Systemic Mastocytosis Associated with Liver Failure in an Adult German Shepherd Dog

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Abstract

A 10-year–old German shepherd dog was presented with right fore limb oedema, ascites and hepatomegaly. A clinical diagnosis of ehrlichiosis and liver failure was made. Response to therapy was unfavourable and with the owner's consent, euthanasia was performed. Necropsy findings revealed a markedly enlarged liver whose surface had numerous cream coloured nodular masses. On histopathology, the liver tissue was destroyed by the infiltrating neoplastic mast cells and eosinophils. Based on the gross and microscopic findings, the condition was diagnosed as metastatic mastocytoma that resulted in liver failure. Occurrence of systemic mastocytosis without overt cutaneous lesions is rare. This article documents a case of liver failure due to malignant mastocytosis of which there are scant reports.

Introduction

Mast cell tumours (MCTs) comprise 20-25% of all cutaneous and subcutaneous tumours in dogs. MCTs therefore, are the most prevalent skin tumours in dogs (London & Seguin, 2003). MCTs occur commonly as benign skin tumours but may metastasize to cause fatal systemic disease (Steffey et al,. 2004). Extracutaneous tumours have been reported in the intestines, liver, spleen, ureters, bone marrow and the spinal cord (Iwata et al., 2000; Steffey et al., 2004). Although MCTs have no sex predisposition, breed predilection has been noted for Boxers, Boston Terriers, Bull Terriers and Labrador Retrievers. The condition affects dogs that are 8-9 years of age (Muller et al., 1983). The lack of scientific reports describing systemic mastocytosis in adult dogs in Kenya and the diagnostic challenges encountered, prompted this case report.

Case History

A 10-year-old female German shepherd dog was presented to the Small Animal Clinic, University of Nairobi on 5th January 2004. The dog was presented with lameness and swelling of the right fore limb. There had been no trauma to the affected limb. Vaccination and deworming history were deemed adequate.

Clinical Findings

Physical examination revealed fever (400c), slight dyspnoea (40 breaths per minute), and an increased heart rate (100 beats per minute). The conjunctival mucous membranes and sclera were congested. Submandibular and prescapular lymph nodes, were markedly enlarged. The abdomen was pendulous and was tense on palpation. The right fore limb had soft tissue swelling from the mid humerus to the metacarpal area making the dog resent its palpation and to knuckle the carpal joint when walked. A blood smear stained with Giemsa revealed Ehrlichia canis initial bodies in the monocytes. On haematological analysis there was a slight leucocytosis due to a granulocytosis. Liver and kidney function tests could not be performed due to the lack of reagents in our laboratories. Cardiac and pulmonary structures were considered normal on thoracic radiography; however, abdominal radiographs revealed ascites that caused fogging of the abdominal organs. The right forelimb radiographs revealed soft tissue swelling. A confirmative diagnosis of chronic ehrlichiosis and a tentative diagnosis of liver failure pending further tests were made.

Clinical Management

The dog was treated by intramuscular injection of 132 mg of 12% Imidocarb Dipropionate (Imizol® Schering-Plough Animal Health, Germany), 300 mg of Amoxycillin Trihydrate (Abbeyvet Ltd. Leeds, United Kingdom), 10 mg of Dexamethasone sodium phosphate (Colvasone®, Norbrook Laboratories) and orally administered 120 mg of furosemide tablets (Lasix® Wellcome, UK), once a day for three days. After 3 days of treatment, the patient improved as the ascites and the right fore limb swelling had resolved. Abdominal palpation revealed an enlarged organ at the right cranial abdomen. The dog was in a stable state and was discharged to return after

2 weeks for the second imidocarb dipropionate treatment. However, the dog returned after a week with a history of anorexia, vomiting and coughing-up blood. On physical examination, the dog had a normal temperature, dyspnoea, congested scleral vessels, polyuria, foul smelling urine and a distended abdomen that was painful on palpation. She was readmitted but her condition rapidly deteriorated. The dog was euthanised at the owner's request with 2,000 mg of pentobarbital sodium (Euthatal®, Merial Animal Health Ltd).

Gross Pathology

On post mortem examination, the skin of the lateral trunk had white, firm, moveable subcutaneous nodules that were 0.5 centimetres in diameter. The abdomen was distended by 3 litres of straw coloured fluid and the liver was enlarged and weighed 4 kilograms (Fig. 1). On the liver surface, there were numerous cream coloured nodular masses that ranged in size from pinpoint to confluent lesions of 5 centimetres in diameter (Fig 2). A few greyish foci were observed on the cortex of the kidneys. The spleen and other organs were grossly congested.

Histological Features

Samples of the liver, spleen and kidneys were collected and fixed in 10% formalin solution for 3 days. The tissues were trimmed, dehydrated in serial dilutions of alcohol and embedded in paraffin wax. Sections of 5 µm thick, were prepared using a microtome, mounted onto microscope slides by water floatation and routinely stained with haematoxylin and eosin. These were examined using a light microscope.

On histological examination the liver tissue was destroyed, displaced and infiltrated by mast cells that appeared as sheets of large round to pleomorphic cells with mitotic figures. Between the neoplastic cells there were numerous eosinophils and few neutrophils and plasma cells. The spleen and kidneys had focal infiltration with tumorous mast cells intermingled with eosinophils.

Discussion

Extracutaneous MCTs without overt skin lesions are rare in dogs (Steffey et al., 2004; Iwata et al., 2000; Oglivie et al., 1995). The lack of an easily observable superficial mass or specific clinical signs in dogs with these tumours delays diagnosis and contributes to a worse prognosis (Moore, et al., 2002; Tyrell & Davis, 2001) as was in this case report. These tumours are quite variable and depend on the location and grade of the tumour (Baker-Gabb et al., 2003; Strefezzi et al., 2003). MCTs have no typical morphology but may be dome-shaped, nodular or penduculated (Muller et al., 1983). Therefore, diagnosis based on physical examination alone is difficult. Clinical signs are also related to the release inflammatory mediators like histamine, heparin and proteolytic enzymes from the intracellular granules. The release of these mediators can cause gastric ulceration, delayed wound healing and local ulceration near the cutaneous neoplasm (Govier, 2003). Clinicians are therefore advised to avoid

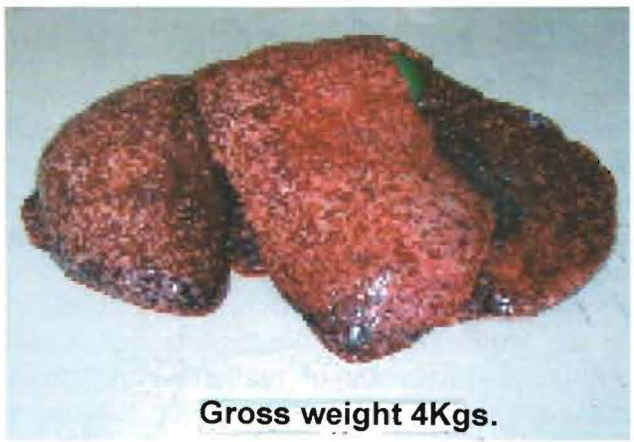

Figure 1: Photograph of a grossly enlarged liver.

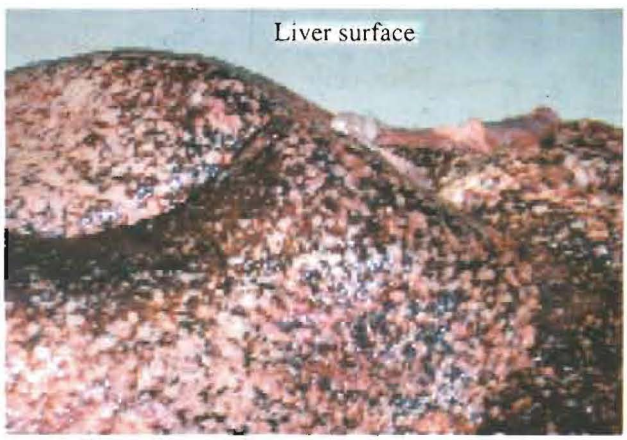

Figure 2: Photograph of enlarged liver showing multiple nodular masses affecting the entire liver surface.

over palpation of cutaneous MCT lesions. The frequency of metastasis is unclear and under certain circumstances those lumps thought as benign and small as was in this case, can have visceral involvement that is undetectable to external examination (Sato & Solano, 2004; Steffey et al., 2004). In general, extracutaneous and mucocutaneous MCTs are associated with a poorer prognosis (Vail, 1996). This could explain the rapid deterioration of the clinical status, leading to euthanasia of this particular case.

Other predisposing causes to MCTs include: chronic diseases that over stimulate the immune system such as flea allergy dermatitis (Patnaik et al., 1998), and genetic link in form of the proto-oncogene; the c-kit receptor protein located on mast cells that may promote uncontrolled growth or survival of mast cells (Reguera et al., 2001)

Diagnosis of MCTs is by cytological or biopsy examination of the lesions (Vail, 1996). Typical MCTs consist of moderate to large population of mast cells with a variable number of eosinophils and neutrophils scattered in the mass of mast cells. Their malignancy is indicated by the degree of mast cell differentiation. Grading is based on the number of granules, mitotic index and cellular characteristic of malignancy (Patnaik et al., 1998). Due to the lack of overt cutaneous lesions in this case, no cytological or biopsy examination was done.

The preferred treatment for cutaneous MCTs is surgery (Baker-Gabb et al., 2003). However, thoracic radiography and abdominal ultrasonography are necessary to rule out metastasis (London & Seguin, 2003; Sato & Solano, 2004). Mast cells are radiation sensitive and radiation therapy is often used as an adjunct to surgery (Vail, 1996). However, radiation therapy for veterinary practice is unclear and not currently feasible as a therapeutic option in Kenya. Old age and the poor prognosis rendered treatment in this case impractical. The prognosis was confirmed by the extensive pathological changes affecting the entire liver parenchyma.

Conclusion

Based on the clinical features, gross and histological appearance of the tumorous cells, a diagnosis of metastatic mastocytoma with liver failure, was made. There are no scientific reports on the incidence and significance of this condition in dogs in Kenya. There is therefore the need for further research to classify and document MCTs and other neoplastic cutaneous cases encountered during small animal practice. This would assist clinicians in making informed decisions on diagnosis, prognosis and management of veterinary cancer patients.

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