TITLE: Leishmaniosis in a dog with no travel history outside of the UK

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TITLE OF CASE

Leishmaniosis in a dog with no travel history outside of the UK.

SUMMARY

A 3-year-old male neutered Shih Tzu cross was presented for investigation of a three-week history of weight loss, seborrhoea, vomiting and diarrhoea. Initial clinicopathological findings included pancytopenia, mild hypercalcaemia and marked hyperglobulinaemia. Subsequent bone marrow and skin biopsies revealed the presence of *Leishmania* amastigotes. Quantitative serology was positive for *Leishmania* spp. and PCR on the bone marrow sample confirmed a *Leishmania infantum* infection. The patient had been in the owner's possession since a puppy, had no travel history outside of the UK and had never received a blood transfusion or been used for breeding. However, another dog in the household that had been imported from Spain had been euthanised six months previously due to severe leishmaniosis. To the authors' knowledge, this is the first reported case of canine leishmaniosis in the UK without a history of travel to an endemic area, and most likely represents a case of dog-to-dog transmission.

BACKGROUND

Canine leishmaniosis is a zoonotic disease caused by the protozoan parasite *Leishmania infantum*. The main route of transmission of the parasite to dogs and humans is by transmission of the infectious stages (promastigotes) from the bite of the female phlebotomine sandfly. Other routes of transmission have been reported including vertical,[1,2,3] venereal[3] and through infected blood transfusions.[4,5] Another reported route of transmission is direct dog-to-dog transmission of *L. infantum* via wounds or dog bites.[6,7,8,9,10] To the authors' knowledge, the latter route of transmission has not previously been reported in the UK. Here we describe a case of leishmaniosis in the UK in a dog without a history of travel to an endemic area.

CASE PRESENTATION

A 3-year-old male neutered Shih Tzu cross was presented to the internal medicine service of the Queen Mother Hospital for Animals (Royal Veterinary College) for investigation of a three-week history of weight loss, seborrhoea, intermittent vomiting and diarrhoea with haematochezia. Haematology prior to referral had documented a moderate pancytopenia, which was confirmed on repeated blood results.

The patient had no prior significant medical history and was confirmed to have no travel history outside of the UK. He had been in the owner's possession since he was 8 weeks of age, had never been used for breeding and had never had a blood transfusion. He was not receiving regular ectoparasite preventative treatment. Another dog in the household, originally acquired from Spain, had been diagnosed with leishmaniosis and was euthanised six months previously.

On physical examination the patient had a body condition score of 2/9. Mild bilateral otitis externa was present with diffuse seborrhoea also noted, most marked periocularly (figure 1). His mucous membranes were pale pink with a normal capillary refill time. No peripheral lymphadenopathy was detected. Examination was otherwise unremarkable.

INVESTIGATIONS

Significant haematological findings included a mild regenerative anaemia [haematocrit 32.9%, reference interval (RI) 37-55%, absolute reticulocyte count 81.6 $X10^9$ /L], moderate thrombocytopenia [90 $X10^9$ /L, RI 150-900 $X10^9$ /L], mild neutropenia [2.6 $X10^9$ /L, RI 3-11.5 $X10^9$ /L] and mild lymphopenia [0.71 $X10^9$ /L, RI 1-4.8 $X10^9$ /L]. Significant biochemical abnormalities included a moderate hypoalbuminemia [20.7g/l, RI 28-39g/l], marked hyperglobulinemia [70.1 g/l, RI 21-41g/l] and mild total hypercalcaemia [2.77 mmol/l, RI 2.13-2.7mmol/l] that was confirmed via ionised calcium measurement [1.44mmol/l, RI 1.13-1.3mmol/l]. Urinalysis (on a cystocentesis sample) revealed a urine specific gravity of 1.030, inactive sediment analysis and 1+ proteinuria quantified with a urine protein:creatinine ratio of 0.3.

Pancytopenia in the presence of hypercalcaemia raised concern for a possible underlying neoplastic process. To investigate this further, computed tomography (CT) of the thorax and

abdomen were performed which revealed no significant abnormalities. In addition, fine needle aspiration of the spleen was suggestive of extramedullary haematopoiesis (likely due to the previously documented peripheral cytopenias) but detected no neoplastic cells. Bone marrow aspiration and core biopsy were then performed to assess for a primary bone marrow disorder as the cause of pancytopenia. On cytology, the bone marrow was hypercellular due to myeloid hyperplasia with erythroid and megakaryocytic normoplasia and a megakaryocytic left shift. Numerous macrophages were seen to contain *Leishmania* spp. amastigotes (figure 2). Histopathology of punch biopsies from areas of seborrhoeic skin revealed a pyogranulomatous perivascular and periadnexal dermatitis with intrahistiocytic amastigotes, consistent with cutaneous leishmaniosis. Quantitative ELISA for detection of IgG against *Leishmania* spp. (Idexx Laboratories Ltd.) was positive at 84.4 test units (>12 units positive). *L. infantum* infection was confirmed with quantitative PCR[11] on DNA extracted from the bone marrow core at the Acarus Laboratory, Diagnostic Laboratories, Langford Vets, Bristol Veterinary School.

TREATMENT *If relevant*

The patient was placed on a 28-day course of miltefosine at 2mg/kg/day PO and allopurinol at 10mg/kg BID PO for 28 days, and thereafter was continued on allopurinol alone.

OUTCOME AND FOLLOW-UP

Re-examination, one month later, showed resolution of clinical signs of vomiting, diarrhoea and seborrhoea and improved body condition score. Haematology, serum biochemistry and urinalysis at this time showed resolution of the previously documented hypercalcaemia, pancytopenia and a decrease in the degree of hyperglobulinemia to 58.2g/l [RI 21-41g/l]. Quantitative serology for *Leishmania* spp. performed 6 months after initiation of treatment showed a persistently positive, but decreased, antibody titre of 40.3 test units. The patient is clinically well and remains on allopurinol therapy at the time of writing.

DISCUSSION *Include a very brief review of similar published cases*

This case of canine leishmaniosis likely represents a case of direct dog-to-dog transmission in the UK.

The distribution of canine leishmaniosis is generally linked to the distribution of appropriate sandfly vectors (*Phlebotomus* or *Lutzomyia)*. In Europe, canine leishmaniosis is known to be endemic in many southern countries including southern France, Spain, Portugal, Italy, Malta, Croatia, Albania, Greece, Cyprus and Turkey.[12,13] Dogs diagnosed in the UK usually have a history of travel to, or importation from, an endemic area.[14] In those areas, dogs seropositive for *L. infantum* represent a source of infection for vectors.[12] However, proven vectors such as *Phlebotomus ariasi and P. perniciosus,* and suspected vector *P. mascitti,* have not yet been reported in the UK. The authors acknowledge the possibility of a thus far undetected phlebotomine vector in the UK, although this is assessed to be unlikely. In addition, non-phlebotomine arthropods, including ticks and fleas, have been proposed as vectors of *L. infantum;* [17-23] however, this route of transmission remains unproven and is also thought to be unlikely in this case.

Given the previous diagnosis of leishmaniosis in another dog in the same household, the authors consider direct dog-to-dog transmission of *L. infantum* between these dogs to be the most likely route of infection. The other dog in the household was euthanised because of the severity of the clinical signs attributed to the leishmaniosis, but despite its confirmed diagnosis, was never treated. It has been reported that the infectiousness of dogs increases with clinical severity,[15] therefore there is a strong probability that this dog acted as a reservoir of infection. Although there was no known history of the dog in this case report being bitten by the other infected dog, we suspect an undocumented dog bite with blood-to-blood contact to be a likely route of transmission. Subclinical infection can persist for months to years; therefore, an episode of blood-to-blood contact may have occurred at any time in the past.

Other potential routes of transmission include vertical,[1,2,3] venereal[3] and through infected blood transfusions[4,5]. This dog had never been used for breeding and had never received a blood transfusion. Because a blood sample from the dam of this dog is not available, vertical transmission cannot be completely excluded but is considered unlikely by the authors. Direct

dog-to-dog transmission of *L. infantum* through bites or wounds has been reported as a possible route of infection in foxhounds in the USA[6,7] and in isolated cases in dogs in Finland,[8] Germany[10] and New Caledonia.[9]

This case report is of epidemiological significance since we believe this to be the first reported case of canine leishmaniosis in the UK in a dog without a foreign travel history. Nonetheless, the authors would like to acknowledge that the possibility of transmission of leishmaniosis between dogs in the UK, in particular non-travelled dogs, has been raised before.[11,16]

In conclusion, clinicians in the UK should include leishmaniosis as a differential diagnosis when appropriate clinical findings are present, even if the dog has no travel history but might have been in contact with a dog that has travelled from an endemic area. Further research is needed to determine the risk and potential routes of direct dog-to-dog transmission.

LEARNING POINTS/TAKE HOME MESSAGES *3 to 5 bullet points – this is a required field*

- A differential diagnosis of canine leishmaniosis should not be excluded by the absence of a travel history to an endemic area
- *Leishmania*-infected dogs may present an infection risk to other dogs even in the absence of natural vectors, as direct dog-to-dog transmission is possible.
- In an era of increased foreign travel of dogs and increased importation of dogs to the UK, it is likely that the prevalence of dogs seropositive for *L. infantum* will continue to increase. As seropositivity increases, dog-to-dog transmission may become a more recognised route of infection in the future.

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FIGURE/VIDEO CAPTIONS *figures should NOT be embedded in this document*

Figure 1: The patient on presentation. Note the bilateral periocular seborrhoea. (Photo credit Professor David Church)

Figure 2: Bone marrow cytology showing macrophages with numerous intracellular organisms consistent with *Leishmania* spp. amastigotes; 100x oil; Modified Wright's stain. (Photo credit Charalampos Attipa)

Figure 1

Figure 2