

Pathology In Practice

In cooperation with

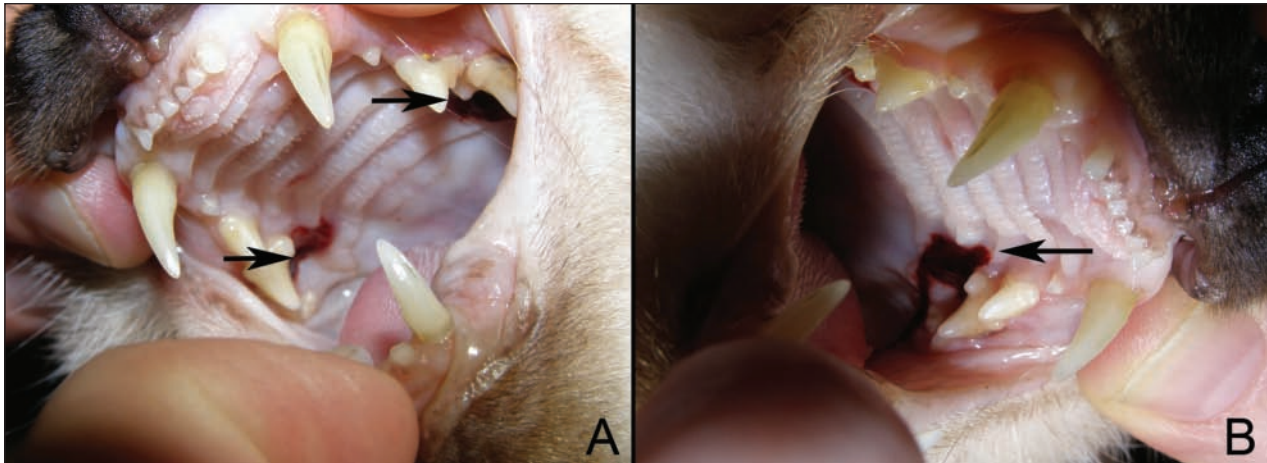


Figure 1—Photographs of a focal, dark red, ulcerated area (arrows) along the gingiva caudal to the last molar that extends onto the palate on both the right (A) and left (B) sides of the mouth of a cat that was evaluated because of intermittent fever and weight loss (despite a good appetite) of 1 month's duration.

History

A 10-year-old spayed female domestic shorthair cat was referred to the Center for Veterinary Health Sciences at Oklahoma State University because of intermittent fever and weight loss (despite a good appetite) of 1 month's duration. Physical examination by the referring veterinarian revealed a high rectal temperature (39.8°C [103.6°F]) and thin body condition. At the time of referral, results of FeLV antigen and anti-FIV antibody tests^a were negative and the cat's serum total thyroxine concentration was 1.3 ng/mL (reference interval, 0.8 to 3.8 ng/mL).

This report was submitted by Catherine G. Lamm, DVM, DACVP; Theresa E. Rizzi, DVM, DACVP; Gregory A. Campbell, DVM, PhD, DACVP; and Jill D. Brunker, DVM, DACVIM; from the Oklahoma Animal Disease Diagnostic Laboratory (Lamm, Campbell) and the Departments of Veterinary Pathobiology (Rizzi) and Veterinary Clinical Sciences (Brunker), Center for Veterinary Health Sciences, Oklahoma State University, Stillwater, OK 74078.

The authors thank Drs. Robin Allison, Mary Bowles, Melanie Breshears, James Meinkoth, Grant Rezabek, and Kuldeep Singh for assistance. Address correspondence to Dr. Lamm.

Clinical and Gross Findings

Abnormal physical examination findings included a body condition score of 3 (scale of 1 to 9), dull coat, rectal temperature of 39.7°C (103.4°F), and pale pink mucous membranes. The cat was quiet and alert; it weighed 2.1 kg (4.6 lb). On auscultation, the heart and lung sounds were considered normal; heart rate was 192 beats/min, and respiratory rate was 48 breaths/min. On palpation, the submandibular lymph nodes appeared mildly large. Examination of the oral cavity revealed a focal, dark red, ulcerated area along the gingiva caudal to the last molar and extending onto the palate on both sides of the mouth (Figure 1). Results of a CBC and serum biochemical analyses were within reference limits, except for high total bilirubin concentration (0.8 mg/dL; reference interval, 0.1 to 0.4 mg/dL) and low albumin concentration (2.3 g/dL; reference interval, 2.5 to 3.9 g/dL). Urinalysis revealed bilirubinuria (2+). Thoracic and abdominal radiography, along with abdominal ultrasonography, revealed no obvious abnormalities.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

Histopathologic and Cytopathologic Findings

Gastroduodenoscopy was performed, and biopsy specimens were collected from several areas of the stomach and small intestine. The samples were immersion-fixed in 10% formalin, routinely processed, and stained with H&E stain. Histologic examination of tissue sections of the small intestine revealed that the lamina propria was expanded by sheets of macrophages, lymphocytes, and plasma cells (Figure 2). Within the cytoplasm of macrophages, there were numerous yeast organisms (2 to 5 μm in diameter) surrounded by clear haloes. Mild villus blunting was evident. Examination of sections of stomach tissue revealed no abnormalities.

Scrapings were obtained from both oral lesions for cytologic evaluation. The prepared slides were routinely stained with a modified Wright-Giemsa stain. Cyto-

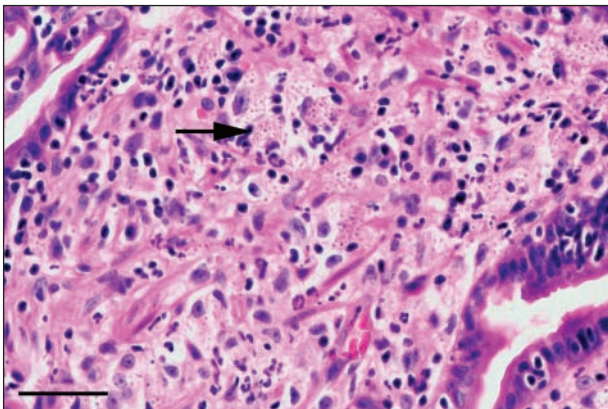


Figure 2—Photomicrograph of a section of tissue obtained from the small intestine of the cat in Figure 1. Intrahistiocytic yeast organisms (arrow) are evident in the intestinal tissue. The yeast organisms are 2 to 5 μm in diameter; in Gomori methenamine silver-stained sections, narrow-based budding of the yeast was evident (image not shown). H&E stain; bar = 50 μm .

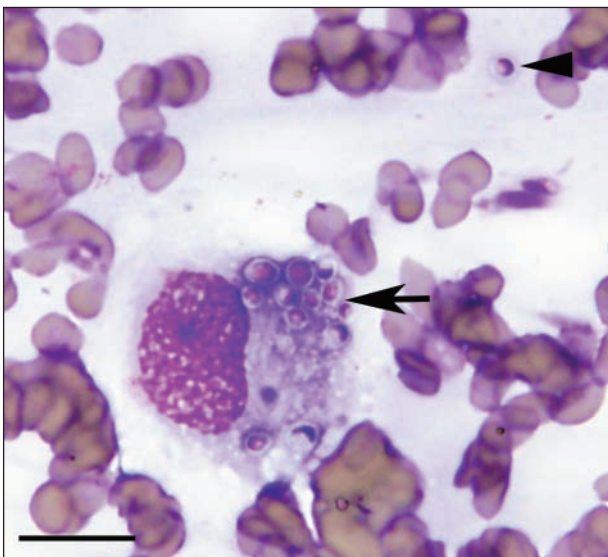


Figure 3—Photomicrograph of material scraped from a lesion in the oral cavity of the cat in Figure 1. Notice the numerous 2- to 5- μm -diameter yeast organisms within the cytoplasm of a macrophage (arrow) and located extracellularly (arrowhead). Modified Wright-Giemsa stain; bar = 20 μm .

logic examination revealed pyogranulomatous inflammation and numerous intracellular and extracellular yeast organisms. The organisms were round (2 to 5 μm in diameter) and surrounded by a nonstaining capsule (Figure 3).

Morphologic Diagnosis

Pyogranulomatous gingival inflammation with intracytoplasmic yeast organisms (consistent with *Histoplasma capsulatum*) and marked, diffuse lymphoplasmacytic and histiocytic enteritis with intrahistiocytic yeast organisms (also consistent with *H capsulatum*).

Comments

Stomatitis and ulceration of the oral cavity in cats may be associated with a wide variety of causes, including metabolic, infectious, immune-mediated, and nutritional diseases; trauma; and foreign bodies.¹⁻³ Immune-mediated diseases include eosinophilic granuloma complex and lymphoplasmacytic stomatitis. Infectious causes of stomatitis in cats include viral (calicivirus, herpesvirus, FeLV, and FIV), bacterial, and fungal infections.^{1,2,4-6} Ulceration of the oral cavity may develop over areas of neoplastic proliferation, such as squamous cell carcinoma, lymphoma, and mast cell tumor.

Cytologic or histologic examination of specimens collected from oral cavity lesions in cats is typically required for definitive diagnosis. Fungal infections within the oral cavity may appear as mass-like lesions or ulcerations. Fungal infections typically induce a pyogranulomatous response, which is detectable via cytologic or histologic examination. If yeast or fungal hyphae are evident, their morphologic features can often be used to definitively identify the infective organism. In some instances, it is necessary to use special stains for fungal organisms or perform mycologic cultures to determine the cause of the inflammation. In the cat of this report, the morphology of the yeast organisms was consistent with the diagnosis of *H capsulatum* infection.

Histoplasma capsulatum infections typically develop via inhalation or ingestion, and most infected animals clear the infection without developing clinical signs of disease.⁷ Cats with histoplasmosis commonly develop respiratory tract signs, such as dyspnea, but can also develop nonspecific signs, such as weight loss and lethargy.⁸ Macrophages are the predominant inflammatory cells in the response to infection with *H capsulatum* and rapidly phagocytose the organism. In dogs and cats, yeast-laden macrophages are able to distribute *H capsulatum* to other organ systems, resulting in dissemination of the organism to visceral organs as well as to the bone marrow and eyes.⁹ *Histoplasma capsulatum* infection can also result in localized lesions within the skin in dogs and cats.⁸

The cat of this report was unusual because the main lesion associated with *H capsulatum* infection was ulceration of the oral cavity; intestinal tract involvement was also present. A review of recent cases of *H capsulatum* infection at our hospital revealed that several cats had these uncommon clinical signs, including focal or multifocal exophytic or ulcerative lesions within the oral cavity. At our hospital, records indicated that oral histoplas-

mosis was diagnosed on the basis of cytologic findings in 3 cats and on the basis of histopathologic findings in 4 cats between August 2005 and December 2007. In our experience, these lesions are typically restricted to the oral cavity and systemic involvement is not apparent.

For cats with histoplasmosis, treatment involves long-term oral administration of antifungal agents such as itraconazole.⁹ The cat of this report was treated with itraconazole (12 mg/kg [5.45 mg/lb], PO, q 24 h). One month following treatment initiation, the cat had not gained weight despite a good appetite. The referring veterinarian reported that the results of a CBC and serum biochemical analyses were within reference ranges, with the exception of mildly low serum albumin concentration (2.1 g/dL; reference interval, 2.2 to 4.4 g/dL). The referring veterinarian did not comment on the status of the oral lesions at that time. During a follow-up conversation 1 year after diagnosis, the referring veterinarian reported that the cat had died. The owner did not permit postmortem examination of the pet, and the extent of *H capsulatum* infection, if any, at the time of death was not determined. As this case illustrates, practitioners within areas in which *H capsulatum* is endemic (central and south central United States) should include infection with this organism as a differential diagnosis for ulcers in the oral cavities of cats.

-
- a. SNAP FIV/FeLV combo test, IDEXX Laboratories, Westbrook, Me.
-

References

1. Lyon KF. Gingivostomatitis. *Vet Clin North Am Small Anim Pract* 2005;35:891–911.
2. Brown CC, Baker DC, Barker IK. Alimentary system. In: Maxi MG, ed. *Pathology of domestic animals*. 5th ed. Edinburgh: Saunders Elsevier, 2007;16–19.
3. Baird K. Lymphoplasmacytic gingivitis in a cat. *Can Vet J* 2005;46:530–532.
4. Pesavento PA, MacLachlan NJ, Dillard-Telm L, et al. Pathologic, immunohistochemical, and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. *Vet Pathol* 2004;41:257–263.
5. Hargis AM, Ginn PE. Feline herpesvirus 1-associated facial and nasal dermatitis and stomatitis in domestic cats. *Vet Clin North Am Small Anim Pract* 1999;29:1281–1290.
6. Diehl K, Rosychuk RA. Feline gingivitis-stomatitis-pharyngitis. *Vet Clin North Am Small Anim Pract* 1993;23:139–153.
7. Valli VEO. Hematopoietic system. In: Maxi MG, ed. *Pathology of domestic animals*. 5th ed. Edinburgh: Saunders Elsevier, 2008;299–301.
8. Taboada J, Grooters AM. Systemic mycosis. In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine*. 6th ed. St Louis: Elsevier Saunders Co, 2005;671–690.
9. Bromel C, Sykes JE. Histoplasmosis in dogs and cats. *Clin Tech Small Anim Pract* 2005;20:227–232.