WHAT IS YOUR DIAGNOSIS?

A six year, female neutered, Labrador Retriever was presented to the R(D)SVS Internal Medicine Service for investigation of pyrexia. The dog had a recent history of coughing and had been receiving treatment with antibiotics and fenbendazole prior to referral.

On clinical examination, the dog was quiet but alert with a body condition score of 6/9. The heart rate was 100 bpm with no arrhythmia, murmur or pulse deficits. The respiratory rate was 32 breaths/minute, with no adventitious lung sounds. Abdominal palpation and peripheral lymph nodes were unremarkable and the rectal temperature was 39.6°C.

Routine hematology serum biochemistry and routine urine analysis were performed. Serum biochemistry and urine results were unremarkable but the following haematology results were obtained.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV</td>
<td>0.36</td>
<td>0.39-0.55 l/l</td>
</tr>
<tr>
<td>WBC</td>
<td>0.33 x10^9/l</td>
<td>5.04-16.76 x10^9/l</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0.02 x10^9/l</td>
<td>2.95-11.6 x10^9/l</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>0.27 x10^9/l</td>
<td>1.05-5.1 x10^9/l</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0.04 x10^9/l</td>
<td>0.6-1.2 x10^9/l</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0 x10^9/l</td>
<td>0.06-1.23 x10^9/l</td>
</tr>
<tr>
<td>Platelets</td>
<td>29 x10^12/l</td>
<td>300-500 x10^12/l</td>
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Smear evaluation confirmed the thrombocytopenia. The few white cells present were morphologically unremarkable. No significant red cell abnormalities were present.

1) **What are your differential diagnoses for pancytopenia in this dog?**
2) **What other diagnostic evaluations would you perform?**
3) **How would you treat this dog pending definitive test results?**
1. **Differential diagnosis for pancytopenia**

- Oestrogen toxicity
- Myelodysplasia
- Idiopathic/immune-mediated disease targeting bone marrow myeloid precursors
- Secondary to infections or neoplasia elsewhere in the body
- Tick borne infections
- Drug reactions
- Myelophthisis secondary to bone marrow neoplasia
- Bone marrow fibrosis
- Septicemia/\textit{Salmonella} infections
- Parvovirus infection

In this case, the dog was well and cardiovascularly stable making septicemia unlikely. The pyrexia may have been caused by infections or neoplastic diseases, although no clear evidence of an inciting cause was present on physical examination. Recent medication administration meant that drug toxicity was a possibility.

2. **Further tests**

The most useful test in a dog with pancytopenia with no obvious apparent course (e.g. recent chemotherapy, evidence of sepsis) is to perform a bone marrow aspirate and core biopsy. This allows many primary bone marrow diseases to be excluded. In addition, thoracic radiographs and abdominal ultrasound scans were performed in this case to investigate a potential underlying neoplastic cause. No abnormalities were apparent. In house serology testing (IDEXX 4DX snap test) for tick borne disease including \textit{Anaplasma phagocytophilum} and \textit{Borrelia burgdorferi} was performed to exclude tick-borne pathogens as serological testing was negative.

Bone marrow biopsies and cytology revealed no dysplastic or neoplastic changes. Myeloid precursors and megakaryocytes were lacking indicating a relatively poorly responsive for a dog with neutropenia and thrombocytopenia. There was no evidence of bone marrow fibrosis.

Based on an absence of evidence for infectious, neoplastic or autoimmune diseases, we suspected the dog an acute toxic insult to her bone marrow. Bone marrow toxicity has been reported in dogs treated with fenbendazole. Following drug cessation, encouraging improvements were seen in the white blood cell population. In a case report of fenbendazole toxicity (Gray et al. Bone Marrow Hypoplasia Associated With Fenbendazole Administration in a Dog. \textit{Journal of the American Animal Hospital Association} May 1, 2004 vol. 40 no. 3 224-229), similar pathological changes are reported. The pancytopenia in this case gradually resolved within two weeks of discontinuation of fenbendazole treatment.

3. **Treatment pending definitive diagnosis**
Considering her pyrexia and profound neutropenia, the dog was treated in hospital with 20mg/kg q8hours with IV potentiated amoxicillin for potential secondary bacterial infection. Prophylactic antibiotics are advisable in dogs with a total neutrophil count of < 1 x10⁹/l.

**Outcome**

A haematology profile taken a week later showed a significant improvement with platelet numbers of 77 x10⁹/l (ref 200-500 x10⁹/l) and neutrophil count of 1.97x10⁹/l (ref 3.6-12.0 x10⁹/l). All other cells lines were within normal reference intervals. With neutrophil and platelet numbers of this magnitude the dog was no longer at significant risk for acquiring secondary infections or for developing spontaneous haemorrhage. Within two weeks all haematology parameters were within normal reference ranges. Notably, the neutrophil count was (6.75 x 10⁹/l, ref 3.6-12) and platelet (246 x 10⁹/l, ref 200-500). Antibiotic therapy was withdrawn once the neutrophil count was within the reference range. The absence of underlying infectious, neoplastic and autoimmune disorders together with resolution of clinical signs and pancytopenia upon cessation of febendazole therapy was highly suggestive of bone marrow hypoplasia associated with febendazole administration in this case.