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Case Report

Chronic eosinophilic leukemia in an African hedgehog (*Atelerix albiventris*)

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Abstract

A 5-year-old African hedgehog (*Atelerix albiventris*) was presented to the veterinarian with history of anorexia and progressive weight loss. On clinical examination the mucous membranes were pale, and the skin exhibited extensive alopecia with crusting in all four limbs and tail. A large subcutaneous mass was palpated on the left lateral femur which subsequently was diagnosed histopathologically as a squamous cells carcinoma. The owner declined further tests and the patient returned home where it continued to deteriorate and finally died 90 days after initial presentation. The carcass was submitted for postmortem examination. Necropsy finding included an enlarged spleen with rounded borders and meaty pulp, hyperplastic bone marrow and multiple white foci in both kidneys. Tissues were submitted for cytology, histopathology and electron microscopy. Splenic cytology revealed a monomorphic population of granulocytes with cellular atypia which were most consistent with neoplastic eosinophils. Similar myeloid cells were also seen histologically in kidneys, liver, intestine, heart, skin and brain. The bone marrow was completely effaced with similar cellular infiltrates. Luna stain for eosinophils was positive in all tissues. Electron microscopy showed that neoplastic cells had granules and electron-lucent crystalloid characteristic of eosinophils. Based on these finding chronic eosinophilic leukemia was diagnosed, and to our knowledge, eosinophilic leukemia in hedgehogs is rarely reported in the literature.

Key words: wildlife diseases, neoplasia, eosinophilic leukemia, African hedgehog, *Atelerix albiventris*.

Introduction

Neoplastic diseases comprise 29-51% of all diseases reported in African hedgehogs (*Atelerix albiventris*) worldwide (1, 11, 12). Mammary carcinoma and skin tumors are the most frequent, following by lymphoma in which the gastrointestinal tract is the most common primary site (1, 4, 7). Little has been reported about myeloproliferative disorders in the hedgehog. The aim of this report is to describe the clinical, pathological and ultrastructural findings of chronic eosinophilic leukemia (CEL) in an African pygmy hedgehog, which showed neoplastic proliferation of eosinophils infiltrating different tissues and in peripheral blood. In the absence of a known cause for reactive eosinophilia, CEL and hypereosinophilic syndrome were the main differential diagnosis (9, 13).

Case report

A 5-year old female African pygmy hedgehog was presented to the Ethology and Wildlife Hospital,

Faculty of Veterinary Medicine and Zootechnic, National University of Mexico (UNAM). The patient had a 3-month history of anorexia and progressive weight loss; at the time of presentation, the hedgehog weighed 352 g. On clinical examination, the mucous membranes appeared pale, and the skin exhibited extensive crusting alopecia involving all four limbs and tail. Also, a non-movable ulcerated cutaneous mass (1.1 x 1.2 cm) was noted in the right lateral femoral region and another small nodule (0.1 cm) in the right lateral upper lip. An incisional biopsy taken from the femoral mass was diagnosed as squamous cell carcinoma. The owner declined further laboratory tests, and the patient went back home.

The hedgehog deteriorated for the following 13 weeks and finally died 90 days after initial presentation. The carcass was submitted for postmortem examination to the Department of Veterinary Pathology, UNAM. On necropsy, the hedgehog was in poor body condition, and internally, the spleen appeared notably enlarged (3x) with rounded margins and a red meaty texture on cut surface. Both kidneys had multiple, small (1 mm) pale yellow foci scattered throughout the renal cortex. Impressions smears were taken from the splenic pulp for cytological examination, and small sections (1 to 2 mm^3) of spleen were fixed in 2.5% glutaraldehyde for ultrastructural studies. Samples of lungs, heart, kidneys, liver, bone marrow spleen, intestine, skin and brain, were fixed in 10% formalin for histopathological examination.

Cytological examination of the splenic pulp revealed numerous round cells with abundant cytoplasm filled with eosinophilic granules. The nuclei of these cells were moderately pleomorphic and frequently displayed lobulated or reniform shape (Fig. 1). Based on cytological morphology, these cells were considered to be eosinophils with cellular atypia.

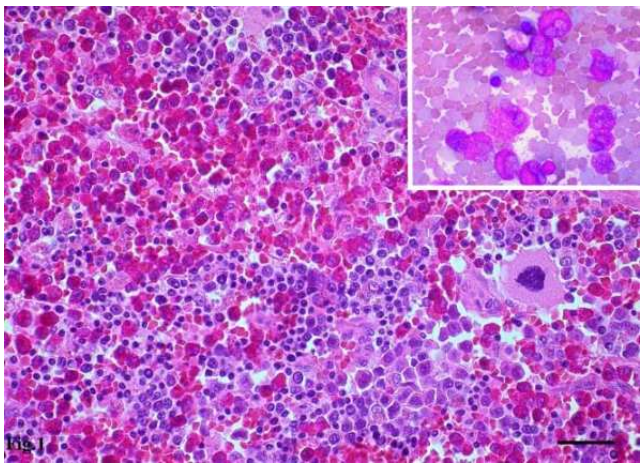


Figure 1. Cytological imprint taken from the spleen. Note round granulated cells with scant cytoplasm and abundant eosinophilic granules. There is a predominance of bands and segmented eosinophils. Romanowsky staining. Bar = 60 µm.

Microscopically, the splenic architecture was effaced and replaced by a homogeneous population of neoplastic cells. These cells were characterized by abundant eosinophilic cytoplasm containing numerous granules and by having pleomorphic nuclei with a finely stippled chromatin pattern. There was moderate anisokaryosis and anisocytosis with occasional binucleation. These morphological features were consistent with malignant eosinophils. Mitotic activity was low (0-1 mitotic figures per high power field), and these cells were positive for Luna stain which is specific for eosinophils (3). Scattered in the hypercellular splenic parenchyma there were also multiple megakaryocytes, a finding that was interpreted as extramedullary hematopoiesis.

Histologically, the bone marrow was markedly hypercellular with 90% cells and 10% adipose tissue. Practically all marrow had been replaced by neoplastic cells that had identical morphology to those previously described in the spleen**.** Similar neoplastic infiltrates were expanding the lamina propria of the small intestine and the renal interstitium, replacing most of the normal cells in the lymph nodes and expanding the hepatic sinusoids. Large numbers of neoplastic cells were present in the lumen of blood vessels of all the tissues already described, as well as in the vasculature of the skin, heart, meninges and brain (Fig. 2). Luna staining for eosinophils was also strongly positive. In addition to the tumoral infiltrates, the skin also had numerous follicular cysts and exhibited diffuse epidermal hyperplasia characterized by acanthosis and orthokeratotic hyperkeratosis.

Ultrastructurally, neoplastic cells had electron-dense cytoplasmic granules, some of which contained conspicuous electron-lucent cylindrical crystals (Fig. 3). Electronic microscopy also revealed that neoplastic cells often had lobulated or multinucleated nuclei. Based on cytological, histological, and ultrastructural findings, the final diagnosis for this hedgehog was chronic eosinophilic leukemia.

Discussion

The term myeloproliferative disease is commonly used in veterinary medicine to describe myeloid neoplastic diseases that originate in the bone marrow or extramedullary sites such as the spleen and liver but excludes lymphoma and lymphoid leukemia which are separately grouped under lymphoproliferative diseases (13). The microscopic findings in this hedgehog fit well with the criteria for a myeloproliferative disorder and unmistakably excludes lymphoma. Myeloid leukemias are divided based on cell morphology and biological behavior in two main types: acute myeloid leukemias in which cells are poorly differentiated and have aggressive behavior, and chronic myeloid leukemias in which cells are well-differentiated and exhibit a less aggressive behavior. Clearly, the myeloid cells in this hedgehog were well-

differentiated eosinophils, thus meeting the criteria for a chronic eosinophilic leukemia (5, 9-13).

The cytological and pathological changes observed in the spleen, bone marrow and other organs of this hedgehog were comparable to those described for chronic eosinophilic leukemia in cats and dogs (8), and to a case recently reported in a hedgehog (5). Cytologically and microscopically, the neoplastic cells in the hedgehog were characteristic for eosinophils, and electron microscopy confirmed the presence of electron-dense crystalloids which are typically seen in eosinophils, but not in other types of leukocytes (3, 6, 10).

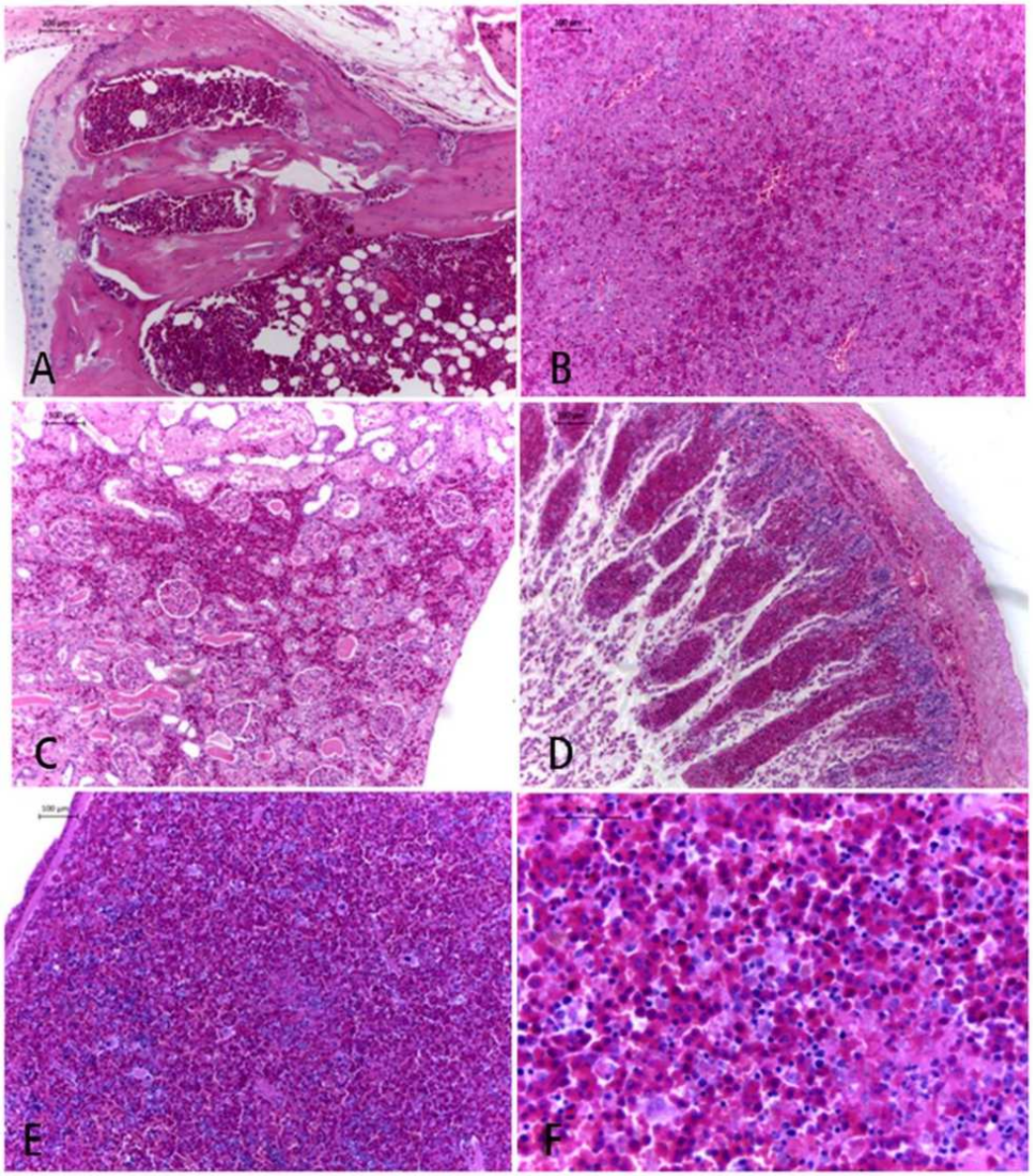


Figure 2. A) Neoplastic proliferation of eosinophils is effacing and replacing the bone marrow. B) Infiltration of eosinophils in hepatic sinusoids. C) Eosinophilic infiltrates expanding the renal interstitium. D) Thickening of intestinal villi caused by diffuse infiltration of neoplastic cells in the lamina propria. E) Extensive infiltration of neoplastic cells is effacing the normal splenic architecture. F) Neoplastic eosinophils characterized by a densely granulated cytoplasm. (H&E Bar = 100 µm).

The main differential diagnoses for chronic eosinophilic leukemia, particularly in cats, are hypereosinophilic syndrome and reactive eosinophilia (9, 13). Hypereosinophilic syndrome is characterized by peripheral eosinophilia and eosinophil infiltrates in multiple organs; the diagnosis of this syndrome is made by exclusion, that is, an absence of true neoplasia and lack of a primary underlying reason for eosinophilia such as allergy and parasitic diseases (2, 14). The cause of the hypereosinophilic syndrome is poorly understood but seems to be related to cytokine dysregulation that disrupt production, migration, and survival of eosinophils (2, 9, 14).

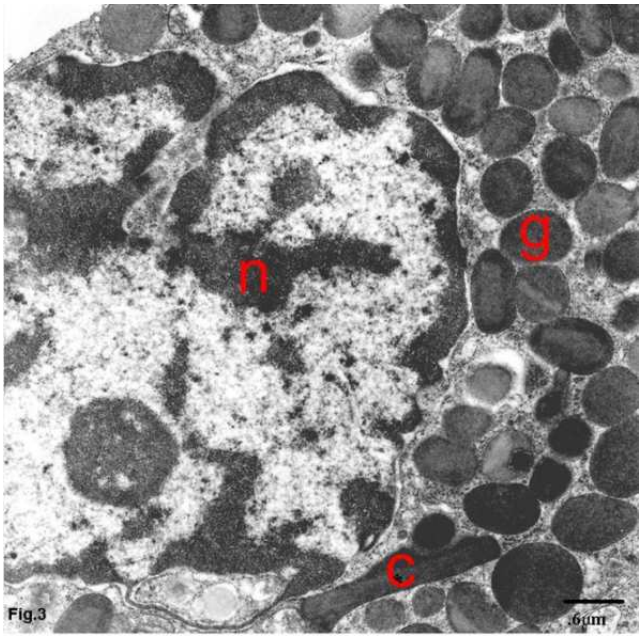


Figure 3. Spleen. Ultrastructural view of a neoplastic eosinophil. Note a reniform nucleus (n), numerous electron-dense granules (g) and cylindrical electron-lucent crystal (c) in the cytoplasm. Transmission electron microscopy (TEM); uranyl acetate and lead citrate 12000x. Bar = 6 µm.

In clinical pathology, there are several guidelines to steer the diagnosis CEL; usually the total leukocyte count is 75 to 155 $x10^9$ /L and patients exhibit marked thrombocytopenia and anemia; in hypereosinophilic syndrome, however, the cell count usually does not exceed 75 $x10^9$ /L (14, 15). The erythroid myeloid ratio in patients with chronic eosinophilic leukemia is usually greater than 10:1 (eosinophilic hyperplasia), which contrasts with the hypereosinophilic syndrome where the ratio is smaller (8, 9). It was unfortunate that no hematologic tests were made in the hedgehog. However, the widespread replacement of hematopoietic tissue with immature eosinophils along with the massive infiltration of eosinophils in virtually all organs and the unequivocal identification of eosinophils by electron microscopy clearly supported the diagnostic of chronic eosinophilic leukemia.

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