PRESCAPULAR MASS IN A CAT WITH ATYPICAL CIRCULATING CELLS

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Signalment

Cat, 7 years old, male neutered, Domestic Shorthair.

History

The cat presented for an oncology consultation with a one year history of mild nonregenerative anaemia, neutropenia and the presence of occasional atypical cells on the blood smear. Presence of a mass of unknown duration in the right prescapular area was also reported. The cat was FeLV positive. No other clinical signs were reported. Lymphoma was suspected based on the clinical picture.

Clinical findings

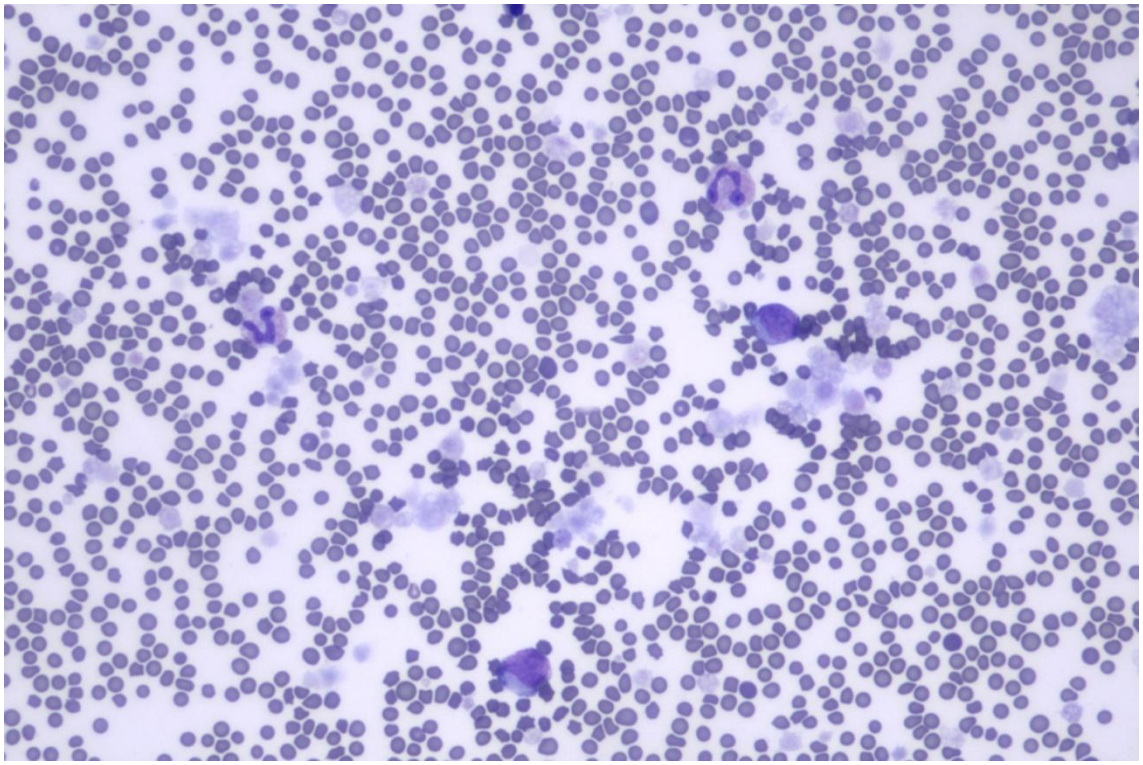
Moderate right prescapular lymphadenopathy was present on physical examination. The cat was otherwise well in himself and did not exhibit any other signs of illness.

Diagnostic procedures

Complete blood count was performed on Sysmex XT-2000iV analyser and a peripheral blood smear was examined. Haematology revealed marked neutropenia (0.98 x10^9/L, reference interval, RI: 3-11x10^9/L) and the presence of atypical cells (9.29x10^9/L). Automated platelet count was within reference intervals (271x10^9/L, RI: 180-550x10^9/L). There were 21 nucleated red blood cells / 100 leukocytes. The most relevant blood smear features are demonstrated in Figure 1 and 2. Biochemistry showed no abnormalities except mild hyperglycaemia (7.88 mmol/L, RI: 5,55-7.22 mmol/L)

Fine-needle aspiration cytology (FNAC) of the right prescapular lymph node was performed (Figure 3-5).

Abdominal ultrasound was performed and showed an enlarged spleen of mixed echogenicity and lymphadenopathy of the mesenteric lymph nodes.

A. 

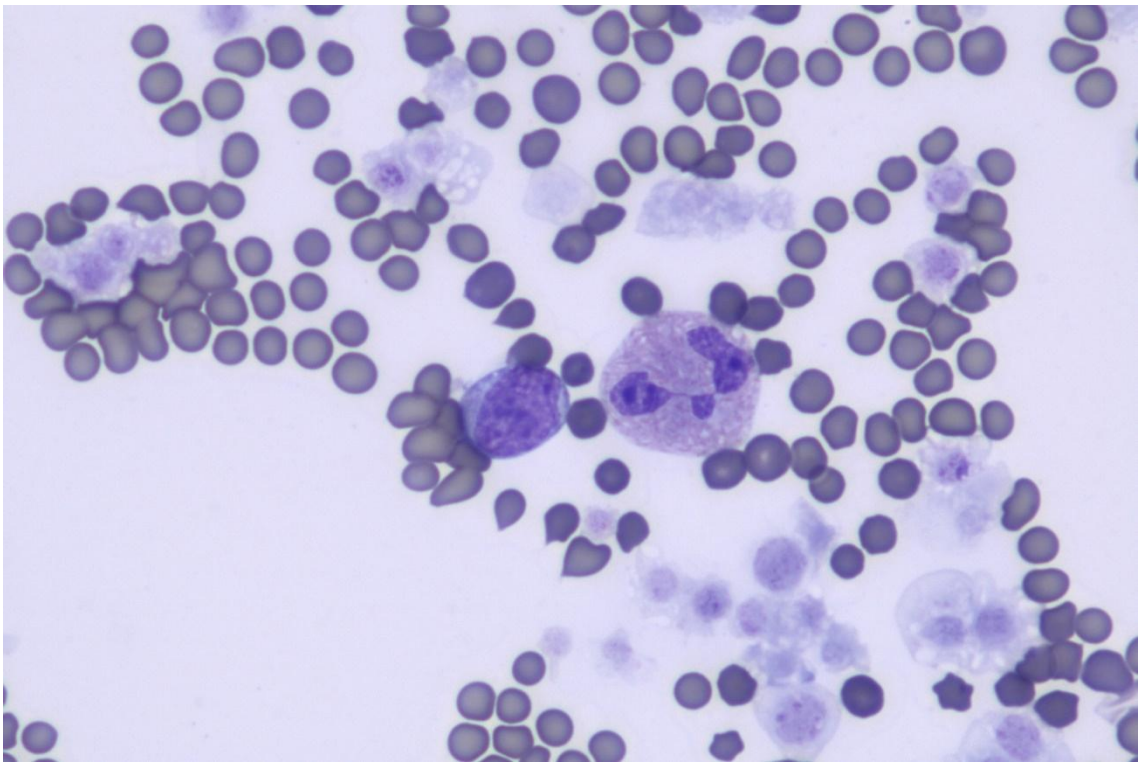
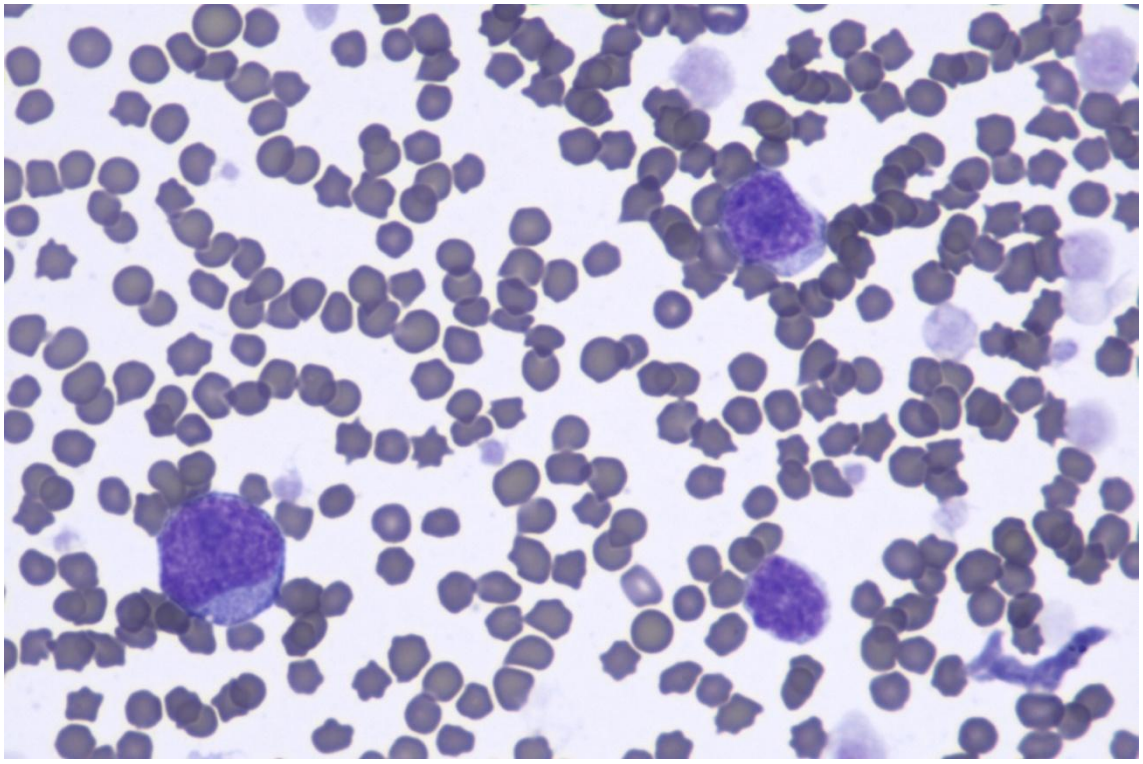
B. 

Figure 1. Peripheral blood smear from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 20x objective (A) and 50x objective (B).

A. 

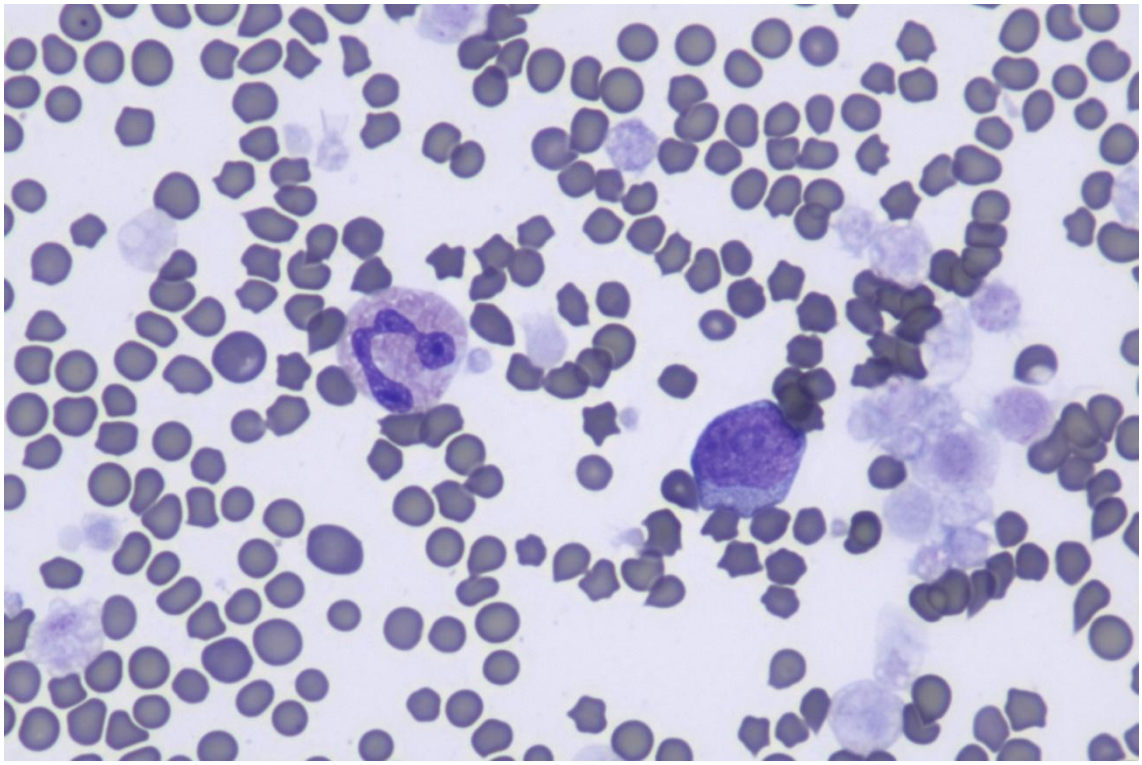
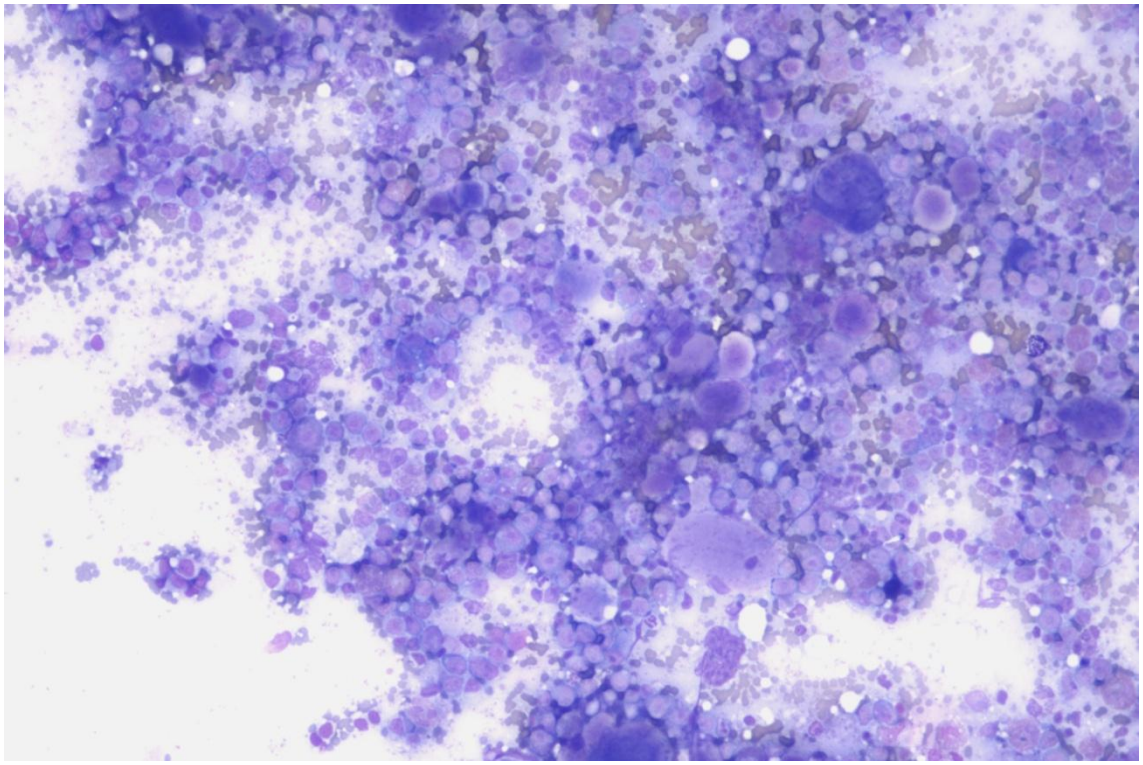
B. 

Figure 2. Peripheral blood smear from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 50x objective.

A. 

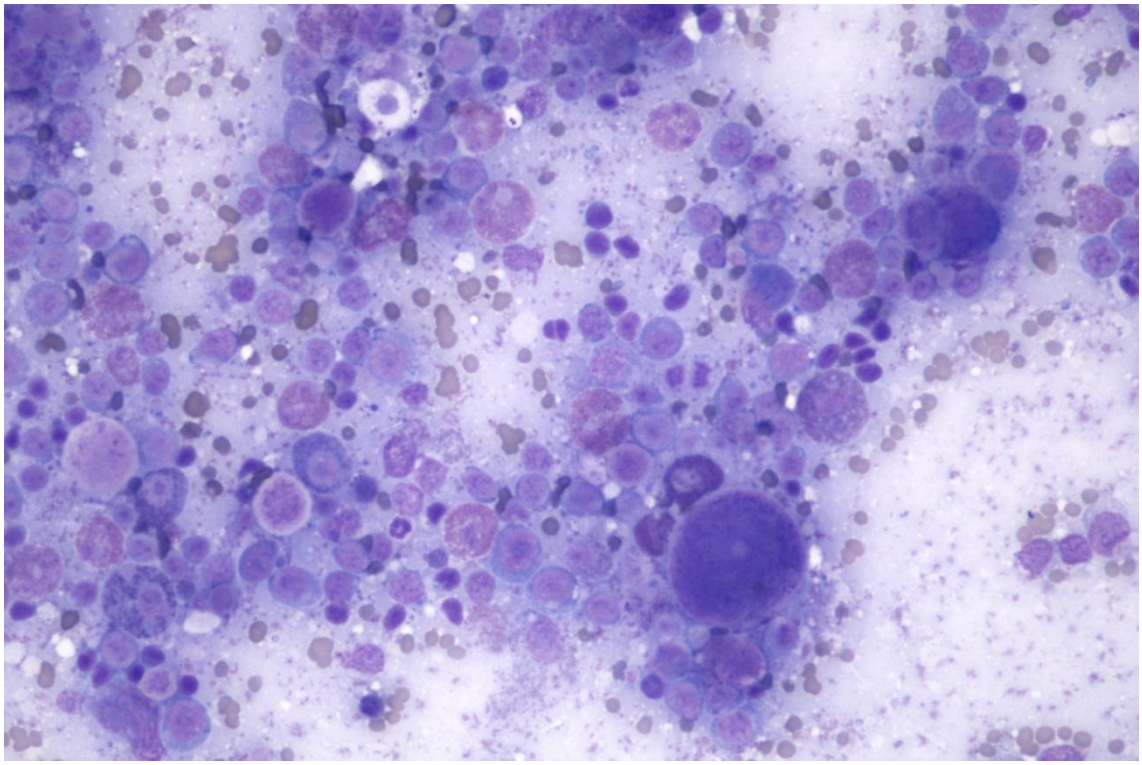
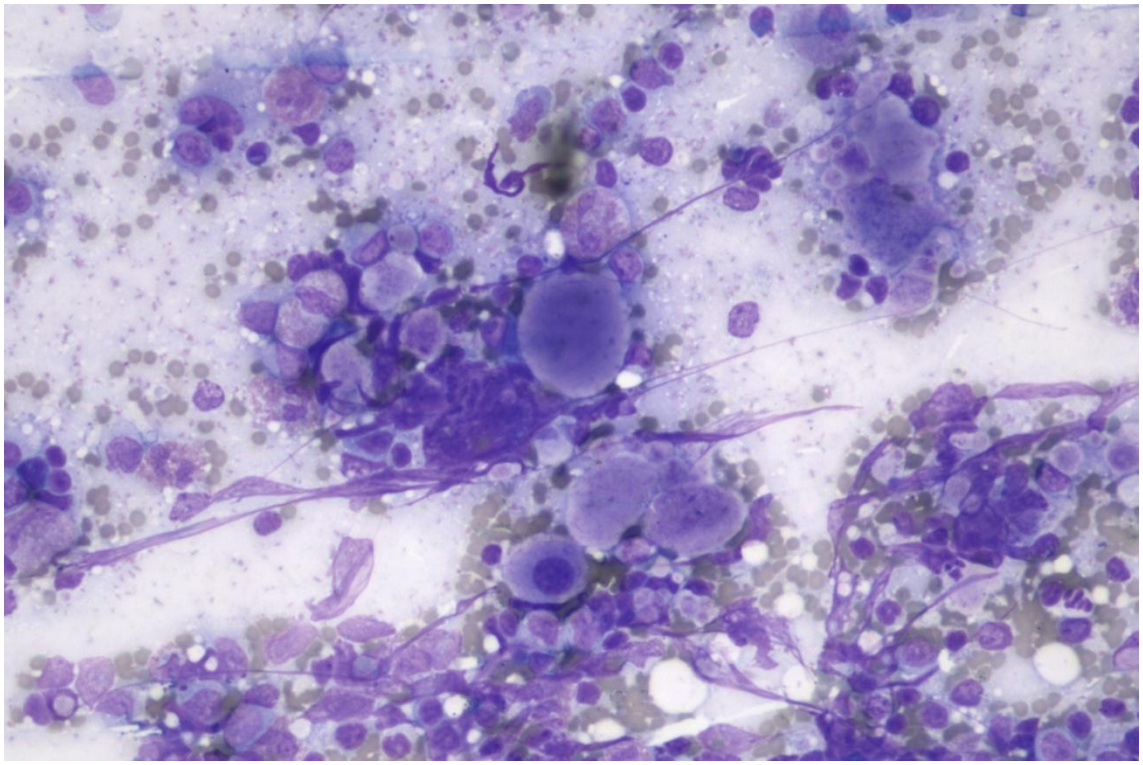
B. 

Figure 3. Fine-needle aspiration cytology of the prescapular lymph node from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 10x objective (A) and 20x objective (B).

A. 

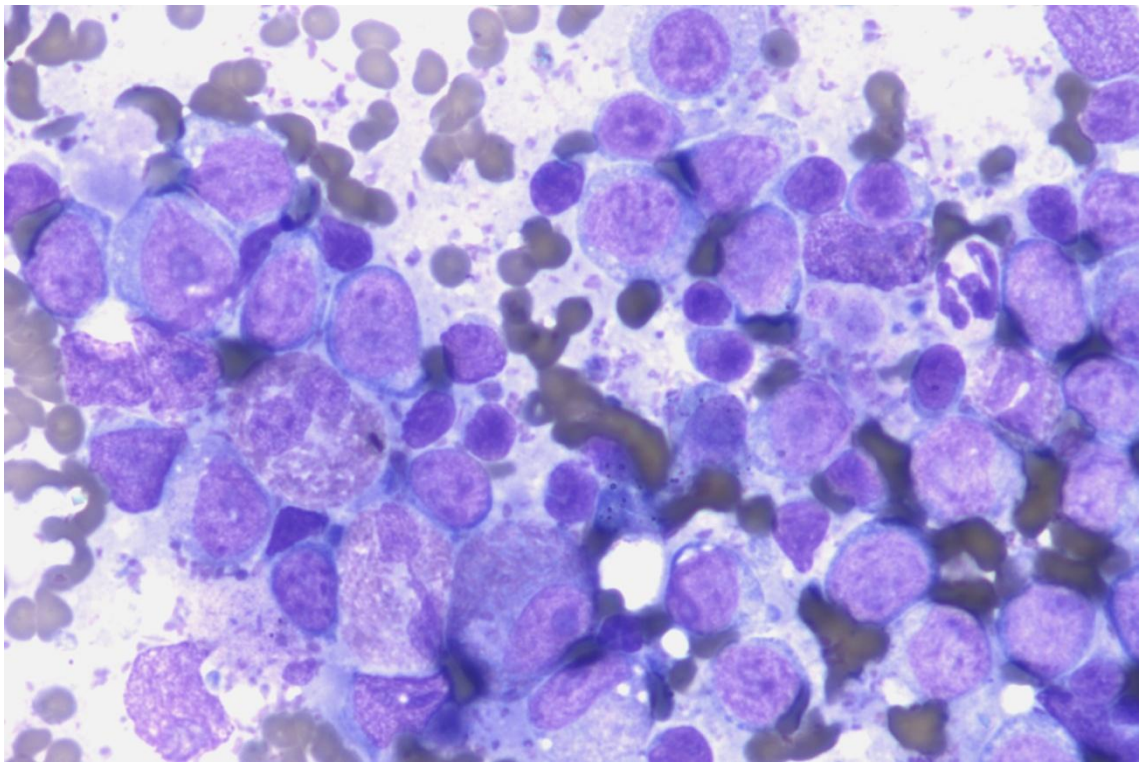
B. 

Figure 4. Fine-needle aspiration cytology of the prescapular lymph node from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 20x objective (A) and 50x objective (B).

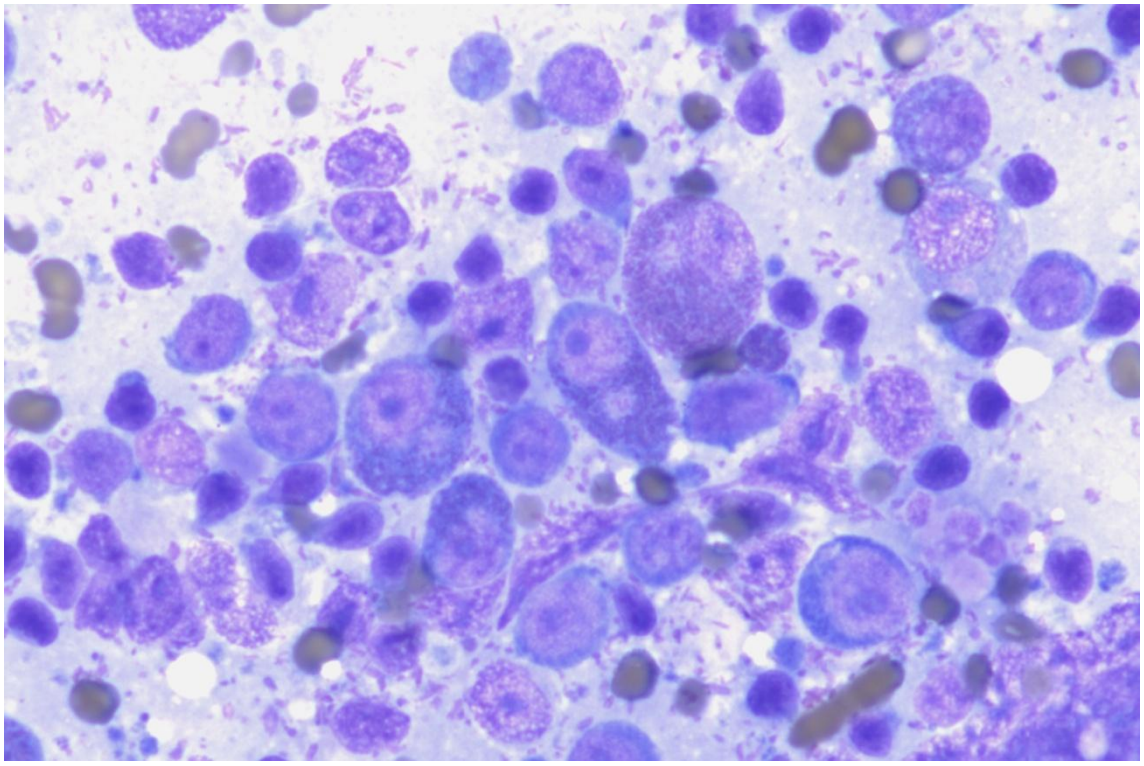


Figure 5. Fine-needle aspiration cytology of the prescapular lymph node from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 50x objective.

QUESTIONS:

1. **What is your description of blood smear findings?**
2. **What is your cytological description?**
3. **What is your interpretation of the haematology and cytology findings and what further tests would you recommend?**

Haematology

Moderate numbers of round atypical cells were observed. These cells were predominantly large and had small amount of mid-blue cytoplasm. Nuclei were round, oval or irregular, paracentrally- or centrally-located. Chromatin was coarse. Nucleoli were mostly single, prominent, medium-sized and round. Rare giant eosinophils were observed.

Erythrocytes were mostly normocytic and normochromic. Mild polychromasia and anisocytosis were observed. Occasional acanthocytes were also present.

Marked platelet clumping and platelet anisocytosis with high numbers of macroplatelets were observed. The true platelet number was likely higher than the automated.

Cytology of the lymph node

Examined slides were of high cellularity. Cellular staining and preservation were good. The background was light blue, slightly vacuolated and contained moderate numbers of pink granules and platelets (including macroplatelets and large bizarre platelets). Only mild haemodilution was observed. High numbers (around 75%) of atypical cells which shared many cytological features with the cells present in the circulation were seen. Moderate numbers (around 25%) of similar cells but with more abundant dark blue cytoplasm filled with small or medium-sized, round or elongated pink granules were also observed. Low numbers of giant eosinophils with segmented or band nuclei were identified. Occasional atypical megakaryocytes were seen, including mono- or multinucleated dwarf megakaryocytes and large megakaryocytes with nuclear abnormalities (e.g. variation in the size of the nuclei within the cell, presence of separate nuclei). Many megakaryocytes had single large prominent nucleoli and exhibited nuclear and cytoplasmic asynchrony. Low numbers of small lymphocytes and neutrophils were also seen.

Interpretation and differential diagnoses

The haematological and cytological findings were consistent with haematological neoplasia and were highly suggestive of myeloid origin. Given morphological features of the cells eosinophilic differentiation was a likely consideration.

The most likely differential diagnosis was an eosinophilic granulocytic sarcoma with concurrent acute myeloid leukaemia (AML). Coincidence of eosinophilic granulocytic sarcoma and myelodysplastic syndrome (MDS) or myeloproliferative neoplasia (MPN) was also possible.

Although the cytological features were not characteristic for other tumours, other haematological malignancies (i.e. lymphoid with an unusual, bizarre extramedullary haematopoiesis) could not have been totally ruled out.

The presence of giant eosinophils, atypical megakaryocytes and bizarre platelets on cytology was likely indicative of extramedullary haematopoiesis with dysgranulopoiesis and dysmegakaryocytopoiesis secondary to myeloid malignancy.

Neutropenia was likely secondary to decreased bone marrow production due to infiltration of the bone marrow with neoplastic cells.

The presence of inappropriate rubricytosis was likely secondary to bone marrow disease.

FURTHER TESTS

Further diagnostic tests recommended in order to reach diagnosis included:

- FNAC of the spleen and other enlarged lymph nodes
- examination of the bone marrow
- histology of the lymph node
- immunochemistry, cytochemistry
- flow cytometry of the peripheral blood

Splenic and bone marrow aspirates and incisional biopsy of the right prescapular lymph node were taken.

Spleen and bone marrow cytology

Similar cell populations were observed in the spleen (Figure 6) and in the bone marrow samples (Figure 7).

Splenic aspirate was of moderate cellularity with good preservation and staining. The background was clear and markedly blood contaminated. Moderate numbers of immature blast cells, moderate numbers of precursor cells (including atypical megakaryocytes and mostly mature erythroid precursors) and occasional cells with eosinophilic differentiation were present.

Bone marrow smears were highly cellular. Cellular preservation and staining were good. The background was clear and mildly haemodiluted. High numbers of spicules were present. Cytology identified the presence of a high number of blast cells (presumed myeloblasts, mostly type I) – they accounted for around 62% of all nucleated cells (ANCs) and for around 88% of nonerythroid cells (NECs). More differentiated granulocytes (many dysplastic and/or exhibiting differentiation towards eosinophils) accounted for around 12% of NEC. Moderate numbers of erythroid precursor cells with rare megaloblastic cells were seen – the maturation was orderly and complete with the majority of the cells being metarubricytes. The myeloid-to-erythroid ratio was 2.41 (increased, normal: 1.21-2.16). Occasional megakaryocytes (many exhibiting dysplastic features) and small lymphocytes were seen.

Spleen and bone marrow cytology supported the presence of a disseminated myeloid neoplasia – most likely an AML with eosinophilic differentiation (AML-M2-Eos). Given the clinical presentation, an early transformation of MDS/MPN to AML was a possible consideration.

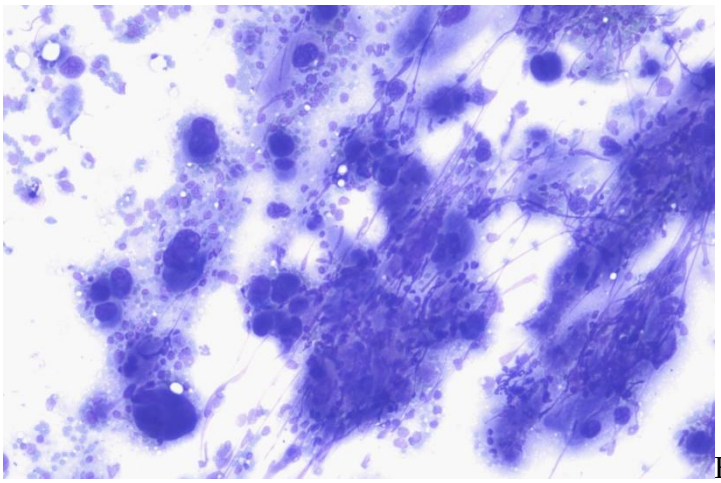
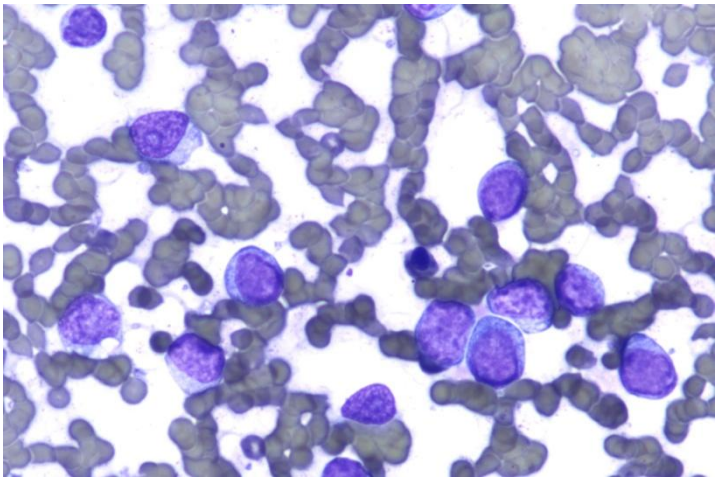
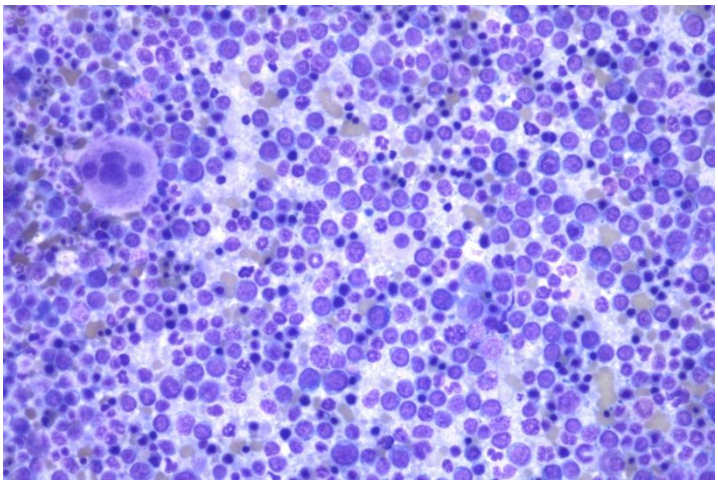
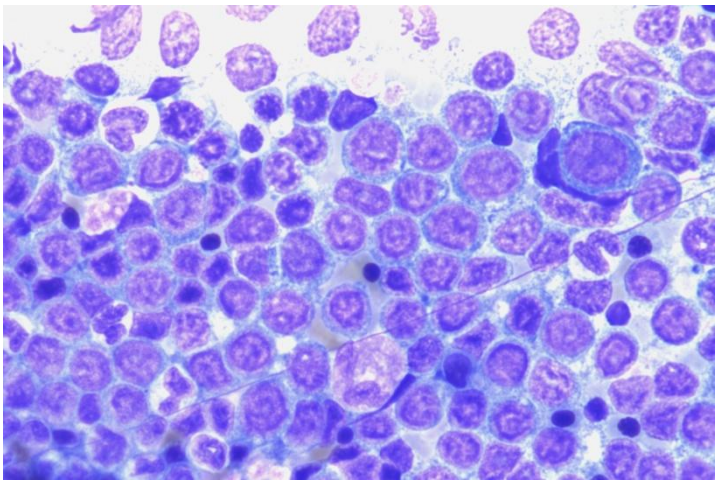
A.  B. 

Figure 6. Fine-needle aspiration cytology of the spleen from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 10x objective (A), 50x objective (B).

A.  B. 

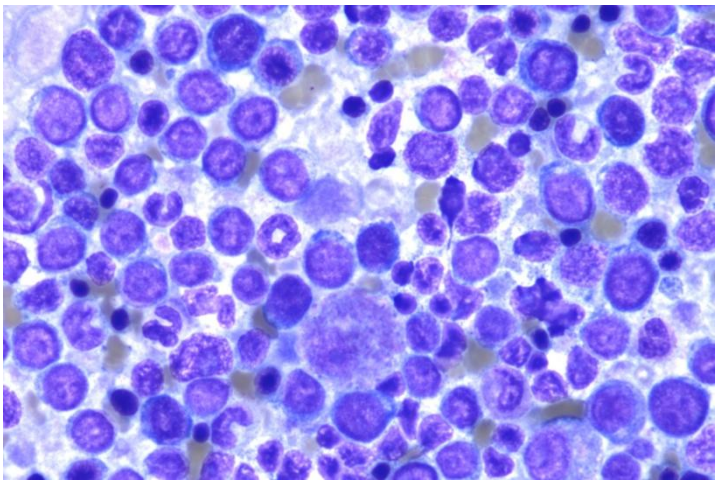
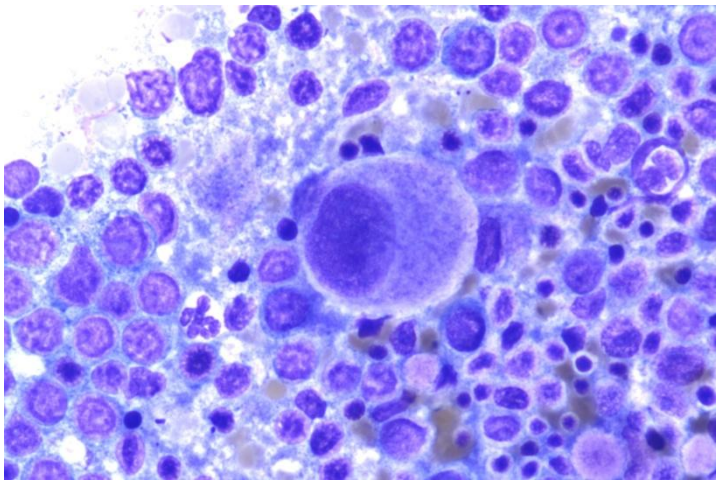
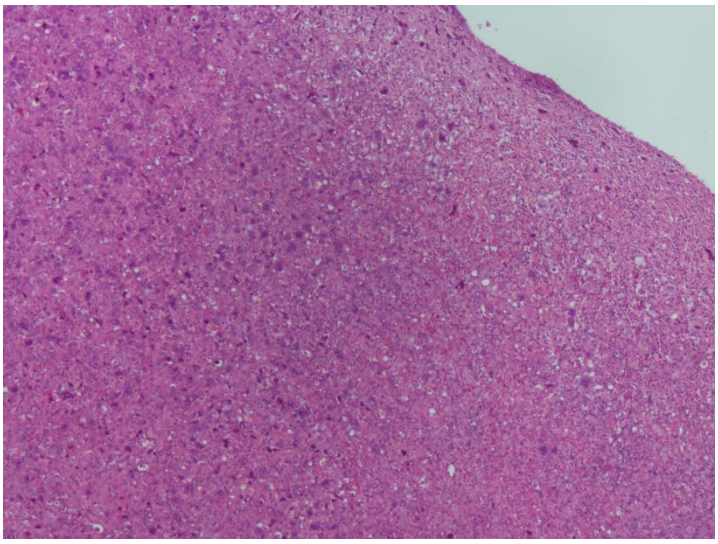
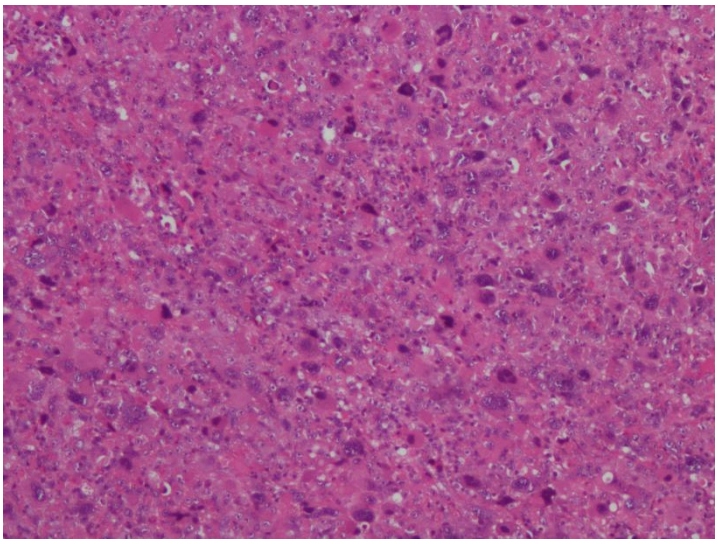
C.  D. 

Figure 7. Fine-needle aspiration cytology of the bone marrow from a 7 years old, male neutered, Domestic Shorthair cat. Hemacolor stain, 20x objective (A), 50x objective (B, C, D).

Lymph node histology and immunohistochemistry

Effacement and replacement of the normal nodal architecture by a mass composed of sheets of round cells was observed. The cells had moderate amounts of eosinophilic cytoplasm and round, ovoid to indented nuclei. There was notable nuclear atypia with bizarre karyomegalic and multinucleated cells being evident. Mitotic activity was moderate. There were low numbers of neutrophils scattered throughout the mass. Histology confirmed the presence of a malignant tumour and was most consistent with myeloid neoplasia.

On immunohistochemistry the neoplastic cell population was negative for CD3, CD20 and CD18 which does not support neoplasia of lymphoid or histiocytic origin.

A.  B. 

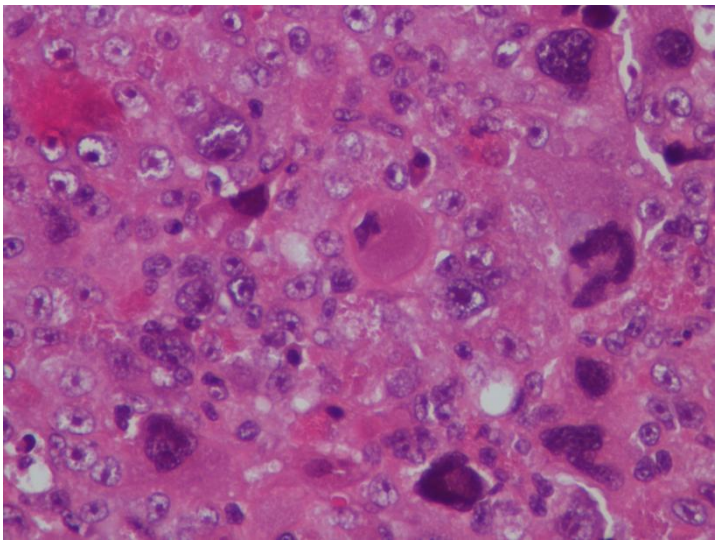
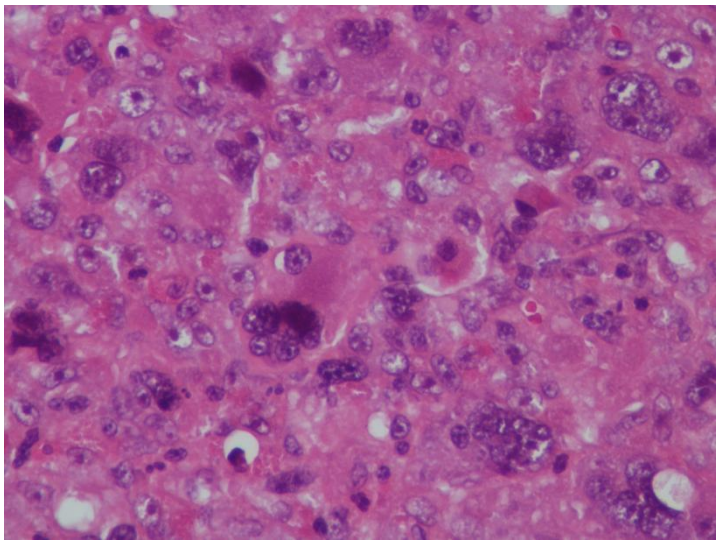
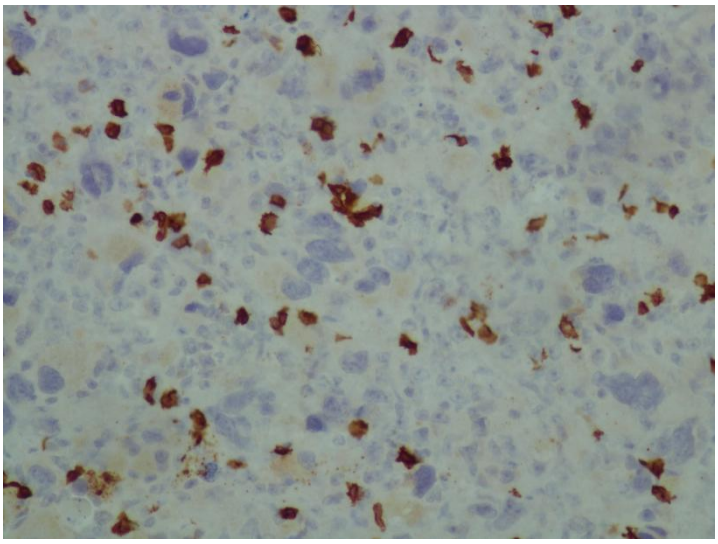
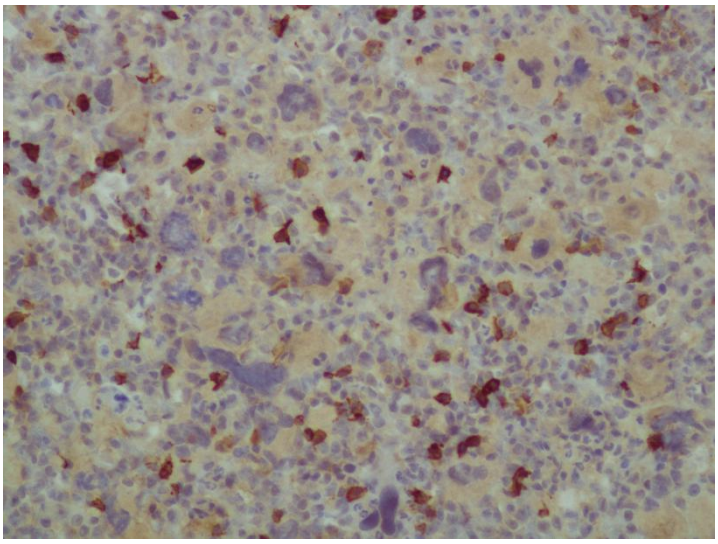
C.  D. 

Figure 8. Histology of the prescapular lymph node from a 7 years old, male neutered, Domestic Shorthair cat. Hematoxylin and eosin stain, 4x objective (A), 10x objective (B), 40x objective (C, D).

A.  B. 

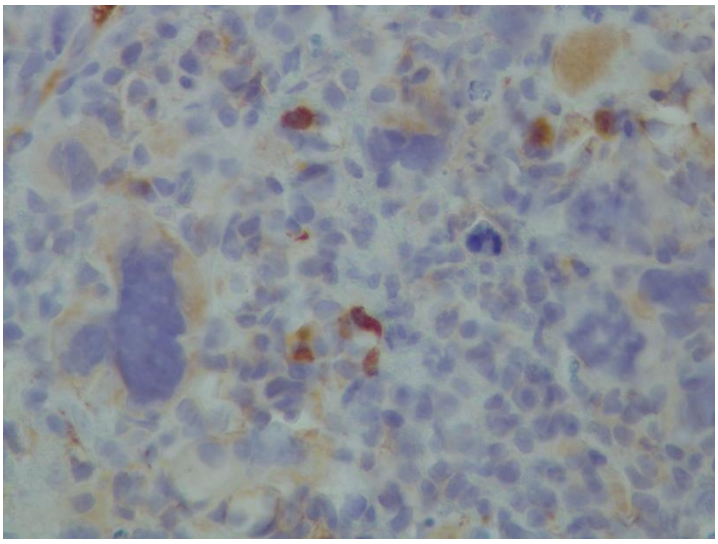
C. 

Figure 9. Immunohistochemistry for CD3 – negative (A), CD20 – negative (B) and CD18 – negative (B) of the prescapular lymph node from a 7 years old, male neutered, Domestic Shorthair cat (10x objective).

Treatment

Treatment with interferon and hydroxyurea was offered. The owner elected not to treat based on the concern that the clinical condition of the patient might deteriorate.

Discussion

Myeloid neoplasms are clonal proliferations of non-lymphoid bone marrow cell lines.[1] These haematological malignancies are subdivided into acute myeloid leukaemia (AML), myeloproliferative neoplasia (MPN) and myelodysplastic syndrome (MDS). In case of both MPN and MDS progression to AML is expected. Myeloid neoplasia can originate from

granulocytic, monocytic, erythrocytic, or megakaryocytic cell lines. Although the proliferation of one type of cells usually predominates, a single cell lineage is rarely affected.[1] A particular form of AML with eosinophilic differentiation (AML-M2-Eos) have been reported in the cat.[2] Myeloid neoplasia in cats is usually associated with FIV and/or FeLV infections.[1,3]

Myeloid sarcoma is a rare solid tumour localised outside of the bone marrow composed of immature granulocytic cells.[4] Typically this disease entity coincides or precedes development of acute myeloid leukaemia.[4] In veterinary patients, myeloid sarcoma has been reported in the dog, cat, cattle, horse and primates.[5,6,7,8,9,10] Its particular eosinophilic subtype was described in the pig and New Zealand White rabbit.[11,12]

Diagnosis of myeloid sarcoma is challenging in both humans and animals. The presumed diagnosis of eosinophilic granulocytic sarcoma was based on cytologic, histologic and immunohistologic characteristics. Distinctive cytologic features included presence of a high number of blast cells with a moderate number of cells exhibiting eosinophilic differentiation. Dysgranulopoiesis, dysmegakaryocytopoiesis and dyserythropoiesis which were also observed in this case are common sequels of myeloid neoplasia in cats.[1,2]

The bone marrow findings fulfilled the diagnostic criteria for AML-M2-Eos:

- presumed myeloblasts accounted for more than 20% of ANCs and for 20 to 89% of NECs,
- more differentiated granulocytic precursors accounted for >10% of NECs,
- there was an increased number of eosinophilic precursors.[1]

Characteristic green discoloration of the mass on gross examination of the biopsy specimen was not observed. Histopathology showed effacement and replacement of the nodal architecture by atypical round cells resembling the abnormal cells in circulation.

The clinical manifestation was not typical for an acute leukaemia – the disease had an insidious onset, the patient was in a good general condition and there was no anaemia or thrombocytopenia. Given the above a disease undergoing blastic transformation was a likely consideration. In this case myeloid sarcoma could be an initial manifestation of an acute leukaemia or could be an early hallmark of transformation of a pre-existing myelodysplastic syndrome or myeloproliferative neoplasia into an acute leukaemia.

Definite diagnosis of myeloid neoplasia and its specific subtype requires determination of the phenotype of the cells by immunochemistry techniques (preferably with a broad panel of antibodies) and detection of distinctive cytochemical features (e.g. positive chloroacetate-esterase staining, alkaline phosphatase).[4] These tests are of restricted usefulness in the cat –

the number of anti-feline or cross-reactive antibodies is limited, e.g. CD34, marker of acute leukaemia is not available in the cat. Flow cytometry and cytochemical staining have not been performed in this case.

In humans myeloid sarcoma is an aggressive condition.[12] Chemotherapy is the recommended treatment.[12] The underlying leukaemia generally has poor prognosis.[12]

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