

Pathology In Practice

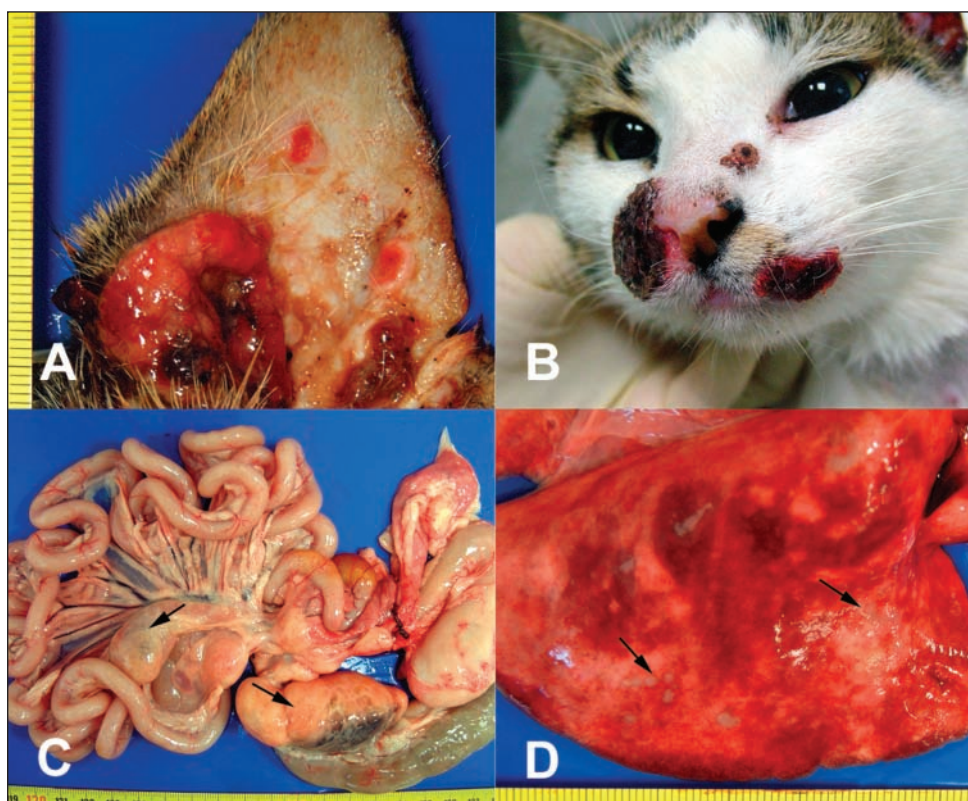


Figure 1—Photographs of the lesions detected before and after necropsy of a cat that had a dermatologic condition that affected the entire body. A—Concave (inner) aspect of the right pinna. Notice the nodular ulcerative lesions with purulent discharge. B—Head. Nodular, ulcerative, crusting lesions are present on the muzzle and nose. C—Stomach, intestines, and mesenteric lymph nodes. The mesenteric lymph nodes are markedly large (arrows). D—Right lung. Multifocal to coalescing, whitish, subpleural nodules throughout the lung tissue (arrows). Scales in panels A, C, and D represent 4.4, 19, and 6.9 cm, respectively.

History

A 2-year-old sexually intact female European shorthair cat that had been rescued by an animal welfare center was evaluated because of a dermatologic condition that affected the entire body. No further information about the cat was available.

Clinical and Gross Findings

Dermatologic examination revealed a proliferative fleshy growth (approx 2 cm in diameter) with bloody discharge in the right inner pinna (Figure 1). There were 2 erosive-ulcerative lesions covered by a thick hemorrhagic crust on the right

side of the muzzle near the nose and on the left superior lip. The lesion on the side of the muzzle was approximately 3 cm in diameter, and the dimensions of the lesion on the lip were approximately 2 × 1 cm. On the dorsal aspect of the muzzle, there was a large (approx 1-cm-diameter) papule that was covered by a serosanguineous crust. Papules of variable size were present in the skin all over the body. Some of these lesions were ulcerated and had a hard core and purulent discharge. No other clinical abnormalities were observed.

A CBC and serum biochemical analyses revealed no abnormalities. Serum was analyzed to detect FeLV antigen, anti-FIV antibody, and IgG and IgM against *Toxoplasma* spp, and results were negative. Radiographic examination of the thorax revealed a miliary pattern in both lungs. Euthanasia was performed because of the cat's poor prognosis. At necropsy, in addition to the aforementioned skin lesions, the most striking changes were markedly large mesenteric lymph nodes (6.5 cm in length) and the presence of multifocal to coalescing, whitish, subpleural pulmonary nodules (approx 3 mm to 1 cm in diameter). The nodules contained a grayish, turbid, viscous exudate.

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

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Histopathological and Microbiological Findings

Antemortem cytologic examination of several cutaneous lesions revealed the presence of yeast-like organisms. Following euthanasia, samples of skin, nasal cavity, trachea, lungs, heart, gastrointestinal tract (ie, oral cavity, esophagus, stomach, small and large intestines, and mesenteric lymph nodes), liver, pancreas, adrenal glands, kidneys, and spleen were routinely processed and stained with H&E, periodic acid-Schiff, or Grocott methenamine-silver nitrate stain for histologic examination. Immunohistochemical analysis was performed by use of the avidin-biotin-peroxidase complex technique and anti-*Cryptococcus neoformans*,^a anti-CD3,^b anti-CD79,^b anti-major histocompatibility complex (MHC) II,^b and anti- λ ^b and anti- κ ^b light chain antibodies.

Histologically, numerous, spherical, pale-centered, thin-walled periodic acid-Schiff- and Grocott methenamine-silver nitrate-stained yeasts (8 to 12 μ m in diameter) that had mucous capsules were detected in the skin of the ear and muzzle and in mesenteric lymph nodes (Figure 2). Similar yeasts were also observed in several foci in the medulla of the right kidney. Multiple granulomatous lesions were present in alveolar spaces of the lungs in association with adult and larval nematodes (detected in cross section) that were compatible with *Aelurostrongylus abstrusus*. The parasites were surrounded by a mild inflammatory infiltrate that was composed of eosinophils, macrophages, plasma cells, and lymphocytes. The immunohistochemical characterization of the inflammatory infiltrate in the perivascular and peribronchial spaces revealed small groups of CD3-positive cells (T lymphocytes) and a greater number of CD79-positive cells (B lymphocytes). Large numbers of λ -light chain-positive plasma cells and MHC II-positive cells (alveolar macrophages) were ob-

served in the alveolar spaces, alveolar walls, and perivascular and peribronchial spaces. Very low numbers of κ -light chain-positive plasma cells were scattered within the inflammatory infiltrate. Severe fibromuscular hyperplasia of bronchiolar, alveolar, and arteriolar walls was also detected. Necrotizing vasculitis was evident. Occasionally, in alveolar spaces and vascular lumens, a few periodic acid-Schiff-stained yeasts were also detected. By use of the avidin-biotin-peroxidase complex technique, the yeast organisms had an intense immunoreaction.

Samples of skin and CSF collected from the cat of this report were cultured on Sabouraud agar at 37°C for 15 days. Creamy-white colonies characteristic of *C neoformans* grew from the skin samples on the agar plates after 72 hours. No growth was obtained from samples of CSF.

Morphologic Diagnosis

Systemic cryptococcosis caused by *C neoformans* with concomitant severe pulmonary aelurostrongylosis.

Comments

Aelurostrongylus abstrusus (Nematoda, Metastrongyloidea) is a common agent of verminous pneumonia in cats that are infected by paratenic hosts or by ingesting infected molluscs,¹ and infection is usually clinically inapparent. Cryptococcosis is a fungal disease caused by several opportunistic species of the saprophytic yeast-like basidiomycete fungus, *C neoformans*. Infection with *C neoformans* can develop in animals with apparently normal immune functions,² but is more severe in immunocompromised animals. In the cat of this report, the ELISA results were negative for infection with FeLV, FIV, and *Toxoplasma* spp and results of a CBC and serum biochemical analyses were unremarkable. On the basis of those findings, we concluded that the cat was immunocompetent. Thus, to our knowledge, this is the first case of systemic cryptococcosis in an immunocompetent cat in Spain.

In cats, the respiratory tract is the primary site of infection with *C neoformans*; the first clinical sign of infection is typically rhinitis. The infection then disseminates hematogenously and can spread to the nervous system, bones, skin, or periarticular soft tissues.³ Because inhalation is the principal infection route, the primary clinical signs and lesions of cryptococcosis are usually localized in the respiratory tract in most cats with the disease.⁴ In the cat of this report, the presence of *C neoformans* yeasts in the lower respiratory tract and the absence of granulomatous lesions and yeasts in the upper respiratory tract were indicative of a primary cryptococcal infection of the lower portion of the respiratory tract. Although clinical signs and lesions in the lower respiratory tract are rare in cats with cryptococcosis, small cryptococcal granulomas have been detected in

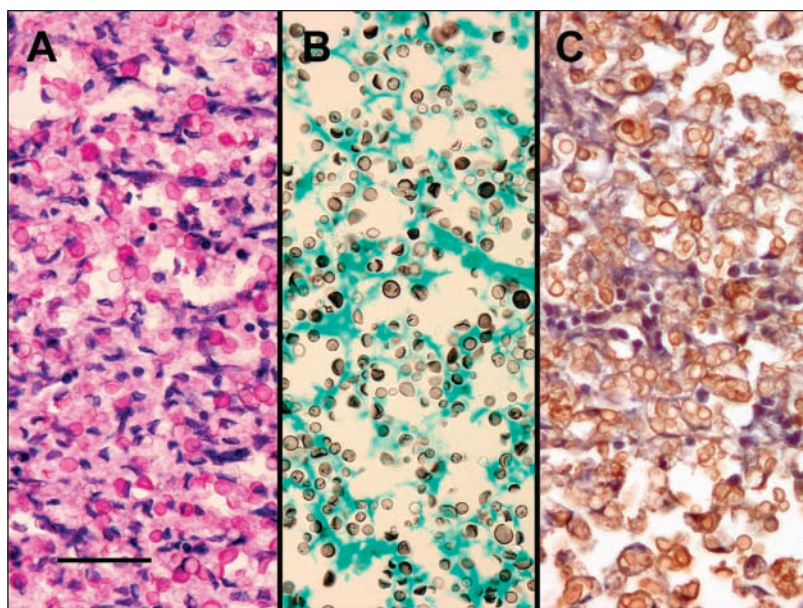


Figure 2—Photomicrographs of sections of mesenteric lymph node obtained from the cat in Figure 1 that were stained with periodic acid-Schiff (A) or Grocott methenamine-silver nitrate stain (B) or processed by use of an avidin-biotin-peroxidase complex technique (C). Loss of nodal tissue architecture is evident; numerous yeasts with capsules are intensely stained and easily detected by use of each staining procedure. Bar = 25 μ m (applies to all panels).

the lungs of healthy cats.⁵ Pulmonary infection possibly develops because of the small particle size of infective yeasts, and the inflammatory granulomatous response against yeasts is generally less severe than that associated with other fungal infections.⁶ However, the severe infestation with *A abstrusus* in the cat of this report might have generated a favorable environment for the systemic dissemination of fungal disease via local vascular damage and either direct inoculation of *C neoformans* into the circulatory system or alteration of the specific immune response against *C neoformans*. The immunophenotypic analysis of the inflammatory infiltrate in the lung revealed large numbers of macrophages, B lymphocytes, and plasma cells and a small number of T lymphocytes. These observations suggest that a predominantly T-helper type-2 (Th2) immunoresponse developed against the parasitic disease, although several cryptococcal structures were detected in the lungs. Because *C neoformans* may act as a facultative intracellular pathogen, infections can be eliminated or become chronic clinically inapparent infections. Resolution of infection in immunocompetent animals is a result of a cellular T-helper type 1 (Th1) immunoresponse, which is mainly composed of CD3-positive T lymphocytes; however, the systemic dissemination of yeasts is associated with Th1 immunosuppression.⁵ Although the humoral immune response (Th2 cells), which is mainly composed of B lymphocytes and plasma cells, is inefficient in resolution of cryptococcosis,⁷ that immunoresponse is classically involved in resolving parasitic diseases. Results of experimental studies^{8,9} involving mice have indicated that allergens or helminthic parasitic diseases can influence the course of several infections caused by intracellular pathogens via the induction of a Th2 immunoresponse, which alters the cytokine expression pattern of the inflammatory infiltrate and favors the systemic dissemination of intracellular pathogens. With this in

mind, we suggest that the severe aelurostrongylosis promoted development of systemic cryptococcal infection in the immunocompetent cat of this report. Although systemic fungal diseases are rare in companion animals, they should be considered by clinicians, especially in rescue animals in which parasitic pulmonary diseases are detected relatively frequently.

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