Disseminated histoplasmosis in an African pygmy hedgehog

Timothy A. Snider, dvm, PhD, dacvp; Priscilla H. Joyner, bvms; Kenneth D. Clinkenbeard, PhD, dvm

Case Description—A 2-year-old captive-bred sexually intact female African pygmy hedgehog (Atelerix albiventris) was evaluated because of vague signs of illness including inappetence, weakness, lethargy, and weight loss over a 20-day period.

Clinical Findings—Abnormalities detected via initial clinicopathologic analyses included anemia, thrombocytopenia, leukopenia, hypoproteinemia, and hypoglycemia. Results of a fecal flotation test were negative. Three weeks after the initial evaluation, splenomegaly was detected via palpation and ultrasonography.

Treatment and Outcome—The hedgehog was treated with broad-spectrum antibacterial agents, resulting in an initially favorable response. Fenbendazole was also administered against possible occult parasitic infestation. After 3 weeks of illness, the hedgehog’s condition had worsened and supportive care and administration of additional antibacterial agents were instituted. The hedgehog died, and pathologic examinations revealed severe splenomegaly; granulomatous infiltrates were evident in multiple organs, and Histoplasma capsulatum yeasts were detected intralesionally.

Clinical Relevance—Histoplasmosis can develop in a wide range of mammalian species. African pygmy hedgehogs are becoming increasingly popular as exotic pets, and vague signs of illness and splenomegaly are often attributed to hemolympathic malignancies, which are somewhat common in this species. Practitioners should be aware that similar clinical signs may be associated with histoplasmosis in these animals. Although the hedgehog of this report was confined indoors, it originated from an area where histoplasmosis was endemic; this indicates that the disease should be included as a differential diagnosis for hedgehogs that develop vague signs of illness and are known to originate from such geographic regions. (J Am Vet Med Assoc 2008;232:74–76)

A 2-year-old 0.42-kg (0.92-lb) captive-bred sexually intact female African pygmy hedgehog (Atelerix albiventris) with a 4-day history of inappetence, weakness, and lethargy was evaluated at the Oklahoma State University Boren Veterinary Medical Teaching Hospital. The only notable physical examination finding was poor body condition. A limited diagnostic investigation including a CBC, assessment of serum glucose concentration, and fecal analysis was performed. Hematologic abnormalities included moderate anemia (Hct, 23%; reference range, 28% to 38%), thrombocytopenia (38 × 10³ platelets/µL; reference range, 241 to 880 × 10³ platelets/µL) with megakaryocytes, leukopenia that involved all leukocyte subsets (4.0 × 10³ WBCs/µL; reference range, 5.8 to 21.0 × 10³ WBCs/µL), hypoproteinemia (4.2 g/dL; reference range, 3.3 to 3.6 g/dL), and hypoglycemia (34 mg/dL; reference range, 81.5 to 116.1 mg/dL). Results of a fecal flotation test were negative. Lacking a definitive diagnosis, the hedgehog was treated for occult parasitic infestation and possible bacterial infections. Treatment consisted of a single dose of fenbendazole (25 mg/kg [11.4 mg/lb], PO) and administration of trimethoprim-sulfamethoxazole (30 mg/kg [13.6 mg/lb], PO, q 24 h) for 1 week.

The owner’s perception was that the hedgehog’s condition worsened initially, but improved during the next week. At an examination 1 week later, the condition of the hedgehog was clinically improving. Eight days following the recheck evaluation, the hedgehog was examined again because of inappetence, weakness, and lethargy accompanied by low body temperature. At this time, physical examination revealed a palpably large spleen, which was confirmed via ultrasonography. The hedgehog was hospitalized and treated with enrofloxacin (10 mg/kg [4.5 mg/lb], SC, q 24 h) and supportive care that included warming and fluid therapy. The hedgehog died the following day.

At gross necropsy examination, the hedgehog was thin with little internal adipose tissue and had generalized pallor. The spleen was markedly large (7 to 10 times as large as the size expected of a clinically normal hedgehog) and weighed 10 g (0.022 lb; 2.4% of body weight). By comparison, the spleen in cats is approximately 0.3% of the total body weight and ranges from 0.12% to 0.2% of body weight in other domestic animals. The hedgehog’s spleen was red and meaty and bulged from the capsule on sectioning. Mild hepatomegaly was also detected.

Specimens of liver, kidneys, spleen, heart, lungs, small intestine, stomach, and uterus were immersion fixed in neutral-buffered 10% formalin, routinely processed, embedded in paraffin, sectioned at 5-µm intervals, stained with H&E stain, and examined via light microscopy. The
architecture of the spleen (the most severely affected organ) was effaced by sheets of epithelioid macrophages interspersed with lymphocytes, plasma cells, megakaryocytes, and rare multinucleated giant cells. Erythrophagocytosis and intrahistiocytic hemosiderin deposition were prominent features (Figure 1). Yeast organisms were detected in splenic macrophages and multinucleated giant cells on H&E-stained sections; these organisms were highlighted by use of periodic acid–Schiff and Gomori’s methenamine silver stains on other sections of spleen (Figure 2). Host cells contained 2 to as many as approximately 30 organisms that had a basophilic nucleus and were surrounded by a nonstaining, clear, thin halo. Narrow-based budding of the yeasts was observed. Their morphology was diagnostic of *Histoplasma capsulatum* var *capsulatum*; specifically, the yeast diameter was sufficient to differentiate *H capsulatum* var *capsulatum* from the larger *H capsulatum* var *duboisii*.\(^3,4\)

The liver, kidneys, small intestine, and lungs were multifocally affected by a similar granulomatous infiltrate and contained similar numbers of yeasts (Figure 3). Yeasts were also evident in macrophages within the myocardial interstitium and the gastric and enteric laminae propriae. *Histoplasma capsulatum* yeasts were also seen within cells of monocyte lineage within intravascular blood in these sections, indicating that diagnosis via hematologic examination may have been possible.

**Discussion**

To the authors’ knowledge, this is the first reported case of histoplasmosis in an African pygmy hedgehog. Histoplasmosis is an infectious, noncontagious, systemic mycotic disease caused by *H capsulatum* var *capsulatum*. Although the disease has a worldwide distribution, histoplasmosis is endemic in the Americas, particularly in the Mississippi and associated river valleys of North America.\(^3,5,7\) Histoplasmosis in humans, dogs, cats, horses, pigs, and cattle has been reported.\(^6,8\) Zoonotic, exotic, and small mammal pet species affected with histoplasmosis include domestic rodents, skunks, woodchucks, raccoons, baboons, Kodiak bears, badgers, red and gray foxes,\(^9\) llamas,\(^9\) rabbits,\(^10\) chinchillas,\(^11\) owl monkeys,\(^12\) rhesus monkeys,\(^1,13\) Atlantic bottlenose dolphins,\(^14\) sea otters,\(^15\) harp seals,\(^16\) marine iguanas,\(^1,6\) and Fennec foxes.\(^18\)

The body of literature relating to medicine and surgery for African pygmy hedgehogs is limited, but it is known that neoplasia is common in this species.\(^1\) There have been reports of splenic extramedullary hematopoiesis\(^19\) and hemolymphatic malignancies involving the spleen,\(^20,21\) both of which result in splenomegaly, in these hedgehogs. On the basis of the reported information and the principal gross finding of marked splenomegaly, a provisional diagnosis of neoplasia was initially made for the hedgehog of this report. However, detection of *H capsulatum* yeasts in multiple tissues provided the basis for the final diagnosis of disseminated histoplasmosis. Therefore, disseminated histoplasmosis should be considered a differential diagnosis for splenomegaly and other vague signs of illness in African pygmy hedgehogs.
Histoplasmosis results from inhalation of microconidia and mycelial fragments of the saprophytic soil fungus *Ajello- nyces capsulatum*, a teleomorphic of *H capsulatum* var *capsula- turem*. Conversion of the inhaled microconidia to yeast at body temperature results in pulmonary infection.1-5 This pulmonary phase may not be initially detected, but rapid dissemination to lymphoid tissues and the liver usually follows. This pathogenesis is typical of the disease in cats.6 Disseminated histoplasmosis in cats is accompanied by anemia, lethargy, weight loss, anorexia,6 leukopenia, thrombocytopenia, and hypoproteinemia;7 these signs are similar to those that developed in the affected hedgehog of this report. Clinical diagnosis is made via cytologic or histologic identification of *Histoplasma* yeasts in affected tissues;8 examination of Buffy coat smears, rectal mucosa specimens, and bone marrow samples is particularly useful.3,8 Buffy coat smears and rectal mucosa specimens were not acquired from the hedgehog of this report; among small exotic mammals,1 antemortem collection of bone marrow samples has been limited to chinchillas, and feasibility of the procedure in hedgehogs is unknown. Immunodiagnostic tests are available, but anti-*H capsulatum* antibody detection is considered unreliable. An *H capsulatum* antigen detection test has been widely and reliably used in humans, and although it may be useful in veterinary species, it has not been validated in other animals.3 Dogs and cats with histoplasmosis are usually treated with itraconazole;8 however, there is limited information on the use of this drug in hedgehogs.

The features of this case raise an interesting question regarding transmission of histoplasmosis to indoor pets that lack an opportunity for typical exposure to the environmental teleomorph of *Histoplasma*. Husbandry of many exotic pet species such as hedgehogs is, with rare exceptions, an indoor pursuit. Transmission of the fungal agent to animals that are kept outdoors is believed to result from exposure to dusts from *Histoplasma*-contaminated areas, particularly those contaminated with bird feces or bat guano.3,6-8 Although the history for the hedgehog of this report did not include typical outdoor exposures, the intermixing of indoor air with outdoor air that contained dust particles laden with *Histoplasma* mycelia is considered the most likely source of infective material. Indeed, the pet was housed in an area of Oklahoma that is positioned on the western fringe of a region where histoplasmosis is endemic.3 Alternatively, the pine wood shavings used as bedding could have been contaminated. Unfortunately, the remaining bedding was unavailable for culture techniques, and a comprehensive analysis of residential air quality was not feasible. Therefore, the role of the bedding in this case is not known. Although bedding material or the immediate environment has been previously incriminated in reports11,18 of histoplasmosis among animals, often the source of exposure cannot be specifically identified.

Histoplasmosis appears to be a successful pathogen of most Eutherian mammalian orders. However, to the authors’ knowledge, the present report represents the first description of the disease in a representative of the order Insectivora and perhaps might indicate that other insectivores, such as moles and shrews, could also be susceptible. More importantly, this case report suggests that histoplasmosis should be a differential diagnosis for vague signs of illness in African pygmy hedgehogs and, perhaps, should be considered in the diagnostic investigation of illnesses in other increasingly popular, indoor small mammal pet species such as sugar gliders, degus, and prairie dogs, despite the fact that histoplasmosis in those species has not been reported. Histoplasmosis is classified as a zoonosis but is best considered a saprozoososis, a disease in which a non-natural reservoir (eg, soil) is involved. Direct animal-to-human transmission is not believed to happen;2 contamination has been identified only under exceptional circumstances, such as handling laboratory culture specimens or performing a necropsy.6 Zoonotic pathogens reportedly transmitted from African pygmy hedgehogs to humans include pathogenic dermatomycetes and *Salmonella* spp.23

References