. The study areas included the Accident and Emergency department, wards and outpatient clinics, and the Haematology and Immunology laboratories.

Participants: Male and female adult patients diagnosed with venous thrombosis confirmed by Doppler ultrasound or MRI.

Main outcome measures: Age, gender, presence or absence of lupus anticoagulant, and titres of anticardiolipin (ACL) and anti-β_2-GP1 antibodies (anti-β_2GP1).

Materials and Methods: Demographic and clinical information was collected by direct interview of patients. Every patient was examined for clinical manifestations of APA and blood drawn for laboratory tests. A proforma questionnaire was used to collect all the information. The data collected was pooled, screened and entered into SPSS v.19 software for analysis.

Results: A total of 60 patients were studied. Majority of the patients, 52 (86.7%), were females, while males were 8 (13.3%). The mean age was 38.3 years (± 13.7), with a median (IQR) of 52 years (38.8, 58) for males vs. 32.5 years (24.8, 43.5) for females, p value <0.05). The mean APTT value was 38.4 seconds (± 15.1) with 20 patients (33.3%) having prolonged values. Two patients (10%) had a prolonged KCT (RI >0.16; positive for LA), and all 20 (100%) who had a prolonged APTT had a negative DRVVT (NR <1.30; negative for LA). The mean anticardiolipin IgG titre was 107.4 U/mL (SD ± 62.4); 55 patients (91.7%) had a positive ACL result. The media anti-beta-2-glycoprotein IgG titre was 5 G units (IQR= 4.5, 6.5); 55 patients (91.7%) had a negative result. A significant positive correlation existed between APTT and ACL (r=0.39) and between ACL and β_2GP1 (r=0.30).

Conclusions: Antiphospholipid antibodies (LA and anti-β2GP1 IgG antibodies) are present in a very small proportion of patients seen at KNH with venous thrombosis. ACL IgG antibodies may be induced by numerous factors and may not be related to thrombosis. Pathological antiphospholipid antibodies are uncommon in patients seen at KNH with VTE.

Introduction

The Antiphospholipid Antibodies (APA) are a heterogenous family of immunoglobulins directed against anionic phospholipids or protein phospholipid complexes. Lupus Anticoagulant (LA) and Anticardiolipin Antibodies (ACL) are the two best clinically characterized antiphospholipid antibodies[1].

The frequency of APA in the normal population is approximately 3.6%, with most of these antibodies being induced by either infections or drugs. A high prevalence is seen in conditions such as peripheral vascular disease, recurrent foetal loss in women of reproductive age, acquired thrombotic episodes, autoimmune disorders, malignancies and cardiovascular disease, among others[1].

Evidence shows that the presence of antiphospholipid antibodies is associated with the development of venous or arterial vascular thrombosis[2,3]. The most frequent site for venous thrombosis is the lower limb[2]. Other sites that may be involved include retinal, renal and hepatic veins. The most frequent manifestation of arterial thrombosis is ischaemic stroke or transient ischaemic attack. Antiphospholipid antibodies are also associated with a significant risk of recurrent thromboembolism, especially on discontinuation of anticoagulants. Patients with APA-associated venous thrombosis therefore require prolonged or lifelong anticoagulant therapy[4].

This study was designed to determine the presence and types of antiphospholipid antibodies in patients with venous thrombosis at Kenyatta National Hospital. This information provides some measure of the presence of APA in patients with DVT in our setting, as these are patients who would benefit from prolonged anticoagulant prophylaxis.

Materials and Methods

Approval for the study was obtained from Kenyatta National Hospital Ethical and Research Committee prior to commencement of the study. In addition, informed consent was obtained from each study participant.

Consecutive adult patients seen at Kenyatta National Hospital Accident and Emergency department, wards and outpatient clinics with DVT confirmed by Doppler ultrasound or MRI between January and November 2011 were potentially eligible for the study. The exclusion criteria included those on anticoagulant medication and those documented as having a bleeding disorder, which would interfere with the coagulation tests.

All patients underwent an examination of clinical history and physical examination, and then blood was then collected for the laboratory tests. Seven and a half millilitres of blood was collected and divided into (i) 3.5 ml into a trisodium citrate vacutainer and (ii) 4 ml into a plain vacutainer. Blood collected into trisodium citrate was immediately transported to the haematology laboratory where platelet poor plasma was prepared by centrifugation at 3000 rpm for 10 minutes. The plasma samples were aliquoted and stored at -80°C, awaiting the coagulation tests (PT, APTT, KCT and LA test), which were done after batching of the samples.

The blood collected into plain vacutainers (4 ml) was transported to the Immunology laboratory, and then allowed to clot undisturbed for 1 hour at room temperature. The serum was separated from the clotted blood by centrifugation at 3000 rpm, then aliquoted and stored at -80°C. Analysis for VDRL, TPHA, ACL and anti-β_2-GP1 antibodies was done after batching of the samples.

Frozen specimens were thawed on the bench or in a water bath at room temperature, and then inverted several times to ensure homogeneity before use for a test. The coagulation tests (PT and APTT) were performed at the Haematology laboratory using an automated coagulation analyser (ACL200). Hemosil™ PT-Fibrinogen HS PLUS and APTT Lyophilized Silica kits were used. Samples with prolonged APTT were subjected to LA detection procedures using two different testing methods, as recommended by the International Society of Thrombosis and Haemostasis guidelines[5], KCT[6,7] (LupoTek KCT kits), and DRVVT[8] (LupoTek DetecTin VL and LupoTek CorrecTin VL kits).

The results of the KCT are expressed as a Rosners Index, with a cut-off of >1.30 being positive. The results of the LA DetecTin and CorrecTin tests are expressed as a Normalized Ratio, with a cut-off value of >0.16 considered as positive.

VDRL test was performed in the Immunology laboratory using the Syphilis RPR Test kit[9], followed by a TPHA test on the VDRL positive samples, using the Syphilis TPHA liquid kit. The tests for detection of anticardiolipin and anti-beta$_2$-glycoprotein 1 antibodies were performed using ELISA kits, the IMTEC-Cardiolipin-Antibodies IgG kit and the REAADS® IgG Anti-Beta 2 Glycoprotein 1 Semi-quantitative Test Kit.

There was strict adherence to protocol during sample collection, storage and processing. All tests were performed in accordance with manufacturers' recommendations. Internal quality control materials provided by the manufacturers were included during analysis. Validation of the ELISA tests was done according to the manufacturers' recommendations.

The data collected using a structured questionnaire and pre-designed extraction sheets was entered into Ms Excel computer database, cleaned and verified, then imported into SPSS (v.19) statistical software for analysis. Descriptive statistics on socio-demographic characteristics was presented using percentages and frequencies for categorical or nominal data. Continuous variables were presented using means (standard deviations) if normally distributed and medians (inter-quartile range) for non-normally distributed variables. Tables and appropriate charts were used to display the results. T-test or ranksum tests were used as appropriate to compare difference in means for two groups of continuous variables. Chi-square or Fisher's tests for independence were used to assess association between two nominal or categorical variables. The level of significance was set at 5% with p-values of $\leq$0.05 being considered significant. Correlation analysis to asses for any linear association was done using Pearson correlation coefficient for the continuous variables, and considered significant at 5% level.

Results

A total of 62 eligible participants were enrolled into the study. Two were excluded due to mislabeling of the specimens. The remaining 60 met the inclusion criteria and were evaluated for the requirements of the study. Majority of the patients were females, 52 (86.7%). The mean age was 38.3 years (± 13.7), with a median (IQR) of 32.5 years (24.8, 43.5) for females and 52 years (38.8, 58) for males (Table 1).

Table 1: Demographic characteristics (n=60)

Characteristic	
Age in years, mean (SD)	38.3 (±13.7)
Gender	n (%)
Male	8 (13.3%)
Female	52 (86.7%)

The mean APTT value was 38.4 seconds (± 15.1), (Table 2), with a majority of the patients having either normal 31(51.7%) or prolonged values 20 (33.3%). (Normal control value was 28.3 – 38.3 seconds).

Table 2: APTT results (n=60)

Characteristic	Results
APTT (seconds), mean (SD)	38.4 (± 15.1)
APTT categories	n (%)
Shortened (<28.3 s)	9 (15%)
Normal (28.3 – 38.3 s)	31 (51.7%)
Prolonged (>38.3 s)	20 (33.3%)

KCT was performed on the 20 patients with prolonged APTT, and the results expressed as Rosners Index (RI). The mean RI was 0 (± 0.3), with majority of the patients 18 (90%) having a negative value and 2 (10%) having a positive value (Table 3).

The Lupus anticoagulant DetecTin and CorrecTin tests were also performed on samples with prolonged APTT, and the results expressed as a Normalized Ratio (NR). The mean NR was 1.2(± 0.1) with all the samples 20 (100%) testing negative for LA, as shown in Table 3.

Table 3: Lupus anticoagulant detection tests (n=20)

Characteristic	Results
Rosners Index (KCT), mean (SD)	0 (± 0.3)
Rosners Index KCT categories	n (%)
Negative	18 (90%)
Positive	2 (10%)
Normalized Ratio (LA) , mean (SD)	1.2 (± 0.1)
Normalized ratio DRVVT categories	n (%)
Negative	20 (100%)

Fifty-five patients (91.7%) tested negative for VDRL, (Table 4). Out of the 5 who tested positive, 4 (80%) also tested positive for TPHA. The mean anticardiolipin IgG titre was 107.4 U/mL (SD ± 62.4) with almost all 55 (91.7%) having a positive ACL result. With regard to anti-beta-2-glycoprotein IgG, the median was 5 G units (IQR= 4.5, 6.5) with almost all 55 (91.7%) the patients exhibiting a negative result (Figure 1).

Table 4: Immunology and biochemistry test results (n=60)

Characteristic	Results
VDRL n (%)	
Negative	55(91.7%)
Positive	5(8.3%)
TPHA n (%) (n = 5)	
Negative	1(20%)
Positive	4 (80%)
Anticardiolipin IgG (U/mL), mean (SD)	107.4 (± 62.4)
ACL categories n (%)	
Negative	5 (8.3%)
Positive	55 (91.7%)
Antibeta2 glycoprotein IgG (G units), median (IQR)	5 (4.5,6.5)
Antibeta2 glycoprotein IgG categories n (%)	
Negative	55 (91.7%)
Positive	5 (8.3%)

As shown in Table 5, the male patients were significantly older than the females, median age (IQR) 52 (38.8, 58) vs. 32.5 (24.8, 43.5), p value <0.05.

Figure 1: ACL IgG and anti-β_2GP1IgG box plots

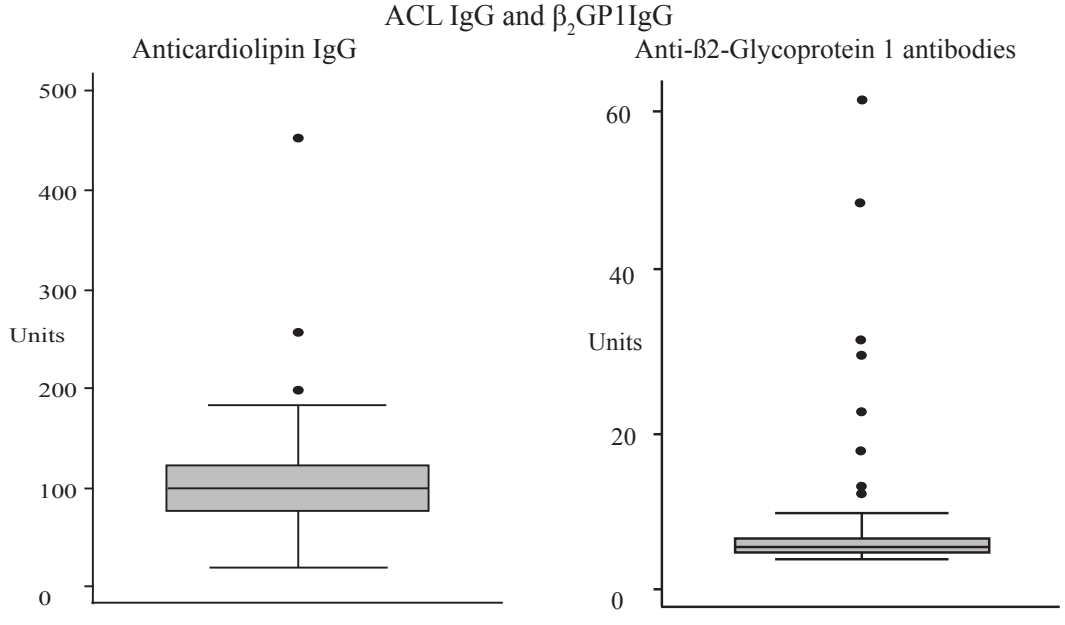
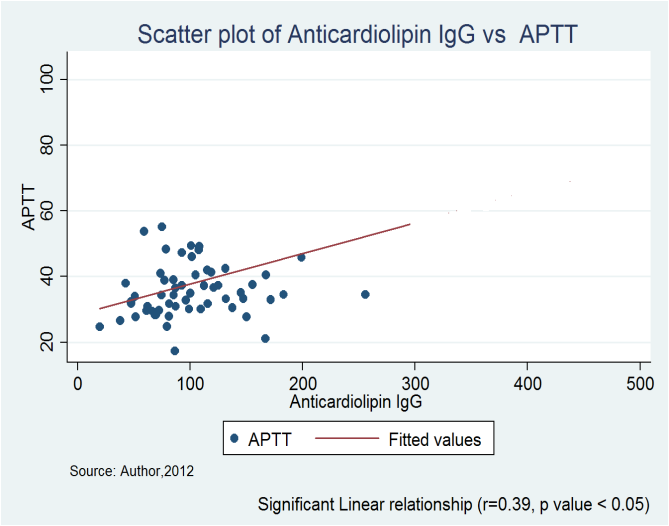


Table 5: Bivariate analysis by gender

Variable	Male	Female	Test statistic	p value
Age in years Median(IQR)	52 (38.8,58)	32.5 (24.8,43.5)	Ranksum test	0.013*

* Significant result (p <0.05)

Figure 2: Correlation between ACL and APTT



Correlations were done using Pearson correlations coefficients and statistical significance determined at 5% level. A significant positive correlation existed between APTT and ACL (r=0.39; p value <0.05), (Figure 2), and between ACL and β_2GP1 (r=0.30; p value <0.05).

Discussion

This study evaluated 60 patients, most of who were females (86.7%). The male participants were significantly older than the females, with a median age of 52 years and 32.5 years respectively.

The APTT was slightly prolonged in a third of the patients evaluated in this study. The causes of the prolonged APTT in these patients' samples may have been due to the presence of heparin, LA, or a coagulation factor deficiency. Thrombin test would have been useful to confirm for the presence of heparin in these samples, as it would cause prolongation of test. This was a limitation of this study, as the thrombin test was not performed. The DRVVT reagent used in this study contained a heparin neutralizer, but unfractionated heparin in excess of therapeutic levels may not be completely neutralized by these neutralizers, and this would interfere with the LA results. Few patients had a shortened APTT, which may have been due to difficulties during sample collection, with partial clotting of the specimens before analysis.

LA was positive in two patients by the KCT test, while DRVVT was negative for all. However, one of the patients with a positive KCT test had syphillis, which may have interfered with the test results to give a false positive LA. The incidence of LA positivity in this study is low (1.6%), compared to those from the West, and is similar to the incidence found in the general healthy population (1%)[10]. Simioni *et al*[11] found five LA positive patients among 59 unselected patients with DVT (8.5%), while Ginsberg *et al*[12], found nine LA positive patients out of 65 (14%).

VDRL test was negative in most patients. Out of the five with a positive VDRL, only one was a false-positive result, as evidenced by a negative TPHA. The other four were confirmed to have syphilitic infection by the TPHA test. Almost all the patients recruited into this study were positive for IgG anticardiolipin antibodies. Several factors may explain this; firstly, the ACL antibodies were measured in the blood after the thrombosis. An assumption made by this study was that the APA measured after the thrombotic event reflects the antibody status before the event. Transiently elevated ACL antibody levels are found in many patients after a venous thrombosis, suggesting that the antibodies may be a result, rather than a cause of thrombosis in these patients[13].

Secondly, analytic issues in the ACL assays may also contribute to false-positive results. Even when a β_2-dependent ACL assay is used, the recommended dilutions during testing enable other endogenous proteins in the serum, apart from β_2-GP1, to be present in a sufficiently high concentration that allows binding in a non-β_2GP1-dependent fashion, thus reducing the specificity of the test. Thirdly, the cut-off values used in this study for interpretation of the ACL assay were those recommended by the manufacturer of the reagent used. It is recommended that local cut-off values be used whenever possible[14]; however, local reference ranges for ACL have not been established for this population.

Five patients (8.3%) were positive for anti-β_2-glycoprotein IgG antibodies. This finding is similar to that of a study by Zanon *et al*[15], who found a prevalence of 8.4% of anti-β_2GP1 antibodies in patients with acute thromboembolic events.

In conclusion, this study shows that antiphospholipid antibodies (LA and anti-β2GP1 IgG antibodies) are present in a minority of patients seen at KNH with venous thrombosis, with the positive tests for anti-β2GP1 being more common than for LA. ACL IgG antibodies may be induced by numerous factors and may not be related to thrombosis. Screening for antiphospholipid antibodies in patients with venous thrombosis at KNH should therefore be limited to relatively young patients with unprovoked thrombosis or recurrent thrombosis. An LA assay together with an anti-β_2-GP1 assay may be more useful than an ACL antibody assay, unless local cut-off values for ACL are established.

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Prevalence of HIV infection among the patients with an avascular necrosis of the femoral head in Ouagadougou, Burkina Faso

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The preliminary results of this work were displayed and presented during the 23rd Congress of the French Society of Rheumatology from November 28, 2010 to December 1, 2010 in Paris-La Defense (France)

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Abstract

Objective: To study the prevalence of HIV infection among the risk factors associated with the avascular necrosis of the femoral head in Ouagadougou, Burkina Faso.
Design: Multicenter retrospective study.
Setting: Rheumatology consultations and Orthopedic-Traumatology Surgery Department Of The University Hospital Yalgado Ouédraogo, at the Medico-Surgical Private Clinic "Notre Dame de la Paix" and the Medical Center 'Paul VI' in Ouagadougou, Burkina Faso.
Patients and methods: The study was conducted on recorded cases from January 2007 to December 2009. All patients received during the study period for an avascular necrosis of the femoral head that was confirmed by X-ray and / or CT were included. The search for HIV antibodies was performed for all patients by the ELISA test confirmed by the Western Blot test.
Results: There were 79 men (56%) and 62 women (44%). It shows a sex ratio of 1.2. The average age of patients was 43.95 ± 15.36 years with extremes of 7 and 79 years. The average duration of disease before diagnosis was 6 ± 6.5 years with extremes of 1 and 39 years. The affected area involved the left hip in 67 cases (47.5%), the right hip in 48 cases (34%) and was bilateral in 26 cases (18.5%). Among the risk factors, alcohol consumption was reported in 30/67 (44.8%), steroids in 09/67 (13.4%), sickle cell disease in 12/141 (8.5%). Six patients (4.25%) among the 141 had an HIV infection.
Conclusion: HIV infection has a place among the risk factors of an avascular necrosis of the femoral head. A HIV serology test should be systematically carried out in all patients with an avascular necrosis of the femoral head in sub-Saharan Africa, particularly in the absence of other risk factors.

Key words: Avascular necrosis of the femoral head, HIV, sickle cell disease, sub-Saharan Africa.

Introduction

The aseptic osteonecrosis of the femoral head is an ischemic degeneration of a wide epiphysis area. Its location at the femoral head causes an Avascular Necrosis (AVN). It represents 1.11% of rheumatology consultations in Burkina Faso[1]. If in the Western countries, etiologies are dominated by alcoholism and corticotherapy[2], in Black Africa, the sickle cell disease seems to be the primary risk factor[3,4]. For many years, HIV infection has been recognized as another risk factor for the AVN[5]. An American study on 38 patients with non-traumatic AVN of the femoral head reported in seven cases (18.4%) an association with infection by Human Immunodeficiency Virus (HIV); among these seven patients, 4 (10.5% with AVN of the femoral head) had no other classic risk factors [6]. Despite Africa being the continent most affected by HIV infection[7], the prevalence of this infection during the AVN of the femoral head is unknown, to our knowledge, in sub-Saharan Africa. Recently, Eholié *et al*[8] in Ivory Coast reported three cases of AVN of the femoral head in patients infected with HIV but with sickle cell disease[8].

The objective of this study was to describe the prevalence and semiological features of HIV infection among the risk factors associated with AVN of the femoral head in Ouagadougou, Burkina Faso.

Materials and methods

This was a multicenter retrospective study conducted on recorded cases from January 2007 to December 2009 at the rheumatology consultation and Orthopedic-Traumatology Surgery Department Of The University Hospital Yalgado Ouedraogo, the Medical and Surgery Clinic Private 'Notre Dame de la Paix', the Medical and Surgery Center 'Paul VI', in Ouagadougou, Burkina Faso. The latter two hospitals receive once a year services provided by an international team specialized in prosthetic hip surgery.

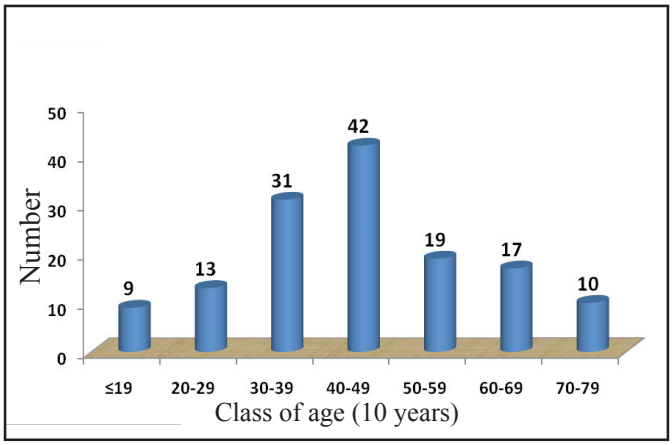
All patients received during the study period for AVN of the femoral head confirmed by X-ray and / or CT were included. The infectious, inflammatory coxites, the septic osteonecrosis of the femoral head were excluded. All patients underwent a complete blood count, erythrocyte sedimentation rate, a C-reactive protein (CRP), a hemoglobin electrophoresis and serology testing for anti-HIV antibodies.

All these patients recruited consecutively, have previously had, on venous blood at the elbow a hemoglobin electrophoresis test at alkaline pH and an Emmel test in the presence of hemoglobin S. The HIV serology test was performed by the ELISA test and confirmed by the Western Blot test. Patients were defined as "consuming alcohol", when they regularly drank more than two glasses of beer per day. Data confidentiality was assured. The various variables were entered using a pre-computerized form, then analyzed with an Epi Info version 3.5.1.

Results

Characteristics of the study population: One hundred and forty-one patients were included during the study period. There were 79 men (56%) and 62 women (44%) giving a sex ratio of 1.2. The average age of patients was 43.95 ± 15.36 years with extremes of 7 and 79 years. The age group 40 to 49 years was most concerned. The distribution of patients by age is shown in Figure 1.

Figure 1: Distribution of patients by age



The average duration of disease before diagnosis was 6 ± 6.5 years with extremes of 1 and 39 years. The affection concerned the left hip in 67 cases (47.5%), the right hip in 48 cases (34%) and was bilateral in 26 cases (18.5%). The amyotrophy was investigated in 71 patients; it was present in 10 (14.1%) and involved the quadriceps. The shortening of the affected lower limb, studied in 75 patients, was observed in 38 (50.7%) cases. The average shortening was 1.5 cm ± 0.4 cm with extremes of 1 and 5 cm, resulting in an average reduction of the walking distance to 800 ± 250 m with extremes of 100 and 2000 m; 19.73% was at a stage of functional impairment. On radiographs, 118 patients (83.7%) were at stage IV of the classification of Arlet and Ficat. Table 1 shows the distribution of patients according to the classification of Arlet and Ficat. Thirty three patients (23.4%) underwent a total hip prosthesis with 16 cemented and 17 un-cemented. A girl-patient of 19 years old was treated with an osteotomy of varization.

Table 1: Distribution of patients according to the classification of Arlet et Ficat

	No.	(%)
I	0	0
II	4	2.8
III	19	13.5
IV	118	83.7
Total	141	100

Risk factors associated to the AVN of the femoral head: Among the 67 patients who underwent a complete search of the traditional factors, 15 (22.4%) had no risk factors. Table 2 shows the distribution of patients according to risk factor.

Table 2: Distribution of patients according to risk factors associated with AVN of the femoral head

	Number n/N*	(%)
Classic		
Alcohol consumption	30/67	44.8
Steroids**	09/67	13.4
Femoral neck fracture	09/141	8.9
Sickle cell SC	12/141	8.5
HIV infection	06/141	4.25
Dislocated hip	01/67	1.5
Discussed		
Obesity	14/53	26.4
Smoking	08/67	11.9
Gout	02/67	2.98

* n / N: number of cases over the total number of patients surveyed. ** Four (04) molecules were involved: betamethasone, prednisone, metylprenisolone, and triamcinolone prescribed for sinusitis (4 cases) dermatitis (2 cases), asthma (1 case), renal disease of unknown aetiology (1 case), a chronic gout (1 case) for a period of two years to 15 years.

Table 3: Characteristics of the HIV infected patients with AVN of the femoral head

Case	Age (years)	Sex*	Others RF**	HIV subtype	Treatment***	Duration (years)	Localization
1	54	M	Alcohol	HIV_1	AZT+3TC+NVP	2	Bilateral
2	39	F	Sickle cell SC	HIV_1	None	-	Right
3	46	M	None	HIV_1	None	-	Left
4	42	M	None	HIV_1	D4T+3TC+NVP	8	Right
5 †	30	F	None	HIV_1	D4T+3TC+NVP	2	Bilateral
					D4T+3TC+LPV/r	3	
6	48	M	Steroids	HIV_1	D4T+3TC+NVP	6	Bilateral

*sex : M= male, F= female ; **RF= risk factors ;
***AZT : zidovudine ; 3TC : lamuvidine ; NVP : névirapine ; D4T : stavudine ; LPV/r : lopinavir boosted by ritonavir.
† Because of a failure in the treatment at the end of 2 years, the nevirapine was replaced by the lopinavir boosted by the ritonavir (both inhibitors of protease).

No cases of sickle cell SS or S beta thalassemia have been reported. Six (4.25%) among the 141 had an HIV infection. Table 3 lists the characteristics of patients with HIV infection.

Discussion

One hundred and forty cases of AVN of the femoral head in a multicenter study conducted in 2 years are reported. This series is, to our knowledge, the most important that was reported in West Africa[9,10]. The risk factors have been dominated by the consumption of alcohol (44.8%), steroids (13.4%), sickle cell disease SC (8.5%). HIV infection was reported in six (4.25%) including three with Highly Active Antiretroviral Therapy (HAART). The average age of patients (43.9 years) was higher than that reported by Oniankitan *et al*[10] (38.5 years) in Togolese patients with hemoglobin AA and AS. Coulibaly *et al*[9] in Mali reported an average age of 31 years in a study involving a pediatric surgery department. The other semiological features were identical to the other African and Caucasian series[2,3] apart from the severity of the cases reported in sub-Saharan Africa[9]. This severity could be caused by the delay before consultation in our series (6 years on average). However an anomaly in the vascularity of the femoral head could contribute to the severity of injury but remains to be confirmed. The risk factors have been dominated by alcohol consumption, steroids and SC sickle cell. The importance of alcohol consumption (44.8%) could result from the given definition.

Six patients (4.25%) had HIV infection. Among these, three had other risk factors (cases 1, 2 and 6), in the other three, no other risk factor could be found. The first cases of AVN of the femoral head in patients infected with HIV have been reported in literature since the 1990s. The association of HIV infection and AVN of the femoral head, now seems established. The crude incidence of osteonecrosis of 1.2 cases per 10 000 persons-years in subjects not receiving HAART treatment increase from 4.0 cases per 10 000 person-years for those with less than 12 months of HAART treatment to 15.9 cases per 10 000 person-years for those with 60 months or more[11]. The mechanism of this association remains unclear. The protease inhibitors have long been accused[12], however, recent studies seem to implicate all classes of anti-retroviral[13]. One patient (case 5) in our series received a protease inhibitor. HIV is known to cause a syndrome of antiphospholipid antibodies that may cause thrombophlebitis and an AVN[14]. Furthermore, patients infected with HIV are likely to cause protein S deficiency which also predisposes to thrombosis[14]. Recently, hyperlipidemia during therapy with protease inhibitors has been mentioned as a possible factor for the development of AVN in patients infected with HIV[15].

HIV infection has a place among the risk factors of AVN of the femoral head, justifying its systematic search in all patients with epiphyseal necrosis in sub-Saharan Africa particularly in the absence of other risk factors. Indeed, the virus itself, could stimulate the production of proinflammatory cytkines such as interleukin 6 and tumor necrosis factor involved in bone resorption[16]. In a study on 33 cases of AVN of the femoral head, the virus has been found as the only risk factor in 33%[17]. Ries *et al* [6] also reported seven patients with AVN of the femoral head associated with HIV, four (57%) with no other risk factor for epiphyseal necrosis. In case 3 of our series, AVN of the femoral head was the circumstance of the discovery of the HIV infection and no other risk factor was found. In a previous study of 366 patients infected with HIV and on treatment for more than 12 months, no cases of AVN of the femoral head had been reported, probably because of the absence of systematic X-ray of the pelvis[18]. Yombi *et al*[19] in a similar study of 815 patients had reported a prevalence of 0.74% of AVN of the femoral head. Furthermore, magnetic resonance imaging and scintigraphy remain the ideal means of early diagnosis[20]. Indeed, Miller *et al*[21], in a comparative study of 339 HIV-infected patients and 118 healthy patients, had reported 15 cases (4.4%) of AVN of the femoral head in the group infected with HIV and no cases in the control group, using MRI as a diagnostic tool. HIV infected patients are at 100 fold greater risk of developing osteonecrosis than the general population[22].

Nevertheless, the results of our study have been limited by biases due to the absence of research of

anti-phospholipid antibodies, protein S deficiency and lipid profile. However, these results are suggestive and demand the setting up of a multidisciplinary team to be in charge of the adverse effects of HIV and HAART treatment in the various countries of sub-Saharan Africa. Besides, the absence of study in population concerning the AVN of the femoral head, does not allow to assert that its prevalence is more higher in our series than in the general population.

Conclusion

HIV Infection has a role as a risk factor in AVN of the femoral head in Burkina Faso. Its mechanism (viral or iatrogenic) remains controversial. Considering the extent of the HIV pandemic in sub-Saharan Africa, studies of a larger scale are needed to define the exact place of this affection. Multidisciplinary teams are needed for the management of adverse effects related to the virus or the HAART. A HIV serology test should be performed routinely in all patients with AVN in sub-Saharan Africa, particularly in the absence of other risk factors.

Conflict of interest: The authors declare no conflict of interest.

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Health related Quality of Life in Libyan patients with rheumatoid arthritis

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Abstract

***Background**:* In order to measure therapeutic effects or assess disease course, outcome measurement parameters are commonly used in patients with Rheumatoid Arthritis (RA). Quality of Life (QoL) is important outcome measure. There is a paucity of data on the impact of chronic rheumatic diseases on functional disability, as well as Health-Related Quality of Life (HRQOL) in Africans (1). Unfortunately there is no available data about HRQOL in Libya.

Objective: Evaluation of RA burden in Libya was the aim of the study; the study goal was to determine Health Related Quality Of Life (HRQOL) in patients with Rheumatoid Arthritis (RA), who are on disease modifying antirheumatic drugs (DMARD).

Setting: Rheumatology clinic of Tripoli Medical Center, Tripoli, Libya.

Methods: The inclusion criteria for the study were all patients who were diagnosed to have RA by the American College of Rheumatology ACR criteria of 1987, were on DMARDs (started within 6 months of disease duration), had a 28-joint disease activity score (DAS28) of 2.6-5.1, attended the rheumatology clinic of Tripoli Medical Center, Tripoli, Libya, from 1st June 2010 to 30th July 2010 and consented to participate in the study. The study was done after receiving consent from the Tripoli Medical Center ethical and research committee.

Results: One hundred patients were included in the study. The age at diagnosis ranged from 15 to 73 years; the median age was 39 years. The majority of patients were females 94 (94%) patients and 6 (6%) patients were male. The disease duration (symptoms onset to evaluation) ranged from 6 months to 40 years, the median disease duration was 7 years**.** Rheumatoid factor was positive in 72 (72%) patients. They had a 28-joint disease activity score (DAS28) of 2.6-5.1. They were on DMARDs started within 6 months of disease duration, 85% were on methotrexate, 10% were on hydroxychloroquine and 5% were on sulfasalazine. Sixty five percent were on prednisolone tablets (5mg) in addition to DMARDs. Sixty three percent of patients had score 0-1, 25% of them had score 1-2 and 12% had score 2-3. The mean of HAQ score for all patients was 0.86 with standard deviation (SD) of 0.76. The median was 0.75 (range 0.000-2.625)

Conclusion: After evaluation of the RA burden in Libya, we found that 63% of our patients had HAQ score of 0-1, which means mild to moderate disability. In this study, patients selected were using DMARDs at early stage of the disease, (disease duration ≤ 6 months), in further studies, we will compare these results with results of patients who had used DMARDs at later stage of the disease.

Introduction

Rheumatoid Arthritis (RA) is the most common inflammatory arthritis. RA affects 0.5% to 1% of the general population worldwide[1]. It is a chronic, autoimmune, disease that is associated with inflammation of the articular synovium in the joints, resulting in bony erosions, deformity and ultimately joint destruction[2]. In order to measure therapeutic effects or assess disease course, outcome measurement parameters are commonly used in patients with RA**.** Quality of Life (QoL) is an important outcome measure[3]. According to the World Health Organization (WHO), quality of life is defined as; "the satisfaction of a patient with their situation in terms of health status and their ability to function in daily life". Assessment of Health- Related Quality of Life (HRQOL) has gained much importance in the care of Rheumatoid Arthritis (RA)[4]. A vast array of instruments has been created to measure HRQOL. They are typically divided in to two categories; generic and disease-specific. Generic measurements include health profiles and instruments that generate health utilities, whereas disease-specific instruments include activities of daily living and function specific to the disease in question[2]. The medical outcomes study, 36-Item Short Form (SF-36) and HAQ-DI, are perhaps the most well-known and widely used generic and disease-specific health status measures used in the evaluation of RA

patients, respectively[2]. SF-36 has limited reliability and responsiveness for use in clinical studies[5,6]. There have been two main approaches to the assessment of the effects of RA on patient's lives; quantitative and qualitative. The quantitative approach employs scores obtained by RA patients using standardized measures of health status. The HAQ[7] is the most widely used measure of functional disability in RA. Several instruments, such as, the Arthritis Impact Measurement scale (AIMS)[8], and the subsequent AIMS2[9], the Nottingham Health Profile (NHP)[10] and the Sickness Impact Profile (SIP)[11], these instruments have been designed in an attempt to go beyond the measurement of physical impairment and disability, by addressing more emotional and social aspects of a condition. However, problems have been identified with all three instruments. None have been found to have adequate reliability[10-11]or to be consistently responsive. The EuroQol, primarily intended for use in utility analyses, has also been advocated as a generic measure of health-related quality of life that could be applied with RA patients[12]. Meanwhile, the content of the instrument is rather simplistic and covers function, rather than Qol. It has been found to be crude[13], unresponsive[14] and to yield poor response rate[15].

The HAQ, published in 1980, was among the first instruments based on generic, patient-centred dimensions. The HAQ was designed to represent a model of patient-oriented outcome assessment. Strengthened by its use over the past two decades in diverse settings, the HAQ has established itself as a valuable, effective, and sensitive tool for measurement of health status. It is available in more than 60 languages and is supported by a bibliography of more than 500 references[16]. We used HAQ-DI in this study because it is a good predictor of future disability and it is easily applicable.

Objectives of the study: Evaluation of RA burden in Libya was the aim of the study; the study goal was to determine Health Related Quality Of Life (HRQOL) in patients with Rheumatoid Arthritis (RA), who are on Disease Modifying Antirheumatic Drugs (DMARD).

Materials and Methods

The inclusion criteria for the study were all patients who were diagnosed to have RA by the American College of Rheumatology ACR criteria of 1987[17], were on DMARDs (started within 6 months of disease duration), had a 28-joint Disease Activity Score (DAS28)[18] of 2.6-5.1, attended the Rheumatology Clinic of Tripoli Medical Center, Tripoli, Libya, from 1st June 2010 to 30th July 2010 and consented to participate in the study. The study was done after receiving consent from the Tripoli Medical Center ethical and research committee.

Exclusion criteria: Patients in remission, those with high disease activity and patients on biological treatment were excluded. Demographical details such as age and educational level were recorded. The details of the disease were noted such as the duration of the disease and the type of DMARDs used for every patient. The selected patients were asked to complete a HAQ-DI (translated Arabic version) by themselves and submit it on the same day.

Data analysis: Data was analyzed using SPSS computer software package. Continuous variables were categorized in ranges and summarized in to means, medians and standard deviations.

Results

One hundred patients were included in the study. The age at diagnosis ranged from 15 to 73 years, the median age was 39 years. The majority of patients were females. Ninety four (94%) patients were female and 6 (6%) were male. The disease duration (symptoms onset to evaluation) ranged from 6 months to 40 years, the median disease duration was 7 years (Table1).

Table 1: Demographic and clinical characteristis of the patients

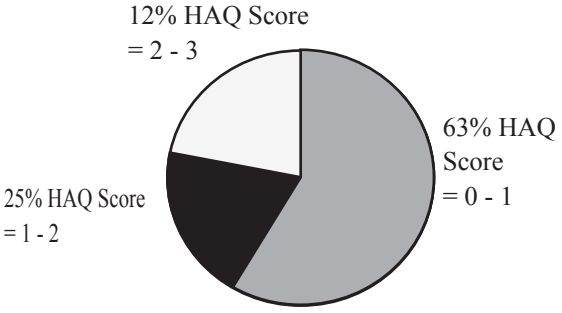
No. of patients	100
Age at diagnosis (years)	
Mean(SD)	40 (SD=12.86)
Median (range)	39 (15-73)
Sex	
Female	94
Male	6
Duration of disease (years)	
Mean	8.17 (SD=6.62)
Median (SD)	7.00 (6 months - 40 years)

Rheumatoid factor was positive in 72 (72%) patients. They had a 28-joint Disease Activity Score (DAS28) of 2.6-5.1.

They were on DMARDs started within 6 months of disease duration; 85% were on methotrexate, 10% were on hydroxychloroquine and 5% were on sulfasalazine, 65% were on prednisolone tablets (5mg) in addition to DMARDs.

Sixty three percent of patients had score of 0-1, 25% of them had score of 1-2 and 12% had score of 2-3 (Figure 1).

Figure 1: HAQ scoring of 100 RA patients



The mean of HAQ score for all patients was 0.86 with standard deviation (SD) of 0.76. The median was 0.75 (range 0.000- 2.625).

Discussion

The utilization of Health-Related Quality Of Life (HRQOL) patient questionnaires by clinical rheumatologists is limited. Although, literature supports the potential value of HRQOL patient questionnaires in

clinical practice, few rheumatologists routinely gather such information as part of patient care[19]. It is cardinal rule that the questionnaire used for assessing HRQL should be regionally applicable and based on the practices of the population from that particular region[4]. We used HAQ-DI to assess the extent of our patient's functional ability, as it has been widely used in research purposes, as well as in clinical setting. It is sensitive to change and is a good predictor of future disability and cost. It has been shown to be reliable and valid in different languages and context[20]. The treatment of RA has seen a paradigm shift in the last decade. More pressure is being put on early detection and aggressive intervention in order to prevent disability and irreversible damage. The pace of radiographic erosion, which progresses very fast in the initial phase of the disease, can be retarded by effective control of the disease activity[21]. Survival per se is no longer the treatment goal for RA. Another goal is control of joint symptoms and thus to improve, restore, or preserve health related quality of life[2].

We compared this study with another study which had been done in South African public health care clinic[22]. In that study, only 17% of patients were completely self sufficient (HAQ-DI 0.00-0.50), 22% were reasonably self-sufficient (HAQ-DI>0.50≤1.25), 26% had many major problems with activities of daily living (HAQ-DI>1.25≤2.00) and 35% could be regarded as severely handicapped (HAQ-DI>2.00-3.00). The median HAQ-DI score was 1.6 compared to our study where the median HAQ-DI score was 0.75.

The median HAQ-DI in South Africa study was worse than our results ($p<0.05$). This might be related to the selection of our patients. We selected patients who were started early on DMARDs and who had DAS28 score of 2.6-5.1.

Conclusion

After evaluation of the RA burden in Libya, we found out that 63% of our patients had HAQ score of 0-1, which means mild to moderate disability. In this study, patients selected were using DMARDs at early stage of the disease, (disease duration ≤ 6 months), in further studies, we will compare these results with results of patients who had used DMARDs at later stage of the disease.

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Assessment of pulmonary function in rheumatoid arthritis patients attending Rheumatology Clinics in Nairobi

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Abstract

Background: Pulmonary involvement is a frequent and among the most severe extra-articular manifestations of Rheumatoid Arthritis (RA) ranking as the second cause of mortality in this patient population. Rheumatoid arthritis can affect the lung parenchyma, airways and pleura. Pulmonary complications are directly responsible for 10-20% of all mortality in RA patients. Spirometry is becoming increasingly available in Kenya and could be used in peripheral areas to screen and monitor for pulmonary function abnormalities in well characterized patient populations such as those with RA. Abnormalities detected by pulmonary function tests may precede symptoms by years and lead to early diagnosis of pulmonary fibrosis in rheumatoid arthritis and hence intervention.

***Objective*:** To determine the prevalence of pulmonary function abnormalities in rheumatoid arthritis patients attending Rheumatology Clinics in Nairobi.

Design: Cross sectional descriptive study.

Setting: Nairobi Rheumatology Clinics in Kenyatta National Hospital, Aga Khan University Hospital and Mater Hospital.

Methods: Rheumatoid arthritis patients aged 13 to 65 years who fulfilled the study inclusion criteria were recruited. Sociodemographic characterictics and respiratory symptoms were assessed using Lung Tissue Research Consortium questionnaire (LTRC) and RA disease activity was established by Disease Activity Score (DAS28). Pulmonary function tests were then done using Spirolab 111 according to the American Thoracic Society recommendations.

Results: One hundred and sixty six RA patients were recruited; the male to female ratio was 1:9.3, with a median age of 47 years. The overall six month prevalence of pulmonary function abnormalities was 38.5% as measured by Spirometry and all our patients did not carry any prior pulmonary disease diagnosis. The predominant ventilatory defect was obstructive pattern at 20.4%, followed by restrictive pattern at 16.8% and least common being a mixed picture at 1.2%. Factors that were shown to be independently associated with pulmonary function abnormalities were age and RA disease activity. Respiratory symptoms that were predictive of PFTs abnormalities were cough, increased frequency of chest colds and illnesses and phlegm.

Conclusion: High prevalence of pulmonary function abnormalities was observed. Respiratory symptoms, older age and ongoing disease activity can identify patients in greatest need of further pulmonary evaluation.

Key words : Rheumatoid Arthritis, Pulmonary function test, Nairobi Rheumatology Clinics

Introduction

Rheumatoid Arthritis (RA) is the most commonly encountered connective tissue disease. It is a chronic inflammatory and systemic disease which mostly affects the synovial joints with a prevalence ranging from 0.5% to 2%. It is a progressive autoimmune process characterized by symmetrical erosive synovitis. Although the central pathology of RA develops within the synovium of diarthrodial joints, many nonarticular organs become involved, particularly in patients with severe joint disease. The female to male ratio of RA is 2.5:1 most frequently seen in the 25-55 years age group[1]. In recent cohort studies, nearly 40% of patients with RA suffered from some type of extra-articular manifestations[2-4]. Extra-articular manifestations can be detected in almost all organ systems as cutaneous, ocular, haematological, cardiovascular and pulmonary lesions[4].

Pulmonary involvement is a frequent and among the most severe extra-articular manifestation of RA[5]. It is a leading cause of excess death in patients with RA and the second cause of death in this patient population[6,7]. Pulmonary complications are directly responsible for 10 to 20% of all mortality[8,9]. When compared with control populations, patients with RA and with a respiratory disease have an

estimated standardized mortality ratio that ranges from 2.5 to 5.0[6,9]. The majority of lung disease occurs within the first 5 years after the initial diagnosis, and may be a presenting manifestation in 9 to 20% of patients. The onset of respiratory manifestation may even precede the onset of symptoms of arthritis.

Lung disease directly associated with the underlying RA is more common, even though pulmonary infection and drug toxicity are frequent complications of RA. The lung is involved in rheumatoid disease because of the abundant vasculature and connective tissue which is involved in collagen vascular diseases. RA can affect the lung parenchyma, airways, and the pleura, with variable amounts of pathological inflammation and fibrosis. The well-characterized pulmonary disorders in RA include: RA-associated Interstitial Lung Disease (ILD), pleural effusions and pleuritis, rheumatoid nodules, Caplans syndrome, pulmonary vasculitis and pulmonary airway involvement. Bronchiectasis and an increased incidence of chest infections have also been reported[10,11].

The prevalence of a particular complication varies based on: The characteristics of the population studied, the definition of lung disease used and the sensitivity of the clinical investigations employed. However, all studies concur in that a high prevalence of abnormality can be found. Furthermore, while the prevalence of other serious extra-articular manifestations is declining, RA-associated lung disease is increasing[13] both pulmonary infection and drug-induced lung disease included[14,15]. In the USA, a study done in John Hopkins University by Pappas *et al*[16] on 159 RA patients, found a 28% prevalence of pulmonary function abnormalities on spirometry. The most common ventilatory defect was obstructive at 11.3%, restrictive pattern was observed in 7.6% and an isolated impaired diffusing capacity of carbon monoxide in 9.6%. He identified factors such as seropositivity to rheumatoid factor, high titres of Anti-cyclic citrulinated peptide antibodies and ongoing corticosteroid use and some respiratory symptoms as predictive of abnormalities on spirometry.

The aim of this study was to determine the prevalence of pulmonary function abnormalities in RA patients and certain correlates (clinical and demographic) in rheumatoid arthritis patients attending Rheumatology Clinics in Nairobi.

Materials and Methods

This was a cross sectional descriptive study, done in three Rheumatology Clinics in Nairobi; Kenyatta National Hospital, Aga Khan University Hospital and Mater Hospital. Patients included in the study were above 13 years of age, confirmed to have RA as per ACR criteria and gave an informed consent. Those excluded were patients with documented active pulmonary lesions e.g pulmonary tuberculosis, pneumonia, asthma, COPD, patients who had documented cardiac disease and those with contraindications to spirometry. These patients were seen during the period September 2012 to February 2013. A total of 166 patients were recruited and tested for pulmonary function using spirometry according to the American Thoracic Society standards disease activity of RA was scored using (DAS 28) and respiratory symptoms evaluated by Lung Tissue Research Consortium questionnaire.

Results

Out of the 166 patients recruited, 150 (90.4%) were females and 16 (9.6%) were males with a ratio of 1: 9.3. Their ages ranged from 14 to 65 years with a mean of 47±13years. Rheumatoid factor was positive in 104 (62.7%) and negative in 62 (37.3%). The median duration of RA illness was 5 years, ranging from 4 to 10. Patients who were on DMARDs were 129 (78%), 36 (21.7%) were on steroids, while 27 (16.2%) patients were on NSAIDS. The mean DAS28 score was 3.68 ± 1.5 with a range of 1.5-7.6. Prevalence of pulmonary function abnormalities as measured by spirometry was 38.5%. The common ventilator defect was obstructive pattern at 20.4%, followed by restrictive pattern at 16.8% and then 1.2% with a mixed obstructive and restrictive ventilatory defect (Table 1).

Table 1: Prevalence of PFTs abnormalities with confidence intervals

Prevalence	No. (%)	95% CI of %	Median measurements
Normal	102 (61.4)	53.0-68.1	-
Pulmonary function abnormalities	64 (38.5)	31.9- 47.0	-
Obstructive	34 (20.4)	15.7- 28.3	FEV1/FVC 65%
Restrictive	28 (16.9)	11.4- 22.9	FVC 71%
Mixed	2 (1.2)	0.0- 2.4	-

Certain demographic and clinical factors were observed to be associated with pulmonary function abnormalities in this patient population. Those who showed abnormalities on PFT were significantly older in age; a mean age of 51 years for those who had pulmonary function abnormalities compared with 44.5 years with normal spirometry (p=0.003). Among RA features, the variables shown to be associated with pulmonary involvement were seropositivity to rheumatoid factor, 47 out of the 64 patients with PFT abnormalities had positive rheumatoid factors (p= 0.03). Fifty six patients with DAS 28 score of 3.2 to 7.6, depicting moderate to high disease activity, were observed to have abnormalities compared to 25 who had mild disease activity (p=0.001). The ESR median value of 36.1 had abnormal spirometry compared with those at 11 who had normal (p=0.001). DMARDs or steroids medications did not show any relationship to the outcome (p= 0.907, p=0.970 respectively) (Table 2).

Table 2: Comparison of patients with PFTs abnormalities and those with normal tests

Variable	PF abnormalities	Normal	OR (95% CI)	P value
Sex				
Male	5 (7.7)	12 (10.9)	0.65 (0.2-2.1)	0.495
Female	59 (92.3)	90 (89.1)	1.0	
Age	51.0 (12.6)	44.5 (14.2)	-	0.003
Duration of illness (years)	5.0 (4.0-10.0)	5.0 (3.0-10.0)	-	0.168
Rheumatoid factor				
Positive	47 (72.3)	57 (56.4)	2.0 (1.0-3.9)	0.039
Negative	18 (27.7)	44 (43.6)	1.0	
Smoking				
Yes	8 (12.3)	10 (9.9)	1.3 (0.5-3.4)	0.626
No	56 (87.7)	92 (90.1)	1.0	
Smoking history				
Yes	4 (6.2)	2 (2.0)	3.3 (0.6-18.3)	0.211
No	60 (93.8)	100 (98.0)	1.0	
Disease activity				
Moderate to high dse activity (3.2-7.6)	56 (69.2)	6 (7.0)	29.5(11.9-76.7)	<0.001
Mild to no disease activity (1.5-3.1)	25 (30.8)	79 (92.9)	1.0	
ESR	36.1 (19.8)	11.0 (9.2)	-	<0.001
Medications				
Methotrexate				0.248
Yes	34(52.3%)	62(61.4%)	0.7 (0.4-1.30)	
No	30(47.7%)	38(38.6%)		
HCQ+MTX				
Yes	10(15.6%)	15(14.7%)	1.0 (0.5-1.8)	0.907
No	54(84.4%)	87(85.2%)		
Prednisolone				
Yes	14(21.5%)	22(21.8%)	1.0 (0.5-2.1)	0.970
No	50(78.5%)	80(78.2%)		
Occupation				
Unemployed	33 (50.8)	31 (30.7)	2.4 (1.2-5.2)	0.020
Formal employment	17 (26.2)	39 (38.6)	1.0	
Business	6 (9.2)	18 (12.9)	1.1 (0.3-3.3)	0.921
Farming	8 (12.3)	14 (13.9)	1.3 (0.5-3.7)	0.609

Table 3: Associations between respiratory symptoms and pulmonary abnormalities

Variable	PFT	Normal	OR (95% CI)	P value
Cough				
Yes	36 (56.3%)	19 (18.7%)	5.6 (2.8-11.5)	<0.001
No	28 (43.7%)	83 (81.3%)	1.0	
Phlegm				
Yes	20 (31.0%)	6 (6.8%)	7.1 (2.6-18.7)	<0.001
No	44 (69.0%)	96 (93.2%)	1.0	
Wheeze				
Yes	3 (4.6%)	3 (2.9%)	1.6 (0.5-5.2)	0.352
No	61 (95.4%)	99 (97.1%)	1.0	
Breathlessness				
Yes	1 (1.5%)	3 (3.0%)	0.5 (0.1-5.0)	1.000
No	63 (98.5%)	99 (97.0%)	1.0	
Frequency of chest colds				
Less than once a year	11 (17.2%)	43 (41.2%)	1.0	
Once a year	11 (17.2%)	24 (22.7%)	1.8 (0.7-4.9)	0.234
2-4 times per year	32 (50.0%)	29 (29.9%)	4.0 (1.7-9.3)	0.001
5 or more times per year	10 (15.6%)	6 (6.2%)	6.1 (1.8-20.4)	0.004

As regards respiratory symptoms, cough was reported in 36 (56.3%) patients with abnormal spirometry compared with 19 who had normal (p= 0.001), phlegm was reported by 20 (31.0%) such patients compared with 6 patients (p= 0.001). A history of increased frequency of chest colds and chest illnesses (> 2 times in a year) was reported by 32 (50%) patients with pulmonary involvement compared with 20 who had normal test (p=0.001). Hence respiratory symptoms observed to be associated with PFTs abnormalities were cough, production of phlegm and frequency of chest colds (Table 3).

Discussion

The overall six month prevalence of pulmonary function abnormalities was 38.5% as measured by spirometry and all our patients did not carry any prior pulmonary disease diagnosis. The predominant ventilatory defect was obstructive pattern at 20.4%, followed by restrictive pattern at 16.8% and least common being a mixed picture at 1.2%. When evaluation of severity was done majority of these patients had mild defects (83.3% in the obstructive pattern and 60.7% in the restrictive).

A study done by Pappas *et al*[16] in John Hopkins University in the United States of America found a prevalence of pulmonary function abnormalities at 28%, nearly a third of the patients he studied, commonest being obstructive pattern at 11.3%, followed by restrictive at 7.6%. He also identified 9.6% with an impaired DLCO. Notably is that the patients studied had a lower disease activity score at a median of 3.1 compared to our study which was at 3.68, depicting that our patients were symptomatic for RA and still had active disease. It has been shown pulmonary involvement is higher in the setting of severe RA disease.

In Africa, Amir *et al*[17] studied 36 RA Egyptian patients and 64% of them demonstrated abnormalities in their pulmonary function tests, Mixed restrictive and obstructive pattern was commonest and reported in 11(30.6%), restrictive pattern at 8(22.2%) and obstructive pattern in 4 (11.1%). The mean disease activity score in his study was 3.63, almost similar to ours, hence the high prevalence of pulmonary impairment but differed in the patterns observed. His study excluded patients who had been exposed to cigarette smoking, since smoking has been shown to be the most consistent independent risk factor predicting the development of ILD in RA in most studies[11]. This could explain the lower incidence of obstructive pattern in his study as compared to our study which included 24 patients exposed to cigarette smoking. The present study found the prevalence of obstructive ventilatory defect to be the most common at 20.4%. This was an important finding since other studies have solely set out to find the prevalence of obstructive dysfunction in small airways in RA.

In France, Thierry *et al*[18] found an obstructive pattern of lung changes in 18% of RA patients using spirometry. He found no significant difference in the proportion of airflow obstruction among smokers and non smokers suggesting a minor role of tobacco smoke in such manifestations. This was also observed in our study where exposure to cigarette smoke had no relationship with the outcome (p=0.626), though we only had a small number of our patients exposed to cigarette smoking. A case control study by Vergnenegre *et al* [19] reported a 16% prevalence of airway obstruction (verses 0% in matched controls). A recent one by Shunsuke *et al*[20] found this to be 30.3%, after excluding 18% of the patients who had abnormalities in their HRCT indicative of interstitial lung disease. However, he included a significant number of smokers.

The reason for the high prevalence of PFTs abnormalities in our study is possibly due to ongoing RA disease activity. However the study took place in sub-Saharan Africa where environmental pollution and the use of biomass as fuel is common. These are known to cause deterioration in the physiological lung function and

though not assessed in our study, may have contributed to our results.

From this study, older age was shown to be associated with pulmonary abnormalities (p = 0.010), the mean age of those affected was 51 years compared to 44 with normal tests. On the other hand, we could not get any conclusion regarding sex of the patients since we only included 16 male patients. Exposure to cigarette smoking, though depicted, showed no relationship to outcome, other factors that were shown to associate with function abnormalities were seropositivity to rheumatoid factor (p=0.039) unemployment (p=0.02), moderate to high score on disease activity (p=<0.001) and ESR (p=0.001). These potentially significant parameters were tested for possible interrelationship by logistic regression analysis. Age remained an independent factor, the older the patient the more likely she had pulmonary involvement (p=0.010). Presence of disease activity as measured by DAS 28; clinical index of joint tenderness and swelling, also remained an independent factor. Patients who had a high and moderate score were more likely to have abnormalities in their tests (P = 0.025).

These findings are comparable to Amir *et al*[17] who observed that pulmonary abnormalities by PFT or HRCT were associated with older age and the RA clinical features that proved to associate with pulmonary involvement were joint tenderness index, duration of morning stiffness, and clinical disease severity. Pappas *et al* [16] did not find any age correlation, but observed that seropositivity to rheumatoid factor, presence of high titres of anti CCP antibodies and ongoing steroid therapy were associated with abnormalities in pulmonary function and identified patients in need of further pulmonary evaluation. These could well infer that symptomatic RA disease and/or disease severity was associated with pulmonary involvement because these are serological markers of disease activity hence supporting our findings. We did not evaluate for disease severity with the use of radiological score (hand and feet X-rays) or serology markers such as anti-CCP as these studies did, instead we used the disease activity score.

As might be expected, respiratory symptoms were statistically more significant in patients with abnormal PFTs. Presence of cough in 56.9% (P=0.001), increased number of chest colds in a year (2-4 times a year) reported by 50% (p=0.001) and production of phlegm by 30.8% were found to be significant. Receiver Operator Characteristic (ROC) curve was constructed to examine the ability of pulmonary symptoms to predict PFTs abnormalities. Area under the curve values for cough was 0.70, frequency of chest colds in a year 0.67, and production of phlegm 0.63 hence these symptoms were found to be predictive.

Our findings were in contrast with Amir *et al*[17] who among respiratory symptoms, dyspnea and cough were associated with any pulmonary abnormalities. He went further to elucidate that when specific pulmonary abnormalities were considered, dyspnoea was identified as predictor for restrictive pattern and for obstructive, both cough and wheezing provided valid prediction. Pappas *et al*[16] found chronic cough was predictive of obstructive pattern, breathlessness for restrictive and chronic phlegm for impaired gas transfer.

The different environments where each study took place could explain these findings. Our study was in the African tropics where the climatic conditions, environmental pollution and presence of communicable diseases may predispose the patients to experience frequent chest colds and illnesses in a year.

Conclusion

We observed a high prevalence of pulmonary function abnormalities as measured by spirometry in this RA population. The commonest ventilator defect pattern was obstructive followed by restrictive. In terms of severity most of the ventilatory defects were mild. There was an increased frequency of reported respiratory symptoms in RA patients with abnormal tests. Rheumatoid disease activity, older age and respiratory symptoms were identified as predictors of lung impairment as determined by spirometry.

Limitations

The study had the following limitations;

(i) PFTs are not the gold standard for detecting respiratory disease. We chose to use PFTs as our marker of lung disease in this analysis as they provide a common and low-risk diagnostic modality that often precedes radiographic evaluation in clinical practice.

(ii) Recruitment of patients from a university hospital rheumatology department could introduce some bias through selection of patients with somewhat more severe articular involvement than that in the overall RA population.

Recommendations

Pulmonary involvement is an important part of the systemic affection of RA. The role of surveillance for lung disease in patients with RA is clear and necessary. Rheumatologists and internists should routinely screen patients for early detection and intervention. Respiratory symptoms, older age and ongoing disease activity can identify patients in greatest need of further pulmonary workup.

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Prevalence of fibromyalgia in ambulatory HIV positive patients with musculoskeletal pain at Comprehensive Care Clinic, Kenyatta National Hospital,

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Abstract

Background: Fibromyalgia is a rheumatic condition that is characterized by chronic widespread musculoskeletal pain with painful pressure points. There are other symptoms that are associated with this condition and they include fatigue, sleep disturbance and depression. The cause of this condition is unknown however chronic viral infections eg HIV have been associated with fibromyalgia.
Objective: This study aimed to determine the prevalence of fibromyalgia in HIV positive patients.
Design: This was a cross-sectional descriptive study.
Setting: The study was carried out at the Comprehensive Care Centre, Kenyatta National Hospital**.**
Methods: The patients attending the clinic between the month of February 2013 and April 2013 were assessed for chronic musculoskeletal pain and subsequently fibromyalgia using the American College of Rheumatology criteria**.** Those found to have fibromyalgia were given the FIQR and those without were given the SIQR for comparison purposes. Clinical details eg WHO clinical stage, CD4 counts and HAART regimen for those on HAART were also documented.
Results: A total of 380 patients were evaluated. The prevalence of fibromyalgia in HIV positive patients at the Comprehensive Care Centre, Kenyatta National Hospital was 68 (17.9%). The mean age of these patients was 42.2 years with a median of 40.5 years.There was a female preponderance of 60 (88.2%). Fibromyalgia was independently associated with female gender, OR=2.75, unemployment status, OR=5.68 and retired status, OR=3.01. A majority of the patients were in WHO clinical stage 3 and the mean CD4 count was 276.2. There was however no association between fibromyalgia and WHO clinical stage, CD4 count and use of HAART or the specific HAART regimens. The mean FIQR was 50.1 which was significantly higher than the mean SIQR score of 12.4 in those without fibromyalgia.
Conclusion: Fibromyalgia is a prevalent rheumatologic condition among HIV positive patients with chronic musculoskeletal pain. It is also associated with a high FIQR score.

Introduction

Fibromyalgia syndrome is an increasingly recognized disorder characterized by chronic, widespread musculoskeletal pain, stiffness, fatigue and sleep disturbance. Physical examination elicits increased tenderness at muscle and tendon insertion sites, known as tender points [1].

The prevalence is related to both age and sex. It is a common condition occurring in the population and mostly seen in women. Older individuals tend to get it more compared to younger people. A study done in Wichita, Kansas[2] found the prevalence of fibromyalgia in the general population to be 2%. They found that the prevalence increases with age from 40 years onwards and it was more common in females.

Locally there is paucity of data on its prevalence; however a study done in 2011 by Dokwe *et al*[3], in Kenyatta National Hospital estimated it to be at about 11% in patients with chronic musculoskeletal pain attending the medical outpatient and rheumatology clinics. The overall prevalence was found to be 1%.

Fibromyalgia has been classified as a neurosensory disorder where central sensitization and abnormal central nociceptive processing have been found in these patients. The overall effect is that the patients have a lower threshold of stimulation of neurons that receive pain[4].

The cause of this condition is unknown. However, certain infectious agents for example chronic viral infections have been linked with fibromyalgia. This connection has been documented with regard to agents like Hepatitis C[5], Lyme disease[6], and HIV[7]. It is suggested that these infectious agents act as triggers for fibromyalgia [8].

In a study done by Simms *et al*[7] in a hospital in Boston City, out of 140 HIV positive patients investigated for rheumatologic conditions, 15 of them had probable or definite fibromyalgia; a prevalence of 41% in those with musculoskeletal pain, and overall prevalence of 11%. Fibromyalgia was associated with a longer duration of the HIV infection. There were more females compared to male and the mean age of the patients was 37 years . Patients who were on zidovudine based therapy did not have an increased frequency of fibromyalgia. This was also noted in another study done by Buskila *et al*[9] where they did not find an association between fibromyalgia and use of AZT.

The diagnosis of fibromyalgia is based on the 1990 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia; and includes:

(i) The presence of widespread pain lasting 3 months or more

(ii) The presence of more than 11 out of 18 possible tender points[10]

Other symptoms associated with fibromyalgia can be assessed using the FIQR whose three domains asses for symptoms, functionality and overall impact of the condition. The SIQR can be used to compare patients who don't have fibromyalgia as it has similar questions as that of the FIQR[11].

Serge Perrot[12] and his colleagues used several investigative tools to assess the burden of this disease. These included the Fibromyalgia Impact Questionnaire (FIQ), EuroQol, the Medical Outcome Study (MOS) Sleep Scale, the Brief Pain Inventory- Short Form (BPI- sf) and the Hospital Anxiety and Depression Scale (HADS). It was demonstrated that fibromyalgia patients incurred costs mainly on physician office visits and prescription medication. There was gross poor health related quality of life in these patients due to the attendant pain, poor functionality, sleep disturbance, anxiety and depression.

Materials and Methods

Subjects: Participants in this study were a consecutive sample population of HIV positive patients with chronic musculoskeletal pain at Kenyatta National Hospital (KNH) Comprehensive Care Clinic(CCC). A total of 2644 patients were assessed between the months of February 2013 and April 2013. Three hundred and ninety eight had chronic musculoskeletal pain among which 5 were excluded due to being below 18 years of age, 2 were in CCC for Post Exposure Prophylaxis hence HIV negative, 4 had neurocognitive impairment and 7 did not give consent. This left us with 380 patients for enrolement into the study.

We obtained wtitten consent from those who we recruited. Approval to conduct the study was undertaken from KNH/UoN-Ethics and Research Committee.

Data collection: Patients attending CCC during the study period were assessed for chronic musculoskeletal pain. This involved interviewing them on the presence of current pain involving any of the parts of the musculoskeletal system which included bones, joints, muscles and tendons. Those who had chronic muscloskeletal pain and fulfilled the rest of the inclusion criteria were enrolled in the study (380 patients). Determination of the HIV status was based on documentation from the file. An interviewer-administered study proforma was used to obtain demographic and clinical data. Clinical data entailed documentation of the current WHO clinical stage, recent CD4 count (within 3 months) and HAART status and regimen were derived from the file.

The ACR criteria was used to establish cases of chronic widespread pain and fibromyalgia. A targeted physical examination was done to establish the number of tender points. A total of 18 specified points were examined for tenderness by digital palpation whereby a force of 4 Kilograms (that which causes blanching of examiner's finger) was applied.

Patients who satisfied the ACR criteria of chronic widespread pain and eleven or more tender points were diagnosed to have fibromyalgia. Thereafter the FIQR was used to assess the frequency and severity of the fibromyalgia related symptoms. Those who did not fit the criteria for fibromyalgia were given the SIQR to assess their overall functionality and symptoms. For those who did not have a recent CD4 count (done within the previous 3 months), blood was drawn at the end of questionnaire administration for this purpose.

CD4 count assessment: Blood was drawn from the antecubital fossa via aseptic means; 3 milliliters was adequate for CD4 count. The blood was put in an EDTA bottle then taken to the laboratory within CCC where it was processed. Since this was done immediately, it did not require any special storage or transport. Determination of CD4 count was done using an automated BD FACSCalibur® machine. Results were available the following day and were also availed in the patients' file.

Statistical analyses: Data was entered and managed in Microsoft Access database. Data cleaning was done and the Access database was exported to SPSS version 17.0 for statistical analysis.

Prevalence was calculated as the number of patients with fibromyalgia divided by the total number of patients with chronic musculoskeletal pain and expressed as a percentage with 95% confidence interval.

Continuous data (age and CD4 count) was summarized into means and standard deviation while categorical data (gender, marital status, occupation, WHO stage and HAART status) was presented as proportions. CD4 counts were also analysed into categories. Comparison between those who have fibromyalgia and those without fibromyalgia was done with Student's T test for continuous data and Chi square test for categorical data. Fibromyalgia-related symptoms were analyzed and presented as mean scores for each patient and then compared with the mean scores of those without fibromyalgia using Student's t test.

Fibromyalgia was correlated with WHO clinical stage and the use of HAART using Chi square test and odds ratios (ORs) calculated to show the estimated risk ratios. Median CD4 count between patients with fibromyalgia

and those without the condition was compared using Mann Whitney U test. For all the variables associated with fibromyalgia, logistic regression analysis was done to control confounding factors and determine independent predictors of fibromyalgia in HIV patients. All the statistical tests were performed at 5% level of significance (95% confidence interval).

RESULTS

A total of 2644 HIV positive patients attending CCC were assessed for musculoskeletal pain between the months of February 2013 and April 2013. This was done by interviewing the patients on the presence of pain in the bones, joints and muscles. Out of these, 1902 did not have any musculoskeletal pain while 344 had pain that had been present for less than three months. Three hundred and ninety eight patients had chronic musculoskeletal pain though 18 were excluded because they did not meet the rest of the inclusion criteria (4 had neurocognitive impairment, 5 were below the age of 18 years, 7 declined to give consent while 2 were HIV negative and they had come to CCC for post exposure prophylaxis). We enrolled 380 patients in the study. Out of the 380, 68 patients had fibromyalgia giving a prevalence of 17.9% (95% CI, 14.2 - 22.1). The mean age of the patients was 41.1 years (SD = 9.9) with a range from 18 to 75 years. Most of the patients (70%) were aged between 30-49 years. Majority of the patients in the study, 282 (74.2%), were female giving a male-to-female ratio of 1: 2.9. Fifty-five percent of the patients were married and 23.4% were single (Table 1).

Thirty one patients (45.6%) were aged between 40-49 years. The mean age of these patients was 42.2 years. Sixty patients (88.2%) were of the females. There was a statistically significant association between fibromyalgia and female gender (p = 0.004). The odds of fibromyalgia was three-fold greater (OR = 3.0, 95% CI 1.4-6.6) among the female. Married patients, 37 accounted for 54.4% of all fibromyalgia cases. None of the marital status was statistically significantly associated with fibromyalgia (all p values > 0.05). There was a statistically significant association between patient occupation and fibromyalgia. The odds of fibromyalgia were significantly higher among unemployed, OR = 5.4 (95%CI 1.1-25) and retired patients, OR= 3.4 (95% CI 2.0-6.0) (Table 2).

Table 1: Demographic characteristics of the patients (n=380)

Demographic characteristics	Frequency n (%)	95%CI
Mean age in years (SD)	41.1 (9.9)	
Sex		
Female	282(74.2)	(69.8-78.6)
Male	98(25.8)	(21.4-30.2)
Marital status, n (%)		
Single	89(23.4)	(19.1-27.7)
Married	212(55.8)	(50.8-60.8)
Separated/ divorced	21(5.5)	(3.2-7.8)
Widowed	58(15.5)	(11.6-18.9)
Daily activities, n (%)		
Manual	188(49.5)	(44.4-54.5)
Not manual	192(50.5)	(45.5-55.6)
Occupation, n (%)		
Employed	277(72.9)	(68.4-77.4)
Unemployed	96(25.2)	(20.9-29.7)
Retired	7(1.8)	(0.5-3.2)

Table 2: Demographic characteristics of HIV positive patients with and without fibromyalgia

Demographic characteristic	Fibromyalgia (n=68)	No Fibromyalgia (n=312)	OR (95% CI)	P value
Mean age (SD)	42.2 (9.2)	40.9 (10)	-	0.34
Sex				
Male	8 (11.8)	90 (28.8)	1.0	
Female	60(88.2)	222(71.2)	3.0(1.4-6.6)	0.004
Marital status, n (%)				
Single	13(19.2)	76(24.4)	0.8(0.4-1.6)	0.55
Married	37(54.4)	175(56.1)	1.0	
Separated/Divorced	5(7.4)	16(5.1)	1.5(0.5-4.3)	0.47
Widowed	13(19.1)	45(14.4)	1.4(0.7-2.8)	0.39
Occupation, n (%)				
Employed	34(50.0)	243(78.9)	1.0	
Unemployed	31(45.6)	65(20.8)	5.4(1.1-25)	<0.001
Retired	3(4.4)	4(1.3)	3.4(2.0-6.0)	0.02
Daily activities, n (%)				
Manual	36(52.9)	152(48.7)	1.0	
Not manual	32(47.1)	160(51.3)	0.8(0.5-1.4)	0.53

Thirty seven patients (54.4%) with fibromyalgia were in stage III of HIV. The mean CD4 counts for those with fibromyalgia and those were 276.2 cells/ml. Fifty six patients (82.4%) of those with fibromyalgia were on HAART. Thirty nine (69.6%) of the patients on HAART therapy with fibromyalgia were on a regimen consisting of tenofovir, while 12 (21.4%) patients were on zidovudine-based therapy (Table 3).

Table 3: Clinical characteristic of HIV positive with and without fibromyalgia

Clinical characteristic	Fibromyalgia (n=68)	No Fibromyalgia (n=312)	OR(95% CI)	P value
HIV clinical staging				
I	7(10.3)	37(11.9)	1.0	
II	12(17.7)	70(22.4)	0.9(0.3-2.5)	0.85
III	37(54.4)	166(53.2)	1.2(0.5-2.8)	0.72
IV	12(17.7)	39(12.5)	1.6(0.6-4.6)	0.36
CD 4 count				
Mean counts(SD)	276(144)	325(203.1)	-	0.06
HAART				
Yes	56(82.4)	248(79.5)	1.0	0.59
No	12(17.6)	64(20.5)	1.2(0.6-2.4)	
HAART regimen				
Tenofovir	39(69.6)	158(63.7)	1.0	
Zidovidune	12(21.4)	78(31.5)	0.6(0.3-1.3)	0.19
Other	5(9.0)	12(4.8)	1.7(0.6-5.1)	0.35

Table 4: Frequency and severity of fibromyalgia related symptoms; FIQR &SIQR Scores

Symptom (n=68)	Frequency (%)	Severity (score out of 10) 0 n(%)	1-3 n(%)	4-6 n(%)	7-10 n(%)
Pain	68(100)	0(0)	11(16.2)	25(36.7)	32(47.1)
Lack of energy	64(94.1)	4(5.9)	17(25)	28(41.2)	19(27.9)
Stiff	51(75)	17(25)	32(47.1)	16(23.5)	3(4.4)
Sleep disturbance	64(94.1)	4(5.9)	4(5.9)	18(26.5)	42(61.7)
Depression	63(92.7)	5(7.3)	13(19.1)	32(47.1)	18(26.5)
Memory	56(82.4)	12(17.6)	28(41.2)	21(30.9)	7(10.3)
Anxiety	58(85.3)	10(14.7)	22(32.4)	23(33.8)	13(19.1)
Tenderness	68(100)	0(0)	22(32.3)	28(41.2)	18(26.5)
Imbalance	57(83.8)	11(16.2)	25(36.7)	21(30.9)	11(16.2)
Sensitivity to noise,light	61(89.7)	7(10.3)	21(30.9)	25(36.7)	15(22.1)

	Fibromyalgia (FIQR)	No Fibromyalgia (SIQR)	P value
Mean scores (SD)			
Total	50.1(17.5)	12.4(8.5)	<0.001
Activity subtotal	16.9(8.3)	4.1(3.3)	<0.001
Impact subtotal	10.4(3.8)	2.6(2.2)	<0.001
Symptom subtotal	22.8(8.6)	5.7(3.8)	<0.001

The average FIQR score for the 68 patients with fibromyalgia was 50.1(SD 17). All the 68 patients with fibromyalgia presented with pain and tenderness. The other frequently reported symptoms occurring in at least 90% of all fibromyalgia cases were lack of energy (94.1%), sleep disturbance (94.1%) and depression (92.7%). Comparison of symptom severity showed that sleep disorder and pain were the most severe fibromyalgia related symptoms. The average FIQR score was higher among patients with fibromyalgia with a mean score of 50.1 (SD = 17.5) compared to the patients without fibromyalgia who had a mean SIQR score of 12.4 (SD = 8.5) (Table 4).

Discussion

The study was carried out at the CCC KNH which offers care to HIV positive patients. We sampled 380 patients with chronic musculoskeletal pain. A majority were females (74.2%) and this may be due to the fact that musculoskeletal symptoms are commonly seen in women[13]. Another explanation could be that according to the KDHS survey (2008-9), women were found to have a higher prevalence (8%) of HIV compared to men (4.3%)[14]. Most of the study population was in advanced stages of HIV (Stage 3 and 4) with CD4 counts below 350cells/ml. We found that a majority of the patients were on Tenofovir which is a first line therapy option according to the Kenyan guidelines[16].

The prevalence of fibromyalgia amongst HIV positive patients with chronic musculoskeletal pain was found to be 17.9%. Simms *et al*[7] in Boston found a higher prevalence of 40%, and this could have been due to population based differences whereby the patients in Simm's study were predominantly Caucasian males.

Simms' study was also conducted among patients who had IVDU[7]. We found that female gender was independently associated with fibromyalgia, OR 5.68. This mirrors findings of other studies on fibromyalgia that show a female preponderance. Females commonly experience rheumatologic conditions and the exact reasons for this remain unclear. However, it is postulated that sex hormones especially estrogen, could play a role in pain perception [13]. The younger age group in our study could be a reflection of the overall study population.. The odds of fibromyalgia were significantly higher among those who were unemployed (OR 5.4) and those retired (OR 3.4). This is relevant because negative life events like being unemployed have been noted to be psychological stressors that could increase one's risk of having fibromyalgia.. Alternatively, the chronicity and severity of fibromyalgia symptoms may make patients unable/unwilling to work or opt for early retirement.

The study did not show any associations with any of the clinical characteristics that we observed in our patients. These included CD4 count, WHO clinical stage or use of HAART. This may have been due to the small number of subjects with fibromyalgia and the fact that this study was not powered to look for these differences. This lack of association has also been seen in other similar studies done in the HIV positive population[19, 20].

The mean FIQR score was 50.1 which meant that overall, our patients were experiencing moderate disease. On analyzing the responses to the third domain of the

FIQR, we found that pain was the predominant symptom. It is thought to be because these patients have a lower threshold of stimulation of neurons that receive pain. The other commonly occurring symptoms included sleep disturbance and lack of energy which occurred in up to 94% of the population. The patients reported that they woke up feeling 'unrefreshed' and the lack of energy meant they were tired most of the days and hence unable to carry out the goals they had set out to do.

Patients with FM have been found to have disturbed sleep patterns. Intrusion of alpha waves into slow delta wave stage 4 sleep has been observed. They thus tend to sleep less at night followed by a day full of painful episodes[17]. In a different study, it was shown that FM symptoms can be induced in normal subjects by intentionally disturbing stage 4 of Non REM sleep[18]. Depression and anxiety were also found to exist amongst 92% of the study population with FM. Patients with fibromyalgia had a higher mean FIQR score of 50.1 compared to those without who had a mean of 12.4 on the SIQR. This showed that those with fibromyalgia had more difficulties in terms of being able to carry out certain activities, overall impact and symptom score.

This study was limited in that self reporting of the severity of symptoms associated with fibromyalgia could have been subjective. Secondly, recall bias may have been introduced when patients had to report the symptoms associated with fibromyalgia in accordance with FIQR.

We recommend that clinicians should be made aware of the presence of fibromyalgia in the HIV positive patients with chronic musculoskeletal pain. Patients found to have the condition should also be assessed for the associated symptoms and hence be offered the available modes of therapy.

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Diffuse alveolar hemorrhage in a young woman with systemic lupus erythematosus: Case report and literature review

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Abstract

Diffuse Alveolar Hemorrhage (DAH) is rarely reported complication of Systemic Lupus Erythematosus (SLE).

A young woman diagnosed SLE, with a previously normal plain chest radiograph, developed acute onset cough, dyspnoea and hemoptysis. The repeat urgent chest radiograph revealed alveolar opacities. The triad of acute onset respiratory symptoms on a background of SLE and previously normal chest radiography raised the suspicion of DAH in her. She made satisfactory clinical response to high dose corticosteroid and pulse intravenous cyclophosphamide.

We conclude that high index of suspicion is required for recognition of DAH. Prompt diagnosis and management are keys to successful outcome.

Key words: Systemic lupus erythematosus, Diffuse alveolar hemorrhage, Rare complication

Introduction

Diffuse Alveolar Hemorrhage (DAH) is an acute, life threatening event and is defined as a clinical syndrome resulting from injury to the alveolar arterioles, capillaries and venules leading to red blood cell accumulation in the distal air spaces characterized by the clinical triad of hemoptysis, anemia, and progressive hypoxemia. Diffuse alveolar hemorrhage can complicate a large number of clinical conditions. It may present in different ways and may be life-threatening[1]. It poses an important challenge for the clinician[1].

It is also known as intrapulmonary hemorrhage, diffuse pulmonary hemorrhage, pulmonary alveolar hemorrhage, pulmonary capillary hemorrhage, alveolar bleeding, or microvascular pulmonary hemorrhage. DAH is a rarely reported condition. At onset up to 11% of systemic lupus erythematosus patients have DAH[2]. It is more commonly seen in SLE than any other connective disease[2]. Although no prospective study has yet identified which cause is the most common, in a series of 34 cases, Wegener granulomatosis accounted for 11 cases, Goodpasture syndrome four cases, Idiopathic pulmonary hemosiderosis four, Collagen vascular disease four, and Microscopic polyangiitis three[2]. DAH has protean clinical presentation and this frequently reflect either alveolar bleeding alone or features of the underlying cause (e.g. arthritis in systemic lupus erythematosus). Hence, its recognition requires a high degree of suspicion. Reported prognosis is poor; with in-hospital mortality ranging from 20% to 100%[4]. Early identification of prognostic factors may be useful in the initiation of appropriate treatment. Hence this case report has been written to create awareness among physicians and refresh our knowledge of rare complication of systemic lupus erythematosus.

Case report

Miss A.M. was a 22 year old lady referred from Federal Medical Centre Abakaliki Ebonyi State Nigeria. She presented to our Rheumatology clinic of University of Nigeria Teaching Hospital Enugu on 22nd March 2010 and was subsequently admitted into the female medical ward. She was suspected to be a case of systemic lupus erythematosus based on American College of Rheumatology classification few weeks to presentation to us. She presented with recurrent fever and polyarthralgia of one year duration. There was also history of paraesthesiae over the feet, recurrent mouth sores, skin rashes over the cheeks and also exposed areas of the body that is worse with exposure to sunlight, hair loss, facial puffiness and leg swelling, progressive weight loss, anorexia, fatigue and an episode of precordial chest pain suggestive of pericarditis. There was no history of reduction in urine output, excessively frothy urine, raynaunds phenomenon, sicca symptoms, skin tightening, proximal muscle weakness and reflux symptoms. She had no history of cough, drenching sweats, abdominal swelling, diarrhea, polyuria, polydipsia, palpitations, heat intolerance, headaches, seizures and no tremors. Her symptoms were not

controlled hence her referral for further evaluation and appropriate management. Her accompanying laboratory results revealed proteinuria and active urinary sediment suggestive of glomerulonephritis, markedly raised ESR and the plain chest radiograph taken on the 15th of March 2010 was normal.

Examination revealed chronically ill-looking young woman that was not in respiratory distress, pallor, patchy alopecia, and bilateral pitting leg oedema. She was febrile with a temperature of 37.8^0 C. There was no jaundice, peripheral lymphadenopathy and dehydration. Examination of her skin revealed malar rash, photosensitive fixed erythematosus patches on the arms and legs. The digestive system examination revealed palate mucosal erythema and erosions and ascites demonstrable by shifting dullness. The central and peripheral nervous system examination revealed only hypoaesthesiae in a glove and stocking distribution. She was Stein-Broker's classification S3 functionally impaired. The cardiovascular and chest examinations were normal. The provisional diagnosis was systemic lupus erythematosus. She was admitted and commenced on oral hematinics. The following investigations were requested: Full Blood Count, reticulocyte count, ESR, urinalysis and urine microscopy, culture and sensitivity, Serum electrolytes urea and creatinine (SEUCR), HIV, anti-HCV, HBsAg, liver function test, Prothrombin time, Activated Partial Prothrombin Time, serum protein and albumin, stool microscopy, fasting blood glucose, mantoux test and abdominopelvic ultrasound scan (Table 1).

Table 1: Investigation results

Full Blood Count: Hb 8.7g/dl, WBC total count 3.6 x 10^9/L , N56 L42 E2 Platelet 120 x 10^9/L (23/3/2010) Repeat hemoglobin: 6.9g/dl (29/3/2010)
Reticulocyte count: 2.4% ESR: 113mm first Hour (Westergren) (17/03/2010)
Prothrombin Time: test (23/03/2010) 9.41sec; control: 11.1 sec International Normalised Ratio 1.1
Blood culture: no growth (29/03/2010) Urinalysis and urine M/C/S: proteinuria 2+; no growth
SEUCr: (23/03/2010) Na 134 K 3.9 Cl 102 HCO 22 mmol/l urea 2.3mmol/l creatinine 120umol/L
HIV: negative for antibodies to HIV 1 &2 (24/03/2010) Anti-HCV: negative HBsAg: negative
Liver function and Serum protein and albumin test: normal:
Fasting blood glucose: 78mmol/l Mantoux test: (26/03/2010)< 2mm induration after 72 hours
Abdominopelvic ultrasound scan: (25/03/2010) normal examination

She had a comprehensive eye evaluation which revealed only refractive error necessitating only corrective lens. With no contraindication, she was commenced on oral hydroxychloroquine 200mg BD for SLE. Her clinical state remained apparently same till the 7th day in admission when she developed sudden onset shortness of breath, cough and transient haemoptysis. A repeat of the plain chest radiograph was requested. This showed widespread new alveolar opacities in both lung fields (Figure 1).

Figure 1: Shows PA view chest radiograph of Miss A.M taken on 30th March 2010. Note the apparent cardiomegaly. This is due to mal-rotation of the patient at the time of the investigation. Her previous chest radiograph that was taken 2 weeks earlier showed normal cardiothoracic ratio. The radiograph also showed widespread alveolar opacities both lung fields.

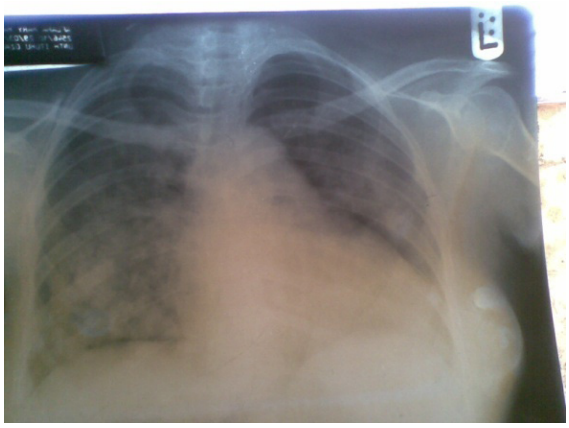
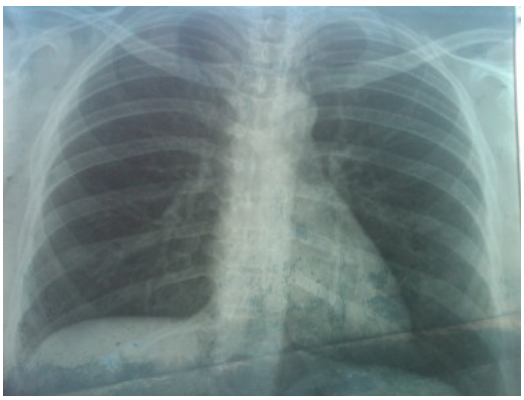


Figure 2: Shows the PA view chest radiograph of Miss A.M. taken on the 15th March 2011. The examination report was normal.



The repeat hemoglobin also showed a downward trend. The diagnosis was modified to SLE complicated by diffuse alveolar hemorrhage. She was started on pulse IV cyclophosphamide 500mg twice weekly for six doses, pulse methylprednisolone 1000mg daily x 3 days then oral prednisolone 30mg daily and oxygen therapy. She subsequently made steady and progressive improvement in the affected systems. The SOB and hemoptysis resolved over the next one week and she was discharged home, a week later, on the following medications: oral prednisolone 25mg daily, hydroxychloroquine

200mg BD, oral hematinics and to complete her IV cyclophosphamide as out patient. She completed her IV cyclophosphamide and was started on maintenance oral hydoxychloroquine 200mg daily, azathioprine 50mg daily and low dose prednisolone 5mg daily till date. She has remained in remission and her last clinic attendance was on 18th October 2012.

Discussion

Dyspnea, cough, and fever are the common initial symptoms of DAH and are most often acute. The fever is usually due to the underlying cause, such as lupus. Hemoptysis may be absent at the time of presentation in up to a third of patients because the total alveolar volume is large and can absorb large amounts of blood, without extending more proximally into the airways. The physical findings are nonspecific and may reflect the underlying systemic vasculitis or collagen vascular disorder. Widespread crepitations may be heard in chest. Our patient with classification of SLE based on ACR classification criteria developed while in the ward on the 7th of admission sudden onset shortness of breath, cough and transient haemoptysis. This triad of acute symptoms on a background of SLE and previously normal chest radiography raised the suspicion of DAH in her. Generally speaking, dyspnea, cough, haemoptysis, and new alveolar infiltrates in conjunction with bloody bronchoalveolar lavage specimens (with numerous erythrocytes and siderophages) establish the diagnosis of diffuse alveolar hemorrhage. The chest radiograph usually provides further support for the diagnosis of DPH, but the draw back is its non-specificity. It most commonly shows the sudden appearance of a diffuse alveolar filling pattern that is often perihilar or basilar and is indistinguishable from pulmonary edema or diffuse infection such as viral or pneumocystis pneumonia[5]. The radiograph is abnormal in 80% of cases and most commonly shows diffuse bilateral patchy consolidation in the mid and lower zones with sparing of apices and costophrenic angles[6]. Resolution, often with a reticular pattern, is rapid and the radiograph may revert to normal in less than two weeks[5]. However, accentuated vascular markings tend to persist after repeated episodes of bleeding due to presence of siderophages in the interstitium and if the bleeding continued over a sufficiently long period, permanent reticulonodular infiltrates develop, resembling the presence of idiopathic pulmonary hemosiderosis[7].

The radiographic abnormalities found in DAH patients are never specific for DAH. This is explained by the fact that a diffuse alveolar filling pattern can be caused by any substance filling the alveoli, which may be edema fluid (pulmonary edema) or inflammatory exudates (pneumonia). The lack of cardiomegaly and pulmonary vascular congestion point away from cardiac pulmonary edema[3]. Our patient had chest radiograph that showed diffuse bilateral alveolar opacities with no evidence of vascular congestion nor pleural effusion. These features resolved and were not evident in the subsequent radiograph taken one year later. It is of note that the radiograph she had done one week to presentation was normal and showed no cardiomegaly. Computed tomography may show areas of consolidation interspersed with areas of ground-glass attenuation and preserved, normal areas. The Diffusing Capacity for Carbon Monoxide (DLCO) may be distinctively increased. Serial increases in the DLCO may indicate progressive alveolar hemorrhage. However, it is worthy of note that the clinical instability of these patients experiencing active alveolar bleeding contraindicates immediate or early performance of the DLCO measurement maneuvers. Thus, the DLCO test is relatively impractical in acute DAH. Those with recurrent DAH may give restrictive pattern of lung function studies. Patients with diffuse alveolar hemorrhage hematology profile generally show falling hemoglobin, rising leucocyte count and elevated acute phase reactants. Active urinary sediment and azotemia may be seen in those with underlying systemic autoimmune disorders.

The diagnostic evaluation in diffuse alveolar hemorrhage usually includes bronchoscopic examination[8] which serves two purposes: to document alveolar hemorrhage by bronchoalveolar lavage and to exclude airway sources of bleeding by visual inspection and to exclude an associated infection. The diagnostic yield of bronchoscopy is higher if the procedure is performed within the first 48 hours of symptoms rather than later. Bronchoalveolar lavage specimens should be sent for routine bacterial, mycobacterial, fungal, and viral stains and cultures, as well as for *Pneumocystis carinii* stains. Our patient had a repeat chest radiography which revealed new onset widespread alveolar opacities. Her repeat hemoglobin level also showed a downward trend.

The sputum culture yielded no growth and mantoux skin testing and accompanying chest radiograph were not suggestive of pulmonary tuberculosis. The DLCO test was impractical in her and in a resource poor setting like ours she could not do CT scan of the chest. There were logistics problems with regards to bronchoscopy within the first 48 hours of onset of her symptoms and because we are aware that the diagnostic yield of bronchoscopy is higher if the procedure is performed within the first 48 hours of symptoms rather than later we decided not to do it. With the results of limited confirmatory test and investigations we strongly felt she had DAH. Effort should be made to find if any underlying cause is present or not present. Management is tailored to presence or absence of underlying systemic cause. For those DAH cases with demonstrable primary multi-systemic autoimmune disorder, corticosteroid with or without disease modifying anti-rheumatic drugs such as azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide and etanercept or other immune biologics may be used in diffuse alveolar hemorrhage. Plasmapheresis may be indicated for DAH associated with Goodpasture syndrome or with other vasculitic processes in which the titres of pathogenetic

immunoglobulins and immune complexes are very high. There are other considerable management measures and these include supplemental oxygen, bronchodilators, reversal of any coagulopathy, intubation with bronchial tamponade, protective strategies for the less involved lung, and mechanical ventilation. Our patient's response to conventional therapy putting into consideration available meager funds was quite remarkable.

The prognosis for diffuse alveolar hemorrhage depends on the underlying cause. Our patient had good outcome mainly because the DAH was recognized and nipped at the bud stage. She is yet to record any recurrence since discharge.

Conclusion

DAH can occur in our patients with multi-systemic autoimmune disorders. High index of suspicion is required for early diagnosis and prompt initiation of appropriate management is strongly recommended. Prognosis is likely to be improved when early diagnosis is made and prompt appropriate management initiated.

Acknowledgments

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Juvenile idiopathic arthritis in a Congolese patient with sickle cell haemoglobin C disease: Case report

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Abstract

Sickle Cell Disease (SCD) presenting with musculoskeletal manifestations may be difficult to distinguish from Juvenile Idiopathic Arthritis (JIA), especially in sub-Saharan area where SCD is endemic and share some clinical aspects with JIA.

We report a case of JIA occurring in a patient with a Sickle Cell Haemoglobin C Disease (SCHCD). The patient was diagnosed as SCHCD at the age of two years and underwent two blood transfusions for anemia at the age of 2 and 3 years. Musculoskeletal manifestations appeared at the age of 12 years and consisted of pain, swelling and deformity of the fingers, tees, wrists and ankles and were suggestive for JIA.

Keys words: Juvenile idiopathic arthritis, sickle cell disease, DR Congo

Introduction

Bones may be affected by both haemoglobin and vasocclusive processes in SCD. Joint symptoms during painful crisis generally result from pain in the juxta articular areas of bones being referred to the knees, ankles, wrists, elbows and shoulder. Occasionally, painful crisis may be associated with one or more warm, tender, swollen joints[1].

Systemic Lupus Erythematosus (SLE)[2,3], fibromyalgia[4], rheumatoid arthritis[5] chronic synovitis with profuse plasma cell infiltration and cartilage destruction[6], Juvenile idiopathic arthritis[7], increased frequencies of rheumatoid factor and antinuclear antibodies have been described[8] in association with SCD.

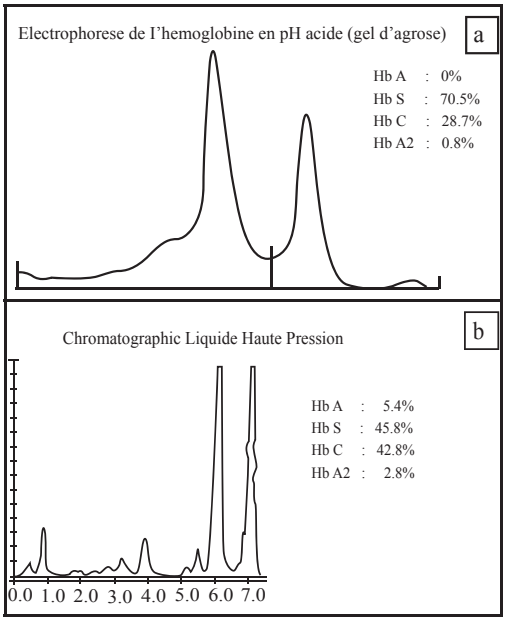
SCD is an endemic haemoglobinopathy in sub-Saharan Africa, SS haemoglobin being the most predominant and severe type in DR Congo and Central Africa while SC haemoglobin, which is less severe is confined to West African population.

In this study we report a case of a Congolese patient suffering from SCHCD with clinical manifestations suggestive for JIA.

Case report

A 16 year old patient was referred to a general practitioner in October 2008 for pain, swelling and deformity of the hands, wrists, feet and ankles. His past history revealed blood transfusions for anaemia at the age of 2 and 3 years. He was diagnosed as SCHCD (Table 1).

Table 1: Haemoglobin type of the patient performed by Agarose gel electrophoresis (Table 1a) and High Pressure Liquid Chromatography (HPLC) (Table 1b)



His mother was of Congolese (DR) origin and her haemoglobin was of AS type while his father was of West African origin (Benin) and his haemoglobin was of AC type. The physical examination revealed a normal physical growth since his weight, height, arm spam and cranial circumference were similar to the values found in a normal Congolese population of the same age and sex (Table 2).

Table 2: Patient anthropometric parameters

Parameter	In patient value	Normal values
Weight	48 kg	48 – 66 kg
Height	173 cm	171 – 173 cm
Cranial circumference	73 cm	70 – 75 cm
Arm span	173 cm	168 cm ± 93 cm

The tangential palpation of metacarpophalangeal (MCP) and metatarso phalangeal (MTP) joints was painful. The swelling of MCPS, MTPS, and of proximal interphalangeal (PIP'S), of the wrists and ankles was observed. A boutonnière deformity of the PIP'S of the fingers II and V of both hands was also noted (Figure 1).

Figure 1: X- Ray and photographs of the hands
Legend: Circle shows boutonniere deformity

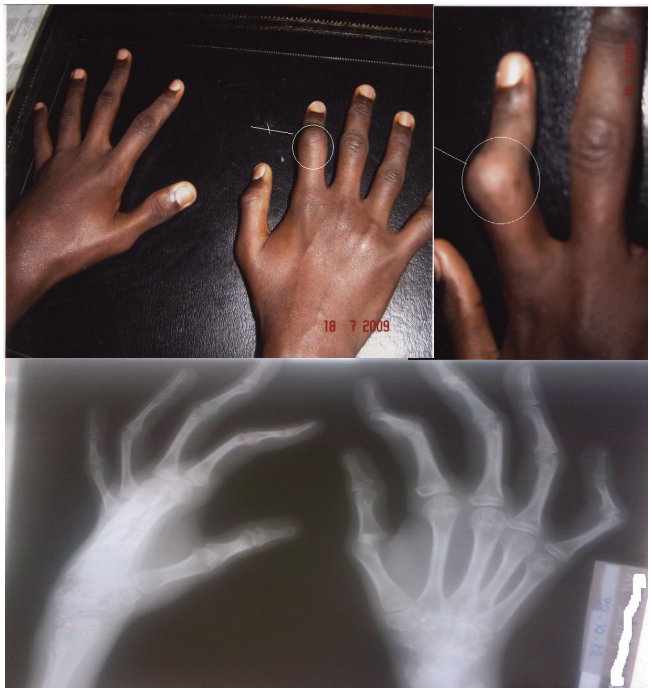


Table 3: Laboratory parameters

Parameter	In patient value	Normal values
Haemoglobin	11gr%	10 – 12 gr %
WBC	80.000/mm^3	4500 – 1100/mm^3
ESR	4 mm / Hour	0 – 15 mm/Hour
Blood sugar	104 mg%	80 – 110 mg%
Rheumatoid factor	Negative	Negative
L.E. Cells	Negative	Negative
HIV anti body	Negative	Negative

Both wrists and ankles were ankylosed and painful. Ankles remained in varus position. Except for haemoglobin level that was slightly low (11g%). Rheumatoid Factor (RF) LE cells and HIV antibody were negative (Table 3).

Discussion

Association of autoimmune disorders and SCD is still a matter of curiosity. SCD is most common in Western Africa while the homozygous type is confined to Central Africa. Its clinical features are less frequent and less severe than in homozygous sickle cell disease[9]. Juvenile Idiopathic Arthritis in this patient fulfilled the American College of Rheumatology (ACR) criteria for diagnosis: age of onset <16 years, arthritis ≥ 1 joints, duration of disease ≤ 6 weeks. The type of onset seems to be of oligo articular type.

As could be seen, hand photographs (Figure 1) showed boutonnière deformity of fingers and X-ray of hands revealed periarticular, osteoporosis. No evidence of erosive arthritis was seen. Likewise, RF and antibody to HIV-1 and 2 were absent. The absence of HIV antibody may exclude reactive arthritis to HIV. Our case highlights that JIA may be associated with SCHCD. Although this association is rare it may be the matter of confusion in endemic area for sicke cell anemia especially at the clinical point of view.

Acknowledgements

We are grateful to the patient and his parents for contributing to this study.

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Actinomycotic mycetoma of the talus with bone involvement: Case report

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Abstract

Mycetoma is a chronic granulomatous infection of bacterial (actinomycetoma) or fungal origin. It is uncommon in Maghrebian countries. We report on the case of a 44-year-old Tunisian woman with a 15 year history of actinomycetoma involving the foot. The diagnosis was based on clinical and bacteriological arguments. An X-ray revealed bone lesions by contiguity. The patient was treated with combined antibiotic therapy.

Introduction

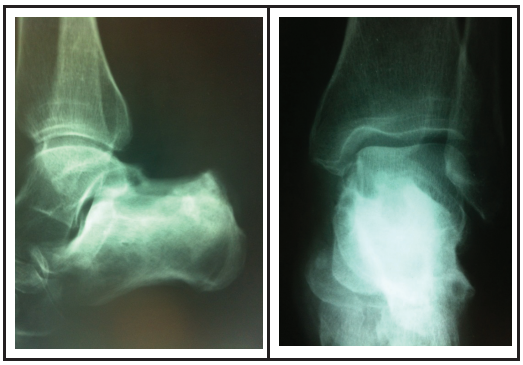
Mycetoma is a chronic granulomatous infection of cutaneous and subcutaneous tissue, in which fungal (Eumycetoma) or filamentous bacterial (actinomycotic mycetoma) causative agents produce grains[1]. It follows penetrating injury inoculating soil organisms. The classic presentation involves tumefaction, multiple draining sinuses, and grain-filled pus. It is endemic in tropical and subtropical regions but uncommon in Europe and Maghreb. The diagnosis is then often delayed, resulting in severe functional consequences. We report on the observation of an actinomycotic mycetoma involving the foot with a prolonged evolution, complicated by an underlying bone involvement.

Case report

The patient was a 44-year-old Tunisian woman, living in a rural area, who consulted for a swollen right foot which hampered walking. Her medical history included hypertension, treated with furosemide.

The history of the disease dates back to 15 years, marked by the appearance of an inflammatory nodule on the sole of the right foot, without prior significant trauma. The swelling continued to expand slowly in spite of repeated antibiotic treatments, resulting in fistulization to the skin. The clinical presentation was an infiltrated and inflammatory plaque of the right sole, affecting the entire heel. It had indistinct limits with a bumpy purplish surface, strewn with fistulas, producing pus, and retractile scars. The pressure of the sinus tracts showed the discharge of soft white grains. There was no popliteal or inguinal adenopathy. Neurological, cardiovascular, pulmonary and abdominal examination was otherwise normal. Routine laboratory tests revealed an elevated erythrocyte sedimentation rate (75 mm/hour). The tuberculin skin test and the patient's chest radiograph were normal. The radiograph of the right foot (Figure 1) showed blurred heterogeneous condensation with an inflammatory aspect of the talus. Bone erosions of the inner edge of the talus with gently sloping connection with the cortex were suggestive of extrinsic impairment.

Figure 1: Radiographic view of foot with blurred heterogeneous condensation and bone erosions of the inner edge of the talus and gently sloping connection with the cotex



There was thickening of the opposite soft parts. The whole of it suggest bone lesions by contiguity.

Microscopic examination of the pus from the discharging sinuses showed an actinomycotic grain. Treatment with oral ampicilline and trimethoprime-sulfamethoxazole resulted in a gradual improvement with drying lesions but subsidence of swelling.

Discussion

Responsible agents for mycetomas are present in the soil or on plants, the contamination being transcutaneous, following a trauma caused by thorny plants. The preferred location is then the foot[2,3] and inoculation is seen more often among the barefoot-walking populations, usually adult males aged 20 to 50 years[2,3]. Trauma may be minor and go unnoticed, which was the case in our patient.

The epidemiology of mycetomas is characterized by an endemic region located between the latitudes of 15 degrees south and 30 degrees north[3]. They are sporadically observed in Tunisia[4]. Within a retrospective study conducted over a period of 13 years in a Parasitologic Department, Kallel and all collected 13 cases[4]. The lesions were localized on the foot in seven cases.

Incubation is silent. As has been reported by our patient, the initial lesion takes the aspect of a firm nodule, developing in the soft tissues and by contiguity progressively invading other tissues, muscles, nerves and bones. At status period, the clinical manifestations are characterized by tumefaction, increased volume, and a firm deformity of the affected area with the presence of nodules, scar tissue, abscesses, fistula, and a purulent exudates[3].

The hallmark of the disease includes extrusion of grains. The analysis of macroscopic and microscopic characteristics of the extruded grains allows distinguishing actinomycotic grains from fungal grains: the size, form, and color, together with the presence or absence of clubs or pseudoclubs offer a clue to diagnosis[3]. Actinomycotic grains were identified in our patient.

Progression to bone and destruction depend on the duration and occur with time. They are responsible for pain and functional impairment. Primary mycetoma of bone can also occur by direct inoculation of the fungus or filamentous bacterium via acute traumatic implantation or by means of contamination or through a site of chronic cutaneous compromise[5]. As shown on X-rays in our patient, bone actinomycetoma causes rarefying and destructive lesions with blurred edges erosions and periosteal apposition. Plain radiographic classification of bone changes in mycetoma of the foot from stage 0 to 6 has been proposed by Abd El Bagi[6]. Our patient had periosteal reaction with cortical erosion which occurs in stage 3. The general condition is maintained, the spread of infection to the lymph nodes or organs is possible but rare. This was not observed in our patient despite a prolonged course for 15 years.

The clinical differential main diagnosis of actinomycetomas arises with fungal mycetomas, leprosy and tuberculosis. The prognosis is good with appropriate antibiotic therapy, preferably by combined drug therapy for 6 to 12 months. Beta-lactams are the first-line treatment. Other active antibiotics can be used in case of allergy or poor clinical response. These are essentially erythromycin, clindamycin, tetracycline, sulfonamides or rifampicin. The evolution of bone actinomycosis during antibiotic treatment is often favorable. Surgical treatment is reserved in case of failure of medical treatment.

Conclusion

We reported the clinical and radiographic presentation of a case of talus mycetoma in a 44-year-old woman. Diagnosis of mycetoma may be missed and should be considered in the differential diagnosis of chronic foot swellings. As in our case, progression to bone invasion and destruction occur with time.

Acknowledgment

We are grateful to the entire staff of Mongi Slim Hospital.

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Steriod abuse; two wrongs don't make a right: A case report

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Abstract

Steroid abuse among patients with rheumatic symptoms is prevalent in developing countries. The sources of the steroids vary with a significant proportion of patients self-medicating. Chronic steroid abuse results in multiple adverse effects and rapid withdrawal in such patients leads to acute adrenal insufficiency. We present a case report of a 47 year old lady who self-medicated her joint pains with steroids for 17 years and subsequently developed acute adrenal insufficiency on their rapid withdrawal.

Introduction

Corticosteroids play a key role in the management of rheumatic diseases. Judiciously used, they are invaluable in the management of several inflammatory diseases and minimum doses should be given for the shortest time[1]. However, corticosteroids becomes dangerous when available over-the-counter and used in an unregulated manner. Increasing trends of steroid abuse have been reported in developing countries due to loosely audited health care systems and lack of sufficient rheumatological training and facilities to cater for the ever increasing rheumatic diseases[2,3]. Studies done in developing countries such as Pakistan, report a prevalence of steroid abuse of 42.5% among patients with rheumatic problems[3]. Such studies have found that 38.2% of the patients on steroids develop side effects, with 29% developing Cushing's syndrome[3]. Rapid withdrawal of steroids in patients with Cushing's syndrome results in acute adrenal insufficiency. This case report is an interplay of the acute and chronic complications of steroid abuse in the background of an undiagnosed rheumatological disease.

Case Report

A forty seven year old lady was admitted at Kenyatta National Hospital with a three day history of facial swelling and one day history of generalized body weakness. The lady had been unwell for seventeen years with generalized joint pains mainly involving the wrist and knee joints. At the first instance of joint symptoms she had sought medical assistance at a pharmacy where prednisolone 10mg twice a day was prescribed. She experienced immediate relief on the medication and as a result self-medicated at the same dosage for seventeen years. Over the seventeen years she had adequate relief of symptoms and hence did not seek further medical assistance. Six years after initiating steroid use, she gained approximately 30 kilograms in weight. In addition, she had emotional liability and muscle weakness especially of the thighs. Six months prior to her admission she was diagnosed to be hypertensive at a pharmacy and initiated on antihypertensives.

On further inquiry she revealed that the right sided facial swelling was recurrent over the past two years. The swelling which started after a tooth extraction persisted despite constant use of various antibiotics. At the time of admission the swelling was discharging frank pus.

Two weeks prior to her admission she sought medical assistance at a local clinic due to worsening joint pains. She reported that the doctor immediately stopped her prednisolone and prescribed new medications for control of blood pressure. She was also instructed not to take the steroids again. One day prior to her admission she reported sudden generalized body weakness and inability to walk or stand without support. In addition she felt dizzy and nauseated.

Physical examination revealed a middle aged lady with cushingoid appearance. She had an abscess on the right maxillary region that was discharging frank pus (Figure 1). Her skin was atrophic with generalized striae. Her blood pressure was reduced at 86/46mmHg. Her pulse and respiratory rates were elevated at 110 beats/min and 26 breaths/min respectively. There was grade 5 weakness of the lower limb proximal muscles. Her joints were neither deformed, nor swollen and had full range of movement. Abdominal examination was normal.

Figure 1: The patient demonstrating the cushingoind appearance and right maxillay abscess

Given the history of long standing steroid use followed by sudden withdrawal a diagnosis of acute adrenal insufficiency was made. In addition, this patient with undiagnosed polyarticular pains had other complications of chronic steroid use- Cushing's syndrome and reduced immunity. A therapeutic trial of glucocorticoid was instituted with 100mg intravenous hydrocortisone. Her blood results revealed slightly reduced random cortisol levels, markedly elevated sugars and leucocytosis (Table 1).

Table 1: Results of the laboratory investigations

Test	Result	Reference range
Serum cortisol	9µg/l	>10µg/l
Potassium	5.0	3.5-5.0mmol/l
Sodium	134.3	135-140
Random blood sugar	23.3	7.8-11.1mmol/l
White blood cells counts	12.5	4-12
Urinalysis	Glycosuria, no ketonuria	
ANA, Rh Factor	Negative	

Radiograph of the right maxillary bone was normal, specifically there was no evidence of osteomyelitis. The patient was continued on glucocorticoid supplementation while in the ward. Titrating doses of soluble insulin were used to control the hyperglycemia. On the third day her blood pressure was found to be elevated and she was started on hydrochlorothiazide 25mg once a day and losartan 50mg once a day (Table 2).

Table 2: Blood pressure recording and fasting blood sugars while in the ward

Day of admission	1	3	4	6	10
BP (mmhg)	86/46	160/100	160/110	150/100	130/95
FBS (mml/l)	23.3	14.1	4.0	9.0	6.9

The abscess was incised and drained. Samples were taken for histology and microbiology analysis including atypical organisms such as mycobacteria and fungi. The histology was reported as chronic inflammatory reaction whereas no growth was obtained on the cultures. The patient was empirically treated with intravenous ceftriaxone 2g once a day and metronidazole 500mg thrice a day.

By the time of discharge ten days later, the patient had markedly improved. Her abscess was resolving and the blood pressure and blood sugar were well controlled. The patient was discharged through the rheumatology clinic on prednisolone 20mg once a day that was to be gradually tapered off. Further investigations to diagnose her underlying rheumatological condition were to be done at the outpatient rheumatology clinic.

Discussion

This case report highlights some complications of chronic steroid abuse. In most patients the signs of steroid abuse are not as overt as in this case. Management of these complications overburdens an already overstretched health care system. It is important that appropriate regulatory measures are put in place to control over-the-counter access of steroids as it is currently estimated that 1-3% of the adults worldwide report long-term steroid use[4].

Chronic steroid use results in two major complications that this patient had developed -Cushing's syndrome and Hypothalamic Pituitary Axis (HPA) suppression. Patients who have been on prednisolone 20mg /day for more than three weeks, have received an evening/bedtime dose of prednisolone for more than a few weeks and have cushingoid features are likely to have HPA suppression[5]. These patients do not need testing to evaluate their HPA function, but should be treated like any patient with secondary adrenal insufficiency, including the wearing of a medical alert bracelet or necklace and carrying an emergency medical information card. Such patients like in this case should have gradual withdrawal of the steroids to avoid developing acute adrenal insufficiency. The goal of tapering is to use a rate of change that will prevent both recurrent activity of the underlying disease and symptoms of cortisol deficiency due to persistent HPA suppression. A suggested regimen involves a 10-20% reduction every 1-2 weeks while accommodating convenience and individual patient's response until the patient is waned off the steroids. Abrupt withdrawal of steroids is only recommended in patients with herpes virus induced-corneal ulceration or steroid abuse psychosis which have been shown not to respond to treatment in the presence of the steroids[5].

A commonly used empiric approach to tapering corticosteroid therapy bases the tapering program on the current daily steroid dose:

(i) At greater than 40 mg/d, one tapers by 10 mg/d every 1 to 2 weeks.
(ii) At 40 mg/d, one tapers by 5 mg every 1 to 2 weeks.
(iii) At 20 mg/d, one tapers by 2.5 mg every 1 to 2 weeks.

Tapering continues until a physiologic dose of prednisone is reached (5 to 7.5 mg/d). The patient can then be switched to 1-mg prednisone tablets or the equivalent dose of hydrocortisone, so that further reductions in dose can be made in smaller steps than is possible when 5-mg prednisone tablets are used. Weekly or biweekly reductions can then be carried out in steps of 1 mg of prednisone at a time, as permitted by disease activity[6].

During the tapering process, a steroid withdrawal syndrome develops in some patients, characterized by depression, myalgias, arthralgias, anorexia, headaches, nausea, and lethargy. Studies have failed to show a relationship between these symptoms and low cortisol levels. In most instances, symptoms are reported when levels are normal, or even elevated, but falling rapidly. HPA responsiveness has also been found to be normal in many of these patients. The mechanisms responsible for this syndrome are unknown but seem to be linked to the rapidity with which the dose is tapered[6].

Another approach involves the use of plasma cortisol measurements to gauge corticosteroids withdrawal[6]. Patients return to the clinic at two to four week intervals for morning plasma cortisol measurement. Tapering is done at a rate of 2.5 mg of hydrocortisone/week down to a single morning dose of 10 mg of hydrocortisone (equivalent to 2 mg of prednisone). Steroid therapy could be discontinued when the morning plasma cortisol concentration rises to greater than 10 mcg/dL. Stress doses of steroids might be needed for infections. This approach, however, has not gained much popularity and is generally not used.

Management of Cushing's syndrome depends on the specific features present. Hypertension and hyperglycemia are managed in the conventional manner with good control achieved after steroid withdrawal[5]. Fat redistribution in the cushingoid habitus occurs gradually over months after steroid withdrawal. Exercises and healthy diet have been shown to aid in the fat redistribution[5].

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Fibroblastic rheumatism

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Abstract

Fibroblastic Rheumatism (FR) is a rare rheumatologic entity of unknown etiology. The pathophysiological mechanism involving fibroblast proliferation is characterized by symmetrical polyarthritis associated with sudden onset of cutaneous nodules, flexion contractures. Bone erosion can occur as the disease progresses and destructive arthropathy is inconstant. The diagnosis of fibroblastic rheumatism is based on histological study of the nodules. Fibroblastic rheumatism treatment is difficult and relies on corticosteroids or immunosuppressive treatment. Given its rarity, we considered necessary to present the diagnostic and therapeutic approach to this disease still imperfectly known.

Keywords: Fibroblastic rheumatism, Sclerodactyly, Nodules, Corticosteroids

Introduction

Fibroblastic rheumatism, is a rare entity in adults and exceptional in children. It was first described by Chaouat and and coworkers[1]. The mechanism remains unknown[2]. It is characterized by the association of arthritis, skin nodules, Raynaud phenomenon, flexion contractures, and sometimes visceral events. The diagnosis is often challenging and must be confirmed by the histological typical features of the nodules[3]. As it is very rare, the therapeutic strategies are not well known and are difficult to establish, primarily derived from observational data reported in isolated cases. We describe the positive diagnosis and treatment of this disease still not clearly known.

Epidemiology

Until 2011, 25 cases of rheumatism fibroblastic have been reported[4,5]. Jurado *et al*[6] published four new cases in 2012. It was originally described in 1980. Rheumatism fibroblastic affects both sexes equally with extreme ages ranging from 8 to 68 years (mean 37.8 years)[7].

Pathophysiological mechanism

The mechanism remains the subject of assumptions. The pathogenic leading to increased dermal fibroblasts has yet to be elucidated. Both exogenous and endogenous factors may drive the observed fibroblast proliferation such as infectious. The limited number of studies have shown that macrophages and lymphocytes could secrete TGF the initial inflammatory stage, which can stimulate the proliferation and differentiation of fibroblasts into myofibroblasts in the skin than in the synovium. The elastic fibers are generally absent. The successive skin biopsies find dermal fibroblastic proliferation, loss of elastic fibers and minimal inflammation, and suggest the existence of several evolutionary phases 6-8. Initial, with presence of inflammatory macrophages, T and B lymphocytes, fibroblast proliferation and collagen disorganization with decreased protein synthesis of collagen and non-collagenous proteins. In the chronic phase, there is a rare mononuclear infiltrates, modest fibroblast proliferation thickening of collagen fibers and a dense dermal fibrosis. In addition, deposits of Immunoglobulin (IgA, IgM), complement (C3 and C1q) were found in the dermal-epidermal junction in some observations.

Diagnosis of rheumatism fibroblastic

The typical clinical presentation of FR is the presence of multiple skin nodules, solid, pink to flesh-colored, may be tender on palpation, display no surface alteration, and are typically 2 to 20 mm in diameter. They seem to have a predilection for the hands and periarticular areas. There is also associated symmetric arthropathy serologically negative, affecting both large and small joints. Destructive arthropathy has been described[9,10] and osteolysis may appear in the RF but only in the form of the distal phalanges. Sometimes the clinical presentation may be with flexion contractures of the fingers, thickened palmar fascia, sclerodactyly and Raynaud phenomenon. The clinical differential diagnosis includes other conditions with associated skin nodules and rheumatologic symptoms such as rheumatoid arthritis, multicentric reticulohistiocytosis, and nodular scleroderma, which can all be excluded on the basis of laboratory testing and histology[11,12]. Concerning the biological labolatory profile, blood tests

are not diagnostic and radiological investigations of the affected joints is usually normal[13]. Typical histological findings are essential for the diagnosis, as explained above. Although the etiology of FR is still unknown, the limited number of studies has shown that macrophages and lymphocytes could secrete TGF-beta during the initial inflammatory stage which can stimulate the proliferation and differentiation of fibroblasts cells[14].

Treatment of fibroblastic rheumatism

There is no satisfactory treatment of FR. Many therapies have been described with highly variable responses, such as aspirin, nonsteroidal anti-inflammatory agents, prednisone, colchicine, hydroxychloroquine, penicillamine, physical therapy, methotrexate, and interferon-alfa. Cases describe response to methotrexate, which has known antiproliferative and apoptosis-inducing effects[15]. There are four cases that responded well to MTX but only one complete regression and there seems to be an effect dose dependant[16]. The development of biological agents has provided a new therapeutic hope. IFN-alfa is capable of inhibiting the production of MMP by synovial fibroblasts and induced by IL-1 and protects the articular cartilage in early arthritis[17]. An antagonist of TGF-beta inhibits both reduced the deposition of extracellular matrix and scarring.

Conclusion

The fibroblastic rheumatism remains an unknown reported condition. It should be considered when patients present skin nodules and arthritis. Based on the clinical and histological features, the fibroblastic rheumatism could belong to fibromatosis. Despite the use of several different therapies, almost all patients eventually have deformations fingers, either due to sclerodactyly or a destructive arthropathy. Biological agents could be beneficial, but require more extensive studies. More information regarding the mechanism and origin are needed for ease of identificationbe identify.

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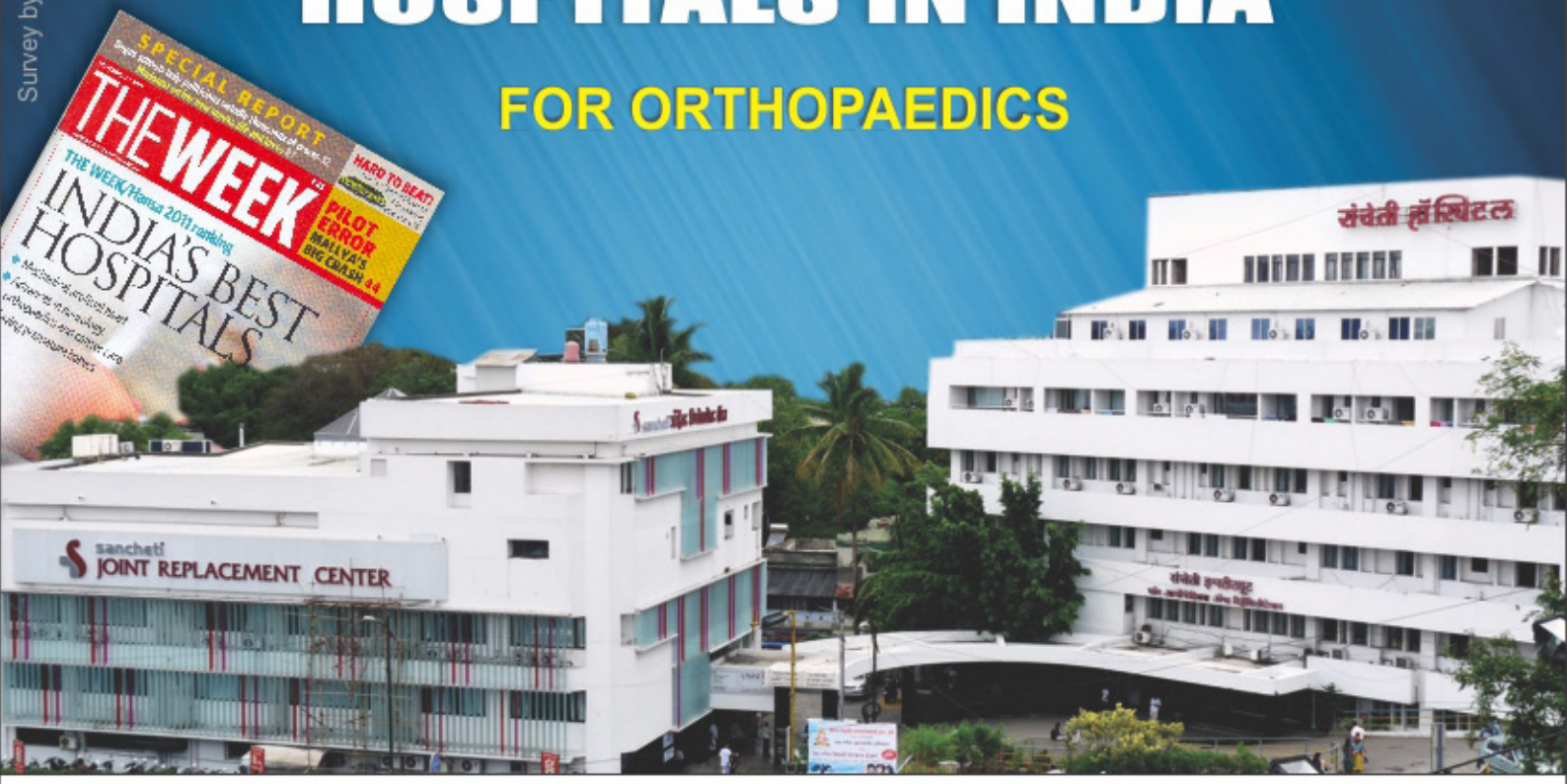

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