Renal T-cell lymphoma with cerebral metastasis in a dog with chronic canine ehrlichiosis

E P Lane[a†] and R G Lobetti[b‡]

ABSTRACT

A renal T-cell lymphoma with exclusive cerebral metastasis was diagnosed in a 5-year-old Staffordshire bull terrier bitch euthanased for aggression. This is the first recorded case of primary renal lymphoma in a dog. Immune suppression, due to chronic canine monocytic ehrlichiosis, may account for the unusual primary site and metastatic pattern of the tumour.

Key words: canine, cerebral metastasis, *Ehrlichia canis,* lymphoma, renal.

Lane E P, Lobetti R G **Renal T-cell lymphoma with cerebral metastasis in a dog with chronic canine ehrlichiosis**. *Journal of the South African Veterinary Association* (2002) 73(2): 83–85 (En.). Department of Pathology, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110 South Africa.

INTRODUCTION

Primary renal tumours are rare in dogs, and those that are seen are mainly epithelial or embryonal in origin. By contrast, metastatic tumours and renal involvement in multicentric lymphoma are common[8]. This report documents an unusual case of primary renal lymphoma in a dog, which metastasised exclusively to the brain and which was associated with concurrent chronic canine monocytic ehrlichiosis (CME).

CASE HISTORY

A 5-year-old female Staffordshire bull terrier was presented at the Onderstepoort Veterinary Academic Hospital with a 2-week history of weight loss, anorexia and vomition. Abnormalities on clinical examination were generalised weakness, the presence of watery, mucoid faeces and papillary mydriasis. Peripheral blood smears revealed the presence of *Ehrlichia canis* morulae. Laboratory tests revealed positive serum IgG (1:5120) and negative IgM *E. canis* titres; mild anaemia (haematocrit 38, normal 40–55 %); lymphopaenia (0.1, normal 1–4.8 $\times$ $10^9/\ell$); thrombocytopaenia (10, normal 200–500 $\times$ $10^9/\ell$) and urinary proteinuria and isosthenuria. In addition, chronic hepatic dysfunction was indicated by hypoalbuminaemia (19.8, normal 27–36 g/ℓ); low blood urea nitrogen (2.9, normal 3.6–8.9 mmol/ℓ) and moderate ammonia tolerance (111.3, normal <30 μmol/ℓ). Hyperalphaglobulinaemia (attributed to acute phase proteins) based on serum protein electrophoresis was also present. Faecal analysis showed large numbers of *Ancylostoma* eggs. On the basis of these results, acute and chronic CME and ancylostomosis were diagnosed and the dog was treated with doxycyline and an anthelminthic. Despite treatment, the dog's mental status deteriorated, she became aggressive, and the owners requested euthanasia.

A full necropsy was performed. The medulla of the right kidney contained a soft, tan mass (1.5 cm diam.) at 1 pole (Fig. 1). A smaller mass of similar tissue (5 mm diam.) was present in the medulla of the left kidney. Multiple small haemorrhagic foci (1–4 mm diam.) were scattered over the ventral surface of the midbrain, cerebellum, and the hypophysis (Fig. 2). In addition, the carcass was pale, with multiple subcutaneous and subserosal petechiae; the lymphoid tissue in the spleen and lymph node cortices were atrophic; the mid-thoracic aorta contained aortic aneurysms (2–3 mm diam.) and a large granuloma (5 cm diam.) containing *Spirocerca lupi* adults was present in the adjacent oesophagus. All other organ systems examined appeared normal macroscopically.

Histologically, both kidneys contained poorly circumscribed, unencapsulated medullary masses consisting of sheets of pleomorphic polyhedral cells, which effaced normal tubular architecture, filling and obscuring tubules. Neoplastic cells had variably distinct cell borders, scanty amphophilic cytoplasm and large round nuclei, clumped chromatin, 1–3 nucleoli and frequent, often bizarre mitotic figures (Fig. 3). Small and large

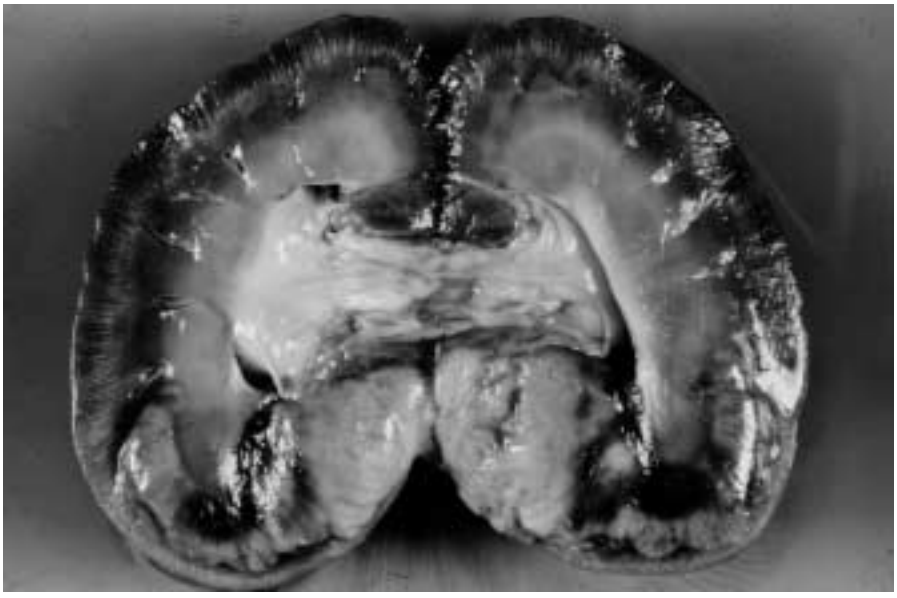

Fig. 1: **Primary T-cell lymphoma at 1 pole of the right kidney of a dog. Note the pale, friable tissue of the neoplasm, and effacement of normal renal architecture.**

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Received: November 2001. Accepted: May 2002.

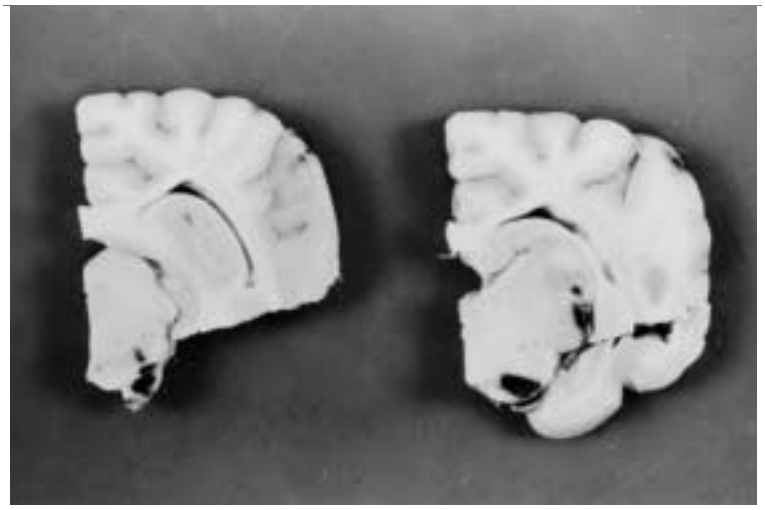

Fig. 2: **Metastatic foci of T-cell lymphoma in the mid-brain of a dog. Note the multiple, dark haemorrhagic foci.**

blood vessels in the haemorrhagic areas of the brain and pituitary gland contained rafts of similar neoplastic cells (Fig. 4). Immunoperoxidase stains for T-cell antigen (CD3) were positive while those for B-cell antigen (CD79a) and epithelial cell antigens (pancytokeratin) were negative.

In addition, mild segmental membranous glomerulonephritis was present, and moderate to large numbers of plasma cells were present around hepatic portal triads, scattered throughout the renal cortical interstitium, along splenic trabeculae, in the lymph node medullary cords and the bone marrow. Splenic periarteriolar lymphoid sheaths and lymph node cortices were depleted of lymphocytes while haemosiderin-laden sinusoidal macrophages were common. Hepatocytes in all zones showed marked fine vacuolar and feathery hydropic degeneration and mild periacinar hepatic fibrosis was present. The bone marrow showed mild hyperplasia of the granulocytic cell lines. Sections of lung, heart and intestine were normal. A final diagnosis of high-grade bilateral renal T-cell lymphoma with metastasis to the pituitary and brain, with concurrent CME was made.

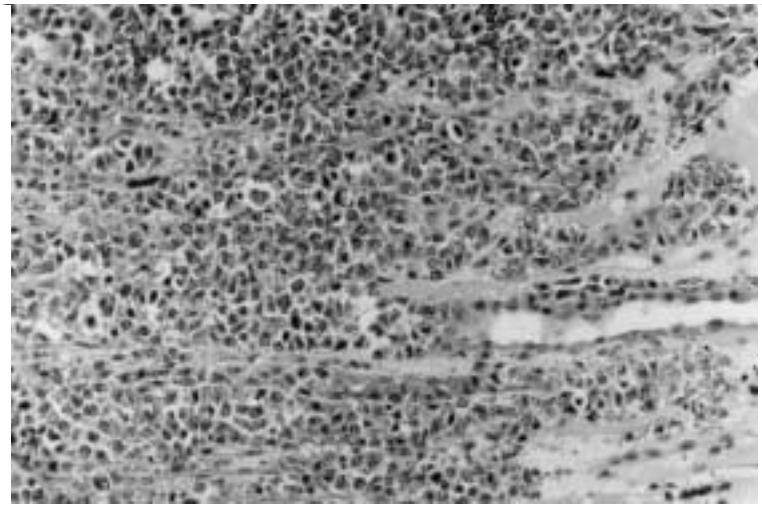

Fig. 3: **Renal lymphoma** (right kidney)**. Note the sheets of neoplastic lymphocytes that efface renal architecture** (H&E, ×40).

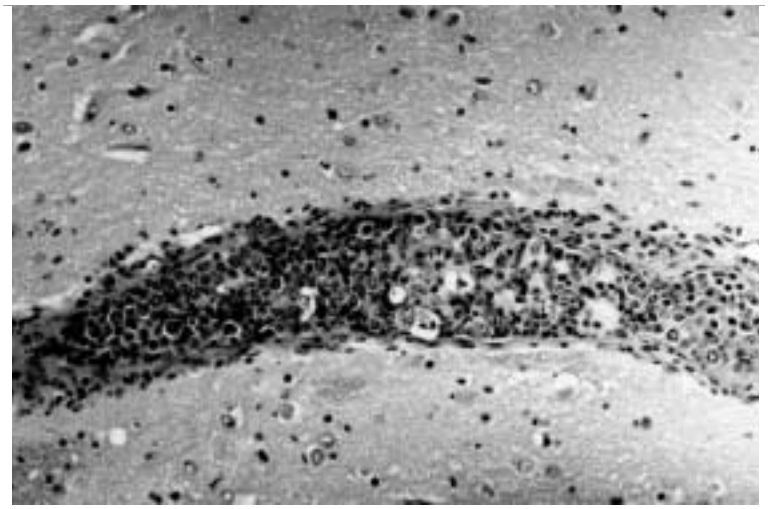

Fig. 4: **Metastatic foci of T-cell lymphoma in the brain. Note the sheets of neoplastic lymphocytes filling a small arteriole** (H&E, ×40).

DISCUSSION

Both the site of origin and cell type of this neoplasm are unusual. Primary renal tumours account for approximately 1 % of all canine neoplasm[8]. To our knowledge, primary renal lymphoma has not been reported previously in dogs. Lymphomas are one of the most common tumours of dogs over 5 years old but renal involvement is always secondary as part of the multicentric and spreading intestinal forms. In these cases, secondary renal lesions are originally perivascular and often in the cortex, in contrast with the medullary location in this case[8,9]. Another unusual feature was that the secondary lesions were restricted to the central nervous system, sparing the spleen, lymph nodes, liver and bone marrow. Both primary and secondary central nervous system lymphoma are rare in dogs and, again, usually a feature of advanced disseminated disease[18].

Primary renal lymphoma has, however, been recorded in a number of species where its occurrence is closely linked with retroviral infections, feline leukaemia virus, bovine leucosis virus and the avian leucosis/sarcoma viruses[10,13]. Canine lymphoma has as yet no proven association with viral infection, but possible aetiological factors include aberrations of the immune system, exposure to chemical carcinogens and chromosomal abnormalities[17].

The role of concurrent CME, if any, in the development of this neoplasm is uncertain. During the acute phase of infection with *E. canis,* lymphoreticular hyperplasia occurs, which is followed in the subacute and chronic states by variable pancytopaenia of unknown pathogenesis[5,11,15]. Apparent increased susceptibility to secondary bacterial, fungal and parasitic infections, reported in advanced cases, have been attributed to both specific and non-specific immune-suppression as a result of infection of

mononuclear cells[3,6,11,14,15]. However, a recent update of CME makes no mention of terminal immune suppression[7].

Immune-suppression has a documented effect on the development of tumours in humans. Patients receiving immune suppressive treatment show, in addition to an increased prevalence of bacterial, fungal and protozoal infections and increased incidence of malignant B and, less commonly, T-cell lymphoma[4,12]. This has been attributed variously to constant antigen stimulation from an implanted organ or opportunistic infectious agent, impaired immune surveillance which allows proliferation of cells that have undergone mutation and viral-induced transformation[4,16]. The mechanisms for the above are as yet unclear[4]. On similar lines, primary and secondary cerebral B and T-cell lymphomas, previously rare, are increasingly diagnosed in human patients with AIDS[1,2]. Owing to similarities in patterns seen in immune-compromised humans, we suggest that an altered immune status as a result of chronic CME may have played a role in the site of development and unusual pattern of metastasis of the lymphoma in this animal. If so, the role of CME in tumour development requires elaboration.

ACKNOWLEDGEMENTS

We thank the technical staff in the Department of Pathology and the Clinical Pathology Laboratory, Faculty of Veterinary Science, for assistance.

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