Systemic Candidiasis Due to *Candida albicans* in a Dog: First Case Reported from Taiwan

**Abstract:** Dermatophytes and *Malassezia* are common pathogen in Taiwan. However, systemic *Candida albicans* (*C. albicans*) infection in animals has not yet been reported here and is rare elsewhere in the world. This report describe a young dog, in which a submandibular pyogranulomatous lymphadenitis caused by *C. albicans* infection progressed to systemic candidiasis. The diagnosis was based on the fungal culture of aspirates from the submandibular lymph node and exudates around the lymph node. The dog did not respond to oral fluconazole therapy and required euthanasia because the dog appeared serious sign of seizure. At necropsy, multiple lymph nodes were also shown to be affected, and the fungal culture of cerebrospinal fluid was positive for *C. albicans*. In this first documented case of systemic *C. albicans* infection in a dog from Taiwan, we assess the possibility of candidiasis as a re-emerging infection in companion animals.

**Key words:** *Candida albicans*, Candidiasis, Dog
Introduction

*Candida albicans* (*C. albicans*), is an opportunistic yeast of skin and a normal inhabitant of gastrointestinal, respiratory and genital mucosa of mammals\(^4\)\(^-\)\(^7\). Infection readily occurs after long-term usage of steroids, antibiotics, or cytotoxic drugs and radiotherapeutics, which may affect a patient’s normal mucosal barrier. Human patients with diabetes mellitus, leukemia, lymphoma, leukopenia or acquired immunodeficiency disease syndrome (AIDS) are predisposed to contracting candidiasis\(^9\). Infection may present as acute, subacute or chronic disease, and most body systems may be involved. Whilst candidiasis of skin and mucosal surfaces in dogs is occasionally reported\(^3\)\(^-\)\(^7\), systemic candidiasis is rarely reported in the veterinary literature\(^2\)\(^-\)\(^5\). Yet, candidiasis is a common complication in hospitalized human patients with cancer or human immunodeficiency virus infection in Taiwan. The purpose of this article is to describe the first systemic canine candidiasis case reported from Taiwan.

Case Report

A one-year-old, 10 kg, spayed, female, mix breed dog had a two-week history of bilateral enlargement of the submandibular lymph nodes. The referral veterinarian concerned about the dog having lymphoma, and referred the case to the author’s clinic for further diagnostic assessment. On physical examination, bilateral enlarged grape-like clusters of submandibular lymph nodes were associated with peripheral subcutaneous oedema. The node on the left had a cluster of four lobules and that of the right had five. These lobules were 1–3 cm in diameter. The dog was otherwise healthy. After anesthesia (Xylazine 1 mg/kg mixed with Ketamine 1 mg/kg, intramuscular injection), an 1 cm diameter nodule was excised for histopathological examination, and fine needle aspirate of the nodes was collected for cytology and culture. The histological examination revealed round yeast bodies that were impossible to identify further. Aspiration samples were inoculated on mycobiotic agar (Difco, Sparks, MD, USA). Yellow-white colonies and budding yeasts were first observed after 72-hour incubation. When they were cultivated with human serum on a slide glass and then incubated at 37°C, the characteristic germ tube structure of *C. albicans* was observed within one hour (Fig. 1).

One firm brown nodule excised was sent for histopathological examination. The nodule looked like a lymph node grossly. On histological examination, it showed the peripheral capsule and internal architecture of a lymph node. However, much of the tissue was effaced by extensive necrosis. Anastomosing bands of eosinophilic cellular debris extended to the cortex and effaced the lymphoid follicles in many areas. The areas of necrosis had a defined structure with central eosinophilic debris containing remnants of nuclei. This was surrounded by pallisading macrophages and epithelioid macrophages and occasional multinucleate giant cells. Some areas at the margin of necrosis had discrete, possibly encapsulated, non-staining bodies of about 5–10 microns. Some of these are part of fungal hyphae. The diagnosis given was chronic pyogranulomatous lymphadenitis with fungal elements (Fig. 2). Lymphadenitis due to *C. albicans* was tentatively...
The dog was hospitalized in the referral vet’s clinic and orally medicated with itraconazole (30 mg/kg once daily) for 4 weeks with poor response, and then switched to fluconazole (15 mg/dog, every other day, orally). Anorexia, vomition, pyrexia and mental dullness ensued, which was believed due to the drug reactions of fluconazole. Because of these side effects, the treatment regime was changed to fluconazole given at 15 mg/dog weekly. During the 4-month therapy, leukocytosis, lymphocytosis, elevated alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were observed. Lesions progressed to generalized subcutaneous lymphadenitis, especially affecting the submandibular and scapular areas with prominent swelling and ulcerations. The exudates aspirated from the submandibular area were purulent and bloody (Figs. 3, 4). The lesion also involved thoracic neck; both eyes (Fig. 5) were infiltrated with nodular lesions. The eye globes shrunk into the sockets and lost their functions. Changes in the animal’s skin included partial alopecia and hyperpigmentation on axilla with moderate itching. After four months, the dog had serious seizure and the owner requested euthanasia.

At autopsy, gross lesions included disseminated white spots on the cerebrum, pancreas, liver, kidney, lung, and heart. All the lymph nodes were enlarged, especially those of the gastrointestinal system (Fig. 6). Caseous appearance was noticed on cross sections of affected lymph nodes (Fig. 7). Numerous white nodules were found in the spleen (Fig. 8). Blood and spinal fluid were collected for fungal culture. *C. albicans* and the germ tube structure were again isolated from spinal fluid cultures.

Multiple organs with gross lesions were sent for pathological examination. Most of the organs were affected similarly. Changes included extensive loss of tissue architecture as coalescing foci and sheets of epithelioid cells spreading out through the tissue. Other
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cells present amongst the infiltrate were plasma cells, neutrophils and aggregates of lymphocytes. In several organs, there were pale staining round fungal yeasts with thick capsules. In the liver, the small granulomatous foci originated in the portal areas. In the lymphoid tissue, the epithelioid cells effaced most of the organ. Multinucleate giant cells were also present. The brain and eyes were extensively and severely affected. However, sections of lung and kidney showed no infection. The final histological diagnosis was systemic mycosis.

Discussion

This young dog was fully vaccinated. There was no history of trauma or penetrating wounds, nor were any underlying diseases detected. Also, the dog did not have history of long-term usage of corticosteroid, antibiotics and/or anti-neoplasm medication or any other history of diseases. The dog was adopted from an animal shelter since puppyhood and kept entirely indoors thereafter. The source of infection was unknown.

Although not widely used in veterinary medicine, fluconazole is suggested as the first-line treatment for candidiasis due to its efficacy and reportedly low incidence of side effects. In veterinary dermatology, recommended dosage of antifungal agents are not based on scientific study but on personal experience of high cure rate. Suggested dosages are 150 mg/dog, 6.25–12.5 mg/kg, 5–10 mg/kg or 2.5–5 mg/kg for dogs and cats, orally administrated daily. For the present case, fluconazole was given at 150 mg/dog which was the highest dosage suggested, but the dog did not respond but accompanied with severe side effects and lesions were worsened. This may be due to the overwhelming infection presented at the time of treatment, the resistance of the organism or could be due to idiosyncratic side effects of the drug itself. It is possible that combination fluconazole and amphotericin B therapy would have been more effective in this case, based on findings from evaluation studies in human medicine. Recent another two reported cases of systemic candidiasis were as similar on end stage of infection revealed neurologic signs. All three dogs did not show evidence of any underlying cause, nor had previous history of medication such as long-term antibiotics, steroid nor immunosuppression and chemotherapy, also no infected sites were found.

*Candida spp.* is an opportunistic fungus. In the past systemic candidiasis were rarely reported in the dog. However, more cases were reported within recent six year. In Taiwan, human medical center had increased lethal AIDS patients accompanies with secondary candidiasis show the *Candida spp.* had resist to most antifungal agents [Dr. Tsong-Yih Ou, personal communication]. Considering the public health and grave prognosis, we need pay more attention to those non typical neurologic and dermatologic signs and enlarged lymph node as a re-emerging infection- systemic candidiasis.

References


