Skin Lump in a Cat

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Signalment: 12-year-old, male-castrated, house cat had a 5 mm lump in the intact skin of the left side of the thorax.

Specimen: Photomicrographs of two smears of a fine needle aspirate (FNA) of the mass, Giemsa stain.

Question/task:

Evaluate the photographs and make as firm a conclusion/ diagnosis as possible.

The most likely diagnosis is:

1. Atypical mast cell tumor (histiocytic type)
2. Squamous cell carcinoma
3: Amelanotic melanoma
4. Plasma cell tumor
5. Tick bite reaction

Figures

Figure 1 Smear of **a** FNA of the lump stained with Giemsa stain. Original magnification 600X.

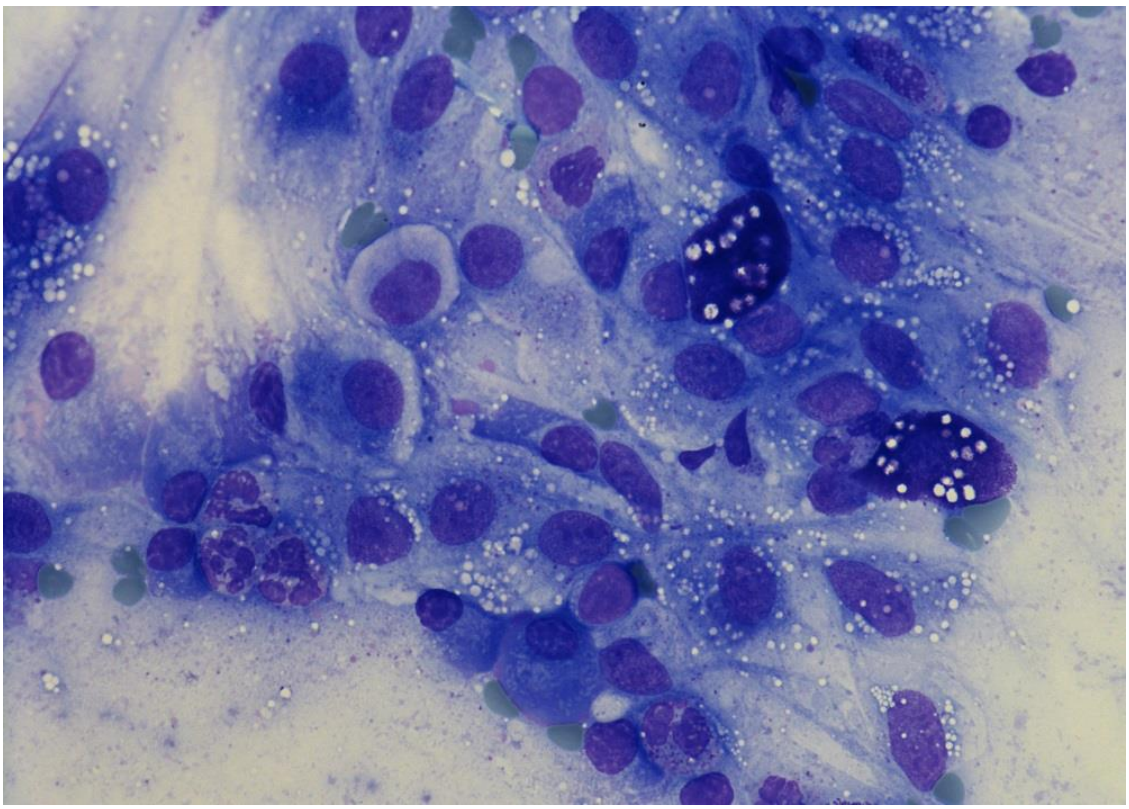


Figure 2 Smear of **a** FNA of the lump stained with Giemsa stain. Original magnification 600X.

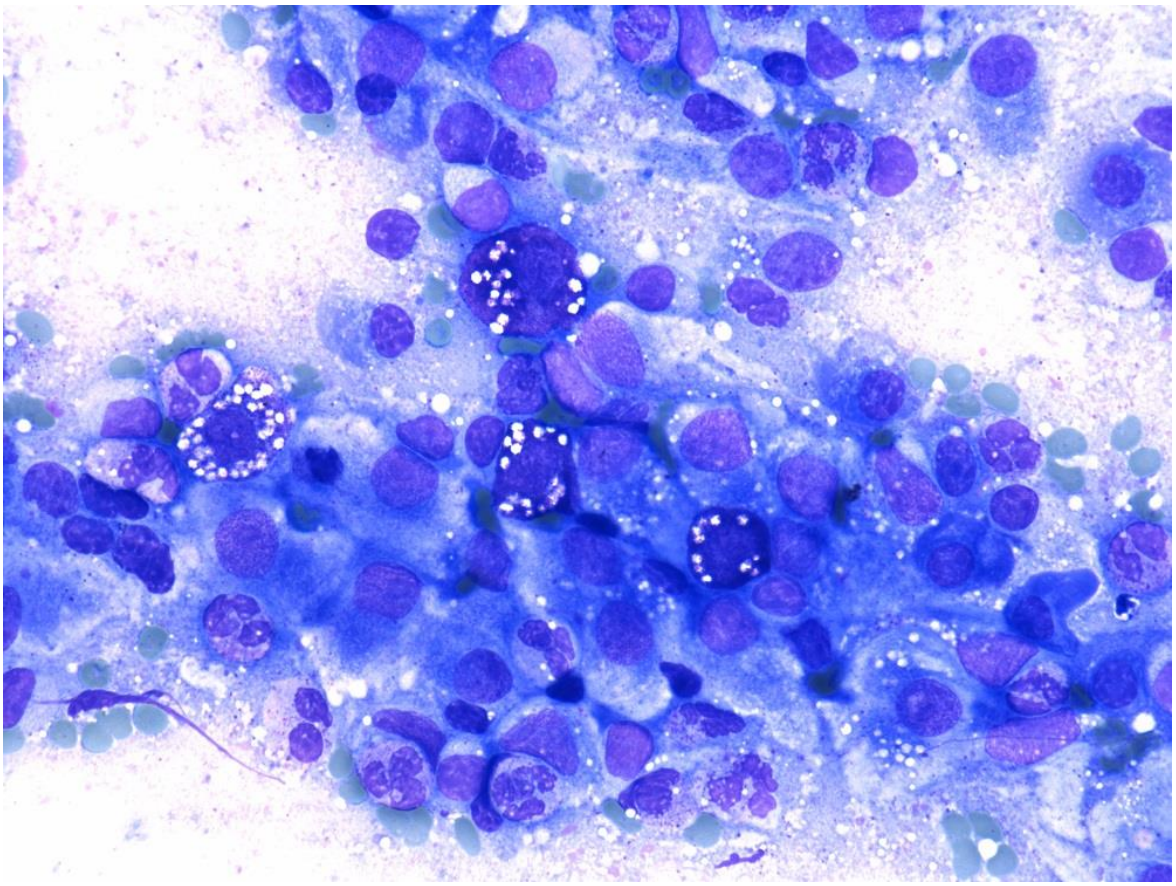
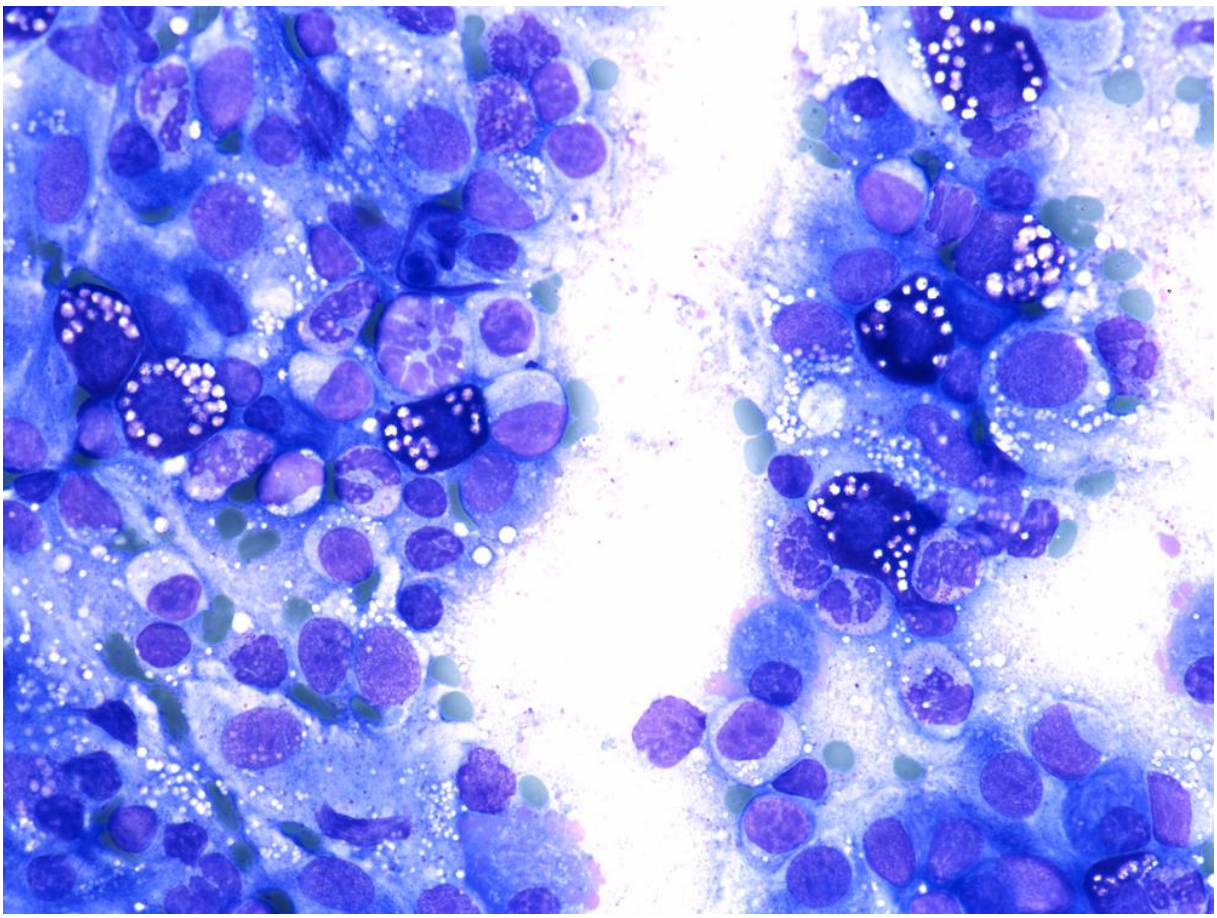


Figure 3 Smear of **a** FNA of the lump stained with Giemsa stain.

Original magnification 600X.



Diagnosis and Discussion:

The cellular reaction was magnificent with very active appearing cells! It is not unreasonable the four diagnoses, returned to the ASVCP list server when this case was presented, were the 4 neoplasms listed in the question for this case. Important to observe is that cellular reaction was mixed and not of one type of cell as expected in a neoplasm. There was a mixture of plasma cells, other lymphoid cells, mast cells with an uncommon feature of a moderate number of clear vacuoles, basophils, and large mononuclear cells with abundant cytoplasm and small vacuoles.

It is the large mononuclear cells which are a very confusing feature of the reaction. They were large, variable, active appearing and not typical of any one cell type. Some were round as expected with macrophages, but some had unusual shapes with small extensions suggesting mesenchymal cells. They had small vacuoles and sometimes granules in the cytoplasm. These were the likely reasons for many who were thinking this was a malignant neoplasm. These were interpreted to mainly be antigen-presenting cells (macrophages) but may include other mesenchymal cells.

Our diagnosis is tick bite reaction. Useful information not included in the case presentation was that that the cat's skin had several scabs and many living ticks (*Ixodes ricinus*) were creeping around the fur. A key feature to note and retain from this case is the role of basophils (Figure 4) in resistance to tick infections.

Basophilia in blood and cytology samples is not rare. Some have commented based on cases we have presented at meetings is there must be something in the water in Sweden that stimulates basophils in our patients. It is more likely that we are effective in recognizing basophils.

Yoshikawa and others wrote a review on the role of basophils in host resistance to tick infestation (2021). It is encouraged that people read their article but their conclusion/summary of their article is as follows.

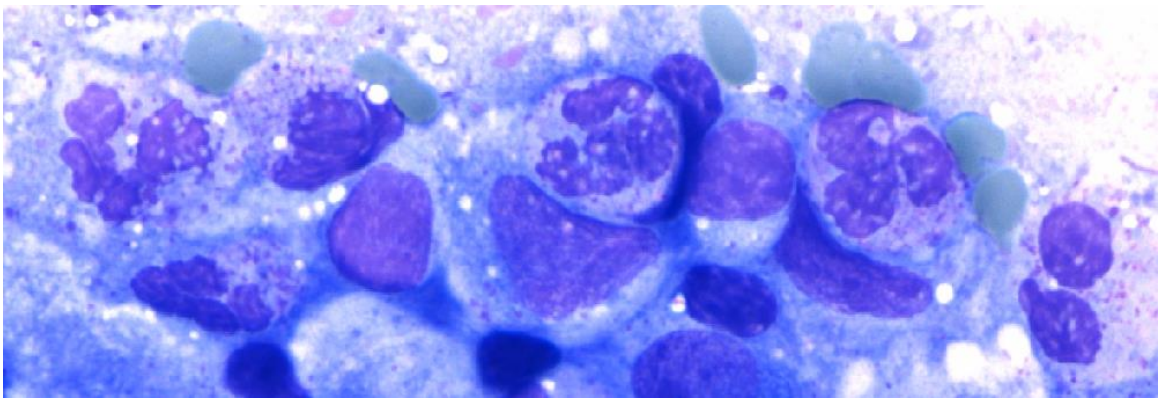
"Accumulating evidence suggests the following stepwise process in the development and manifestation of acquired tick resistance (ATR). During the 1st infestation, antigen-presenting cells (APCs), such as dendritic cells and Langerhans cells, capture tick saliva antigens at tick-feeding sites and then migrate into the draining lymph node. Naïve CD4+ T cells, which can respond to tick antigens presented by APCs, proliferate and develop into type 2 helper T (Th2) cells and follicular helper T (Tfh) cells in the draining lymph node. They help B cells to produce tick antigen-specific IgE antibodies that circulate in the bloodstream and bind to FcεRI on basophils. Some of tick antigen-specific CD4+ effector T cells migrate into the skin throughout the body, and a fraction of them stay in the skin as skin-resident CD4+ memory T cells. Upon re-infestation of ticks, such skin-resident CD4+ memory T cells secrete IL-3, which in turn acts on endothelial cells close to tick-feeding sites and facilitates the transmigration of blood-circulating IgE-armed basophils. Subsequently, skin-infiltrating basophils release histamine upon stimulation with tick antigens and IgE/FcεRI on their surface. Histamine acts on keratinocytes and promotes epidermal hyperplasia at tick-feeding

sites that hampers tick attachment and tick feeding. Several issues remain unanswered, including the role of mast cells in ATR. Further studies on the development and manifestation of ATR are needed to establish effective vaccines against ticks and tick-borne diseases."

What does the vacuolation of the mast cells indicate? A 1983 article described the differentiation of mast cells from a precursor cell, which resembled a large lymphocyte, to the mature cell filled with typical granules. Davidson identified an early stage of development with a vacuolated cell. With time and exposure to fibroblasts, the vacuoles then converted to typical mast cell granules and a concurrent increase in cell content of histamine. This may suggest that the mast cells seen in the cat's lesion were actively developing granules and the histamine needed to respond to ticks. This would indicate an activated mast cell, similar to the other very active appearing cells in the lesion.

Figure 4 Smear of FNA of the lump stained with Giemsa stain. Original magnification 600X.

Note six basophils.



Reference

1. Yoshikawa S, Miyake K, Kamiya A, Karasuyama H. The role of basophils in acquired protective immunity to tick infestation. Parasite Immunology. 2021;43:12804.

2. Davidson S. Mast cell differentiation depends on T cells and granule synthesis on fibroblasts Immunology 1983;48:439