WHAT IS YOUR DIAGNOSIS?

A 10 year old male neutered Bullmastiff was presented to R(D)SVS Emergency Medicine Service for investigation of 10 days progressive history of lethargy, diarrhoea, hyporexia and exercise intolerance. Over the last couple of days the dog became completely anorexic and started showing signs of abdominal discomfort.

Clinical examination revealed tachycardia (160 beats/min) with no arrhythmia, murmur or pulse deficits. Mucous membranes were congested, capillary refill time was reduced (<1 sec) and tachypnoea (40 breaths/min) was observed with no adventitious lung sounds. Additionally the abdomen appeared distended and painful on palpation.

An intravenous catheter was placed and a blood sample obtained for analysis. Results of routine haematology and biochemistry revealed following abnormalities:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>5.7</td>
<td>0-2.0 mmol/l</td>
</tr>
<tr>
<td>PCV</td>
<td>0.25</td>
<td>0.39-0.55 l/l</td>
</tr>
<tr>
<td>Monocytes</td>
<td>1.62</td>
<td>0-1.5 x10^9/l</td>
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<tr>
<td>Platelets</td>
<td>50</td>
<td>200-500 x10^9/l</td>
</tr>
<tr>
<td>Albumin</td>
<td>21.2</td>
<td>26-36 g/l</td>
</tr>
<tr>
<td>ALP</td>
<td>1504</td>
<td>20-60 U/l</td>
</tr>
<tr>
<td>Bile acids</td>
<td>186</td>
<td>0-7 umol/l</td>
</tr>
<tr>
<td>Globulin</td>
<td>14.0</td>
<td>18-37 g/l</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>33.8</td>
<td>0-6.8 umol/l</td>
</tr>
<tr>
<td>Total protein</td>
<td>35.1</td>
<td>58-73 g/l</td>
</tr>
<tr>
<td>Urea</td>
<td>8.6</td>
<td>1.7-7.4 mmol/l</td>
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</tbody>
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Blood smear evaluation confirmed presence of severe thrombocytopenia. There was also normocytic and normochromic anaemia with moderate RBC anisocytosis and a small number of polychromatophils and metarubricytes. Presence of atypical lymphocytes was also detected.

1) What is the problem list for this patient?

2) How would you interpret the findings from the clinical exam and blood results?

3) How would you treat this patient pending further investigations?

4) What further diagnostic tests would you consider?
1) Problem list:
- Tachycardia
- Abdominal pain
- Tachypnoea
- Diarrhoea
- Anaemia
- Moderate panhypoproteinemia
- Marked thrombocytopenia
- Moderate hyperlactatemia
- Moderate increase in ALP, bilirubin and bile acids
- Mild azotaemia

2) Tachycardia with reduced capillary refill time in conjunction with hyperlactatemia indicate hypoperfusion. This patient shows signs of shock that reflect jeopardised delivery of oxygen and nutrients to tissues.
Thrombocytopenia is significant enough to raise a concern over an increased risk of bleeding.
Most common causes of monocytosis include stress response and inflammation but given other abnormalities identified in this patient’s blood results, neoplasia and paraneoplastic response should be considered as well.
Anaemia is only poorly regenerative and together with reduced total protein might suggest recent haemorrhage (e.g. to the gastrointestinal tract) as bone marrow requires between 3 and 5 days to respond to drop in circulating red blood cell count. However, other causes of anaemia and hypoproteinemia cannot be ruled out at this stage. A bone marrow disease concurrently affecting red blood cell and platelet lines could explain poorly regenerative anaemia and thrombocytopenia while ongoing diarrhoea could have led to loss of both albumins and globulins.
The rest of biochemistry results (i.e. increase in alkaline phosphatase and bilirubin) suggest presence of a cholestatic disorder. Differential diagnoses for cholestasis such as functional cholestasis, structural cholestasis or neoplasia should be considered. Interpretation of bile acids levels is helpful in the absence of cholestatic disease, therefore no conclusions can be drawn in this case.

3) Given findings consistent with hypoperfusion and presence of abdominal pain the patient was infused a 10ml/kg bolus of Hartmann’s solution over 15 minutes after which the heart rate reduced to 110 beats/min. Patient was also administered a 0.20mg/kg dose of methadone intravenously.

4) Further diagnostic investigations included:
- Prothrombin time (PT) and activated partial thromboplastin time (aPTT) within normal limits.
- Thoracic radiographs revealed presence of sternal lymphadenopathy.
- Abdominal ultrasound showed normal looking liver, thickening of the gall bladder wall, moderate splenomegaly and small amount of anechoic peritoneal effusion.
• Abdominocentesis was performed and a sample of the peritoneal effusion was obtained. Effusion was highly cellular and consisted of a population of moderate to large atypical cells, raising a suspicion of lymphoma or other neoplasia arising from myeloid precursors.

• Bone marrow aspirates and core biopsies were also obtained to further characterise suspected neoplasia. Evaluation of the samples revealed almost complete effacement of normal haematopoietic population. Bone marrow structure was dominated by medium to large size atypical cells (similar to those found in peritoneal effusion) with paracentral nuclei containing multiple nucleoli surrounded by basophilic cytoplasm with occasional fine granules.
Diagnosis

Possible differential diagnoses for the neoplasia affecting this patient include acute myeloid leukemia, acute lymphoblastic leukemia or stage V lymphoma (lymphoma involving blood/bone marrow). A sample of peritoneal effusion was submitted for flow cytometry to better characterise the type of neoplasia. Unfortunately, due to the low cellularity of the sample the results were considered inconclusive.

Treatment

After identification of atypical cells in peritoneal effusion and bone marrow the patient was started on chemotherapy. The dog received a dose of vincristine, L-asparaginase and prednisolone. In addition he was treated supportively with intravenous fluid therapy and antiemetic injections (maropitant). The patient improved markedly (he was bright, alert, comfortable and the appetite returned) and was discharged home within couple of days of initiation of treatment.

Discussion

Lymphoma is one of the most commonly identified neoplasms in dogs. Malignant proliferation of lymphoid cells is a characteristic feature of the disease. Leukaemia is a malignant disorder affecting stem cells. It can affect lymphoid lineage (T cells, B cells, natural killer cells, plasma cells) or myeloid lineage (monocytes, platelets, neutrophils etc.). Classification of canine leukaemia can be challenging as patients often display signs consistent with involvement of both lineages.

Chemotherapy is the treatment of choice for both lymphoma and leukaemia. Although a complete cure is typically not possible, an appropriate therapy protocol can allow to alleviate clinical signs and gain up to several months of good quality of life. Single agent treatment protocols, using prednisolone, doxorubicin or CCNU, are less likely to lead to complete remission when compared with multidrug protocols. Multi-agent protocols, such as COP (cyclophosphamide, vincristine, prednisolone) or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone), are reported to have higher remission rates and longer survival times. Depending on the type of the neoplasia, degree of the anatomical involvement and treatment protocol, life expectancy can vary drastically and be between weeks (in cases that do not respond to chemotherapy) up to several months.

References