An 8-year-old, castrated, male domestic shorthair cat was presented to the referring veterinarian with a 3-day history of lethargy, inappetance, hyperemic skin nodules, and infrequent coughing and vomiting. Other than a recent 2-week course of Tresaderm (Merial, Athens, GA, USA) for nonspecific ear problems, the cat had no reported medical history. The cat had lived with the present owner for 1 year, had no travel history, and was an indoor cat. Physical examination revealed the cat was febrile (105°F) and had mild upper-airway congestion, increased lung sounds bilaterally, possible right-upper-quadrant abdominal discomfort, and generalized hyperemic skin. Abnormal findings on a CBC and chemistry profile included mild anemia (HCT 29%, reference interval 31–48%), lymphopenia (954 cells/μL, reference interval 1200–8000 cells/μL), thrombocytopenia, hyponatremia, and increased alanine aminotransferase and aspartate aminotransferase activities. Cytology of the skin nodules revealed many spindle- to crescent-shaped protozoal organisms, with morphology consistent with *Toxoplasma gondii* or *Neospora caninum*. Gross necropsy, histopathologic, immunohistochemical, and transmission electron microscopic findings confirmed a systemic protozoal infection; however, the organism exhibited characteristics of both *N. caninum* and *T. gondii*. Diagnosis of a *T. gondii*-like infection was based on internal structures of the organism and positive reaction to rabbit polyclonal antibodies to *T. gondii*. Reports of toxoplastic dermatitis are rare in the cat and dog, and this is the first reported diagnosis of a *T. gondii*-like protozoa in skin aspirates. (Vet Clin Pathol. 2005; 34:156–160)

**Key Words:** Cat, cytology, *Neospora*, skin, *Toxoplasma*
mmol/L, reference interval 3.5–4.8 mmol/L), and marked hypocalcemia (6.6 mg/dL, reference interval 9.1–11.2 mg/dL); ionized calcium concentration was within the reference interval. Also noted was a prolonged prothrombin time (PT, 30.7 seconds, control 8.9 seconds) and partial thromboplastin time (PTT, 48.2 seconds, control 13.8 seconds). Approximately 12 hours after furosemide treatment was initiated, hyponatremia was still present (135 mmol/L, reference interval 147–156 mmol/L) and hypokalemia was marked (2.4 mmol/L, reference interval 4.0–4.5 mmol/L). Dyspnea, hypotension, and anorexia persisted for 36 hours in the ICU with no response to Baytril (Bayer, Pittsburgh, PA, USA), clindamycin, fresh-frozen plasma, or oxygen therapy.

Thirty-six hours after presentation, hyperemic skin nodules on the ventral neck were aspirated, and direct smears were prepared and stained with Wright’s-Giemsa (EMD Chemicals, Inc, Gibbstown, NJ, USA). The specimens were of good quality and low cellularity, consisting of many erythrocytes and few leukocytes. Many spindle- to crescent-shaped protozoal organisms were distributed throughout the smears extracellularly (Figure 2), with an occasional intracellular form detected in macrophages. The protozoal organisms were 5 μm × 2 μm, light basophilic, and contained a dark-staining, eccentric nucleus. Dividing forms containing 2 nuclei were also seen. The morphology of the organisms was most consistent with *Toxoplasma gondii* or *Neospora caninum*. Because of the cat’s declining condition, the owners elected humane euthanasia.

On gross postmortem examination, the skin of the ventral neck and chest contained multifocal, pink-white, alopecic, firm nodules ranging from 1 mm to 5 mm in diameter (Figure 1). The pleural cavity contained 6.5 mL of serosanguinous, clear fluid. The lungs were diffusely firm with multiple, white-grey, very dense, contracted foci within all of the lung lobes. In the right cranial lung an irregularly spheric, 4-cm diameter, firm, white-tan mass with indistinct margins was noted, as well as a similar, 3-cm × 2-cm × 2-cm mass in the left-middle lung lobe. Samples of skin, lung, liver, brain, mandibular lymph node, and small intestine were fixed in 10% formalin, routinely sectioned, and stained with H&E. Histopathologic sections of skin nodules from the ventral neck showed moderate lymphoplasmacytic dermatitis, with sheets of tachyzoites dissecting between the dermal collagen fibers of the superficial dermis and within the subcutaneous fat (Figure 3). Severe, necrotizing interstitial pneumonia with severe,
type-II cell hyperplasia was observed, with numerous free and intrahistiocytic tachyzoites and severe, pulmonary arterial smooth-muscle hypertrophy with invasion of arterial walls by protozoa. Impression smears of the lungs revealed many free and intrahistiocytic tachyzoites (Figure 4).

The lung masses seen grossly corresponded to foci of severe fibrosis with dense inflammatory-cell infiltrates. The brain had moderate, multifocal gliosis and moderate, multifocal lymphocytic meninitis, but no organisms were seen. In the liver, mild lymphocytic portal hepatitis with intrasinusoidal tachyzoites was noted. The mandibular lymph node had mild plasmacytosis with tachyzoites in the medullary and subcapsular sinuses. No significant histopathologic lesions were noted in the small intestine. The renal abnormalities noted on ultrasound examination were not appreciated at necropsy.

Polymerase chain reaction (PCR) assays for *T gondii* and *N caninum* were performed on formalin-fixed tissues and results were negative for both.1,2 Deparaffinized sections of skin were reacted with rabbit polyclonal antibodies to *T gondii* and *N caninum* and with anti-BAG-1 antibodies against *T gondii* and *N caninum*.3,4,5 The latter reacts with bradyzoites of *T gondii* and *N caninum*. Protozoa reacted intensely with *T gondii* but not *N caninum* or anti-BAG-1 antibodies. A piece of deparaffinized skin tissue was processed for transmission electron microscopy. Protozoal tachyzoites were found in several dermal cell types including fibroblasts, mononuclear cells, neutrophils, and epithelial cells (Figure 5a). They were located in parasitophorous vacuoles in host-cell cytoplasm. Tachyzoites had a conoid, few micronemes, a central nucleus, and several rhoptries. Up to 8 rhoptries were seen in 1 plane of section (Figure 5b). The contents of rhoptries were electron-dense in all tachyzoites examined (Figure 5b).
Discussion

Reports of toxoplasmic dermatitis are rare in the cat and dog, and this is the first reported diagnosis of *T gondii*-like protozoa in skin aspirates. Numerous cases of cutaneous neosporosis have been reported in dogs, including a dog with dermatitis and an unidentified *T gondii*-like parasite. The causative agent in the latter was structurally different than *T gondii* and *N caninum* yet stained positively with *T gondii* antibody. In the present case, the organism reacted to *T gondii* but not to *N caninum* antibodies, yet the electron-dense rhoptries were more similar to those of *N caninum* tachyzoites than to those of *T gondii*. Rhoptries in *T gondii* tachyzoites are electron-lucent, and those of *N caninum* are electron-dense. Rhoptries of *T gondii* bradyzoites are electron-dense, yet the lack of BAG-1 immunoactivity confirmed that these organisms were truly tachyzoites and not bradyzoites.

Additional evidence that this case differed from the previously mentioned *T gondii*-like case in a dog was that the protozoa in this cat divided into 2 by endodyogeny, whereas the protozoa in the dog divided into 2 organisms, probably by schizogony. *N caninum* and *T gondii* both divide by endodyogeny. As yet, *T gondii*-like organisms have not been cultured from either the cat or the dog; culture is the gold standard for the diagnosis of *T gondii*.

A diagnosis of Toxoplasma infection was supported by the clinical presentation, the distribution of lesions, and positive immunohistochemistry for *T gondii*; however, the organism was classified as *T gondii*-like because of the electron-dense rhoptries. The negative PCR results cannot be easily explained; however, PCR techniques have much greater sensitivity when assaying fresh, rather than fixed, tissues. Serology could have aided in the diagnosis, although it also has low sensitivity. Considering that as many as 60% of cats in the United States have positive antibody titers to *T gondii*, serologic examination is limited to cases in which the test can be performed repeatedly on the same animal during illness.

*T gondii* is an obligate, intracellular, coccidian parasite that infects virtually all species of warm-blooded animals, including humans. Domestic cats and other Felidae are the definitive hosts. It can be transmitted congenitally, by ingestion of infected tissue, or by ingestion of oocyst-contaminated food or water. The clinical signs of toxoplasmosis have been attributed to cell rupture secondary to organism replication, cell necrosis associated with delayed hypersensitivity reaction, and immune-complex vasculitis. Clinical toxoplasmosis is most severe in transplacentally infected kittens, the clinical signs reflecting inflammation of the liver, lungs, and CNS. Immunocompromised cats with postnatal toxoplasmosis commonly have pneumonia with concurrent anorexia, lethargy, and dyspnea. The hallmarks of postnatal toxoplasmosis are interstitial pneumonia, focal hepatic necrosis, lymphadenitis, myocarditis, and nonsuppurative meningoencephalitis. Necrosis is common and appears to be directly related to the rapid replication of tachyzoites. Tachyzoites may be detected in the peritoneal and thoracic fluids of acutely infected animals, and rarely in blood, cerebrospinal fluid, fine-needle aspirates, and transtracheal or bronchoalveolar washings. It is not fully understood why some infected dogs and cats develop clinical toxoplasmosis, whereas others remain unaffected. Significant factors may include age, sex, strain, number of organisms, stage of the parasite ingested, concomitant illness, or immunosuppression. In cats, clinical toxoplasmosis has been documented concomitantly with glucocorticoid therapy and with infections with *Mycoplasma haemofelis*, FeLV, FIV, and FIP. None of these concurrent diseases were identified in this feline patient; however, additional tests (ELISA for *T gondii* antibodies, mycoplasma titers, FeLV immunofluorescent antibody tests, and bone marrow aspiration) were not performed. This patient had been treated with an otic medication containing 1 mg/mL dexamethasone; however, it is unlikely that the treatment caused significant immunosuppression with a once-daily topical dose, assuming it was administered correctly.

Dubey and Carpenter reported 2 out of 100 *Toxoplasma*-positive cats had cutaneous lesions. One had dermal and subcutaneous nodules, periarticular swelling, and ulcers on its limbs. The other cat had ulcers of the distal limbs and footpad that were caused by toxoplastic vasculitis and subsequent infarction. Disseminated, cutaneous toxoplasmosis and dermatomyositis have been described in severely immunocompromised human patients with erythematous, nodular cutaneous lesions resembling the skin lesions reported in this cat; however, Toxoplasma parasites are rarely demonstrated histologically in skin biopsies of affected human patients. The diagnosis often is confirmed with serology and by response to antitoxoplasmic therapy.

Reported hematologic changes in cats with systemic toxoplasmosis include nonregenerative anemia (anemia of chronic disease); neutrophilic leukocytosis (inflammation, infection, tissue necrosis); lymphocytosis (chronic antigenic stimulation); monocytosis (increased mobilization of marginated cells, necrosis); and eosinophilia (hypersensitivity). Severely affected cats may develop leukopenia that persists until death because of increased tissue demand for neutrophils. This patient had lymphopenia, which we postulated to be secondary either to acute protozoal infection and retention of lymphocytes in the lymph nodes or to corticosteroid-induced redistribution.

The most common biochemical abnormalities during the acute phase of toxoplasmosis include hypoproteinemia and hypoalbuminemia, with hyperglobulinemia reported in some cats with chronic toxoplasmosis. This cat had hypoproteinemia with proteinuria, suggestive of renal loss, although extrarenal causes (eg, hematuria) could have contributed to the proteinuria. More likely, the cat was hypoalbuminemic from a third-space effect caused by the pleural effusion. In addition, acute tissue inflammation may have contributed to hypoalbuminemia, because albumin is a negative acute-phase protein. The cause of hematuria could have included procedural-related contamination (cystocentesis) or hemorrhage into the urinary bladder secondary to hemostatic abnormalities. Potential causes for the prolonged clotting times include consumption of factors secondary to vasculitis, disseminated intravascular coagulation, or decreased hepatic production of coagulation factors. There was no other evidence to support decreased hepatic functional mass; only mild increases in hepatocellular...
enzyme activities and mild hepatitis on histopathology were noted. A normal thyroxine value ruled out hyperthyroidism as a cause of the increased liver enzyme activities.

The majority of the electrolyte disturbances that this patient developed during treatment were attributed to furosemide therapy, which can lead to profound diuresis with water and electrolyte depletion. Hypotension persisted from presentation, signifying sustained hypotonic dehydration and electrolyte loss despite intravenous fluid therapy. Hypoalbuminemia likely contributed to the hypocalcemia, although ionized calcium was also decreased initially, indicative of true hypocalcemia.

In conclusion, we report a rare case of severe, disseminated T. gondii–like infection in a cat, which had moderate lymphoplasmacytic dermatitis with intralesional tachyzoites. It is likely the patient was immunocompromised; however, the cause of immunosuppression was never elucidated. To further identify the T. gondii organism, culture or PCR of fresh or frozen tissues would have been necessary.

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References