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Cutaneous blastomycosis and dermatophytic pseudomycetoma in a Persian cat from Bangkok, Thailand

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ABSTRACT

This is a case report of concurrent of blastomycosis and pseudomycetoma in a 3 year-old Persian cat from Bangkok, Thailand. Histopathology from antemortem and postmortem samples revealed blastomycosis and dermatophyte pseudomycetoma. The PCR analysis of the formalin-embedded tissue of antemortem sample confirmed that blastomycosis was caused by *Blastomyces dermatitidis*. Dermatophyte infection was caused by *Microsporum canis*. According to the author's knowledge, this is the first case of *Blastomyces dermatitidis* and dermatophyte pseudomycetoma in South-East Asia.

1. Introduction

Blastomycosis is a systemic mycotic infection caused by the dimorphic fungus *Blastomyces dermatitidis*, (anamorph, *Ajellomyces dermatitidis* teleomorph). In natural conditions, *Blastomyces* grows in a saprophytic mycelial form that produces infective spores (aleuriocornidia) sexually. The organism is primarily transmitted by inhalation of conidia. Infection in body tissues occurs when these conidias are phagocytosed by pulmonary macrophages, and spreaded to the pulmonary interstitium. At body temperature, the organism transforms into yeast form and replicates asexually [1,4]. The yeast form is characterized by a round, 5–20 μm diameter, broad-based structure with a thick, refractile, and double contoured cell wall [1,4]. The disease may localize in the lungs or may spread hematogenously or lymphatically to other organs [4]. Systemic pyogranulomatous disease is most commonly reported in dogs, humans and infrequently reported in cats. Infected animals showed systemic illnesses such as anorexia, lethargy, respiratory distress, skin lesions and weight loss [1,4]. The endemic areas of blastomycosis are North America, Ohio and Mississippi river valleys, north central Wisconsin and the northern region of Ontario. The organisms favor growing in moist, acidic soil enriched with decaying vegetation or animal excreta. The soil near lakes, rivers or streams is considered a risk location for infection [1,4]. Other than the endemic regions, blastomycosis has been reported in Africa, India, Europe, and Central America [1–4,7,8]. There is one case report each from Israel and Saudi Arabia, and there are many human case reports in India, but only five cases have been conclusively proven to be blastomycosis [7,8]. As of today, there are no confirmed cases of human exposure in Thailand.

Histopathological staining is the gold standard of diagnosis for blastomycosis [1–4]. Chest radiographs support the radiographic changes of lung tissue, which are diffuse miliary or nodular interstitial pattern. There are serology tests to detect either antibody or antigen. Serology antigen detections are Agar Gel Immuno Diffusion (AGID), Radio Immuno Assay (RIA) and Enzyme Immunoassay (EIA) with a sensitivity of 17.4–90, 92 and 76.1% respectively. All serology tests have 100% specificity, and RIA can detect antibody up to1545 day post infection. Enzyme Immunoassay can detect *Blastomyces* antigen in serum and urine specimen. This test can show false positive, resulting from other deep mycotic infections [4]. PCR analysis of formalin embedded tissue can be performed. Treatment of blastomycosis is depended on the severity of disease. For significant pulmonary-involved dogs and cats, the recommended treatment are amphotericin B at the dose of .5–1 mg/kg (dogs) and .25 mg/kg in cats intravenously with itraconazole 5–10 mg/kg for the first 4–7 days, and follow by itraconazole 5–10 mg/kg for 4–6 months. In less severe cases, the recommended treatment is itraconazole at a dose of 5–10 mg/kg twice a day for at least 60 days. The treatment should be continued until 1 month post radiographic resolution of lung tissue [1–4].

Pseudomycetoma, an atypical form of dermatophytosis, is a deeper dermal and/or subcutaneous infection caused by dermatophytes in cats and dogs. Dermatophytic pseudomycetoma (DPM) is most commonly

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caused by *Microsporum canis*. The pathogenesis of the progression from cutaneous dermatophyte infection to pseudomycetoma remains unclear. It has been indicated that Persian cats are predisposed to dermatophytosis due to ineffective grooming of the long hair coat, the cutaneous microenvironment or immunological deficits [5,6]. Lesions of DPM are not restricted to epidermal structures, because the organisms can invade the dermal tissue and rupture the follicular structure causing multifocal nodular dermatitis. Diagnosis of DPM is made by wood's lamp and trichograms of broken hairs which architecture are effaced by fungal hyphae. Cytology of fine needle aspiration demonstrates numerous degenerate neutrophils, activated macrophages, multinucleated giant cells and fungal hyphae. Histopathology will confirm the diagnosis with coalescing foci of pyogranulomatous inflammation surrounding multiple, irregular basophilic hyphae-like elements in a sparse, granular, faintly eosinophilic matrix. These elements are strongly positive on Periodic acid Schiff staining. PCR analysis can be performed to confirm the identification of the organism by using biopsy samples for fungal DNA extraction [5,6]. Dermatophytic pseudomycetoma infection can be difficult to manage and the prognosis is poor. The lesions often recur after surgical excision and the outcome with surgical excision and concurrent use of antifungal treatments (griseofulvin, ketoconazole, and itraconazole) has been variable [5,6]. The purpose of this case report is to report blastomycosis concurrent with dermatophytic pseudomycetoma in an indoor Persian cat, which is also the first case report of blastomycosis in Thailand.

2. Case

A 3-year-old male intact Persian cat was referred to the dermatology clinic with 2 months history of chronic skin lesions. The referring veterinarian suspected dermatophyte infection, but no fungal culture was performed. Initial treatment was oral itraconazole at a dose of 5 mg/kg for 1 month, resulting in some improvement. However, the treatment was discontinued 1 month before referral. According to the owner, the cat was always thin and had dry skin. The owner and the other two cats at the same household had no skin lesions. The infected cat was a completely indoor pet. On day 0, the physical examination revealed that the cat was emaciated. The skin was alopecic and had hyperpigmented and scaling lesions throughout the body. There were multifocal ulcerated nodules all over the body. There were three large nodules at chin, left submandibular, left inguinal areas. The nodules at chin area had draining tract with bloody discharge (Fig. 1A and 1B). Differential diagnoses included deep bacterial infections, deep fungal infections and cutaneous neoplasia. Cytological examination of the draining nodule at the chin revealed a large number of coccoid bacteria, neutrophils, macrophages, and branching septate fungal hyphae. From the history of recurrent dermatophyte infection, a tentative diagnosis of dermatophytic pseudomycetoma with deep bacterial and/ or deep fungal infection was suspected. Skin biopsy was performed on this nodule. Specimen for histopathology samples was fixed in 10% neutral buffered formalin, which was stained with haematoxylin and eosin stain (H & E) and Periodic acid-Schiff stain (PAS). Chest and abdominal radiograph and abdominal ultrasound were performed at the initial exam and the results were within normal limits. Feline leukemia and immunodeficiency tests were negative. The complete blood count, liver enzymes (ALT and ALKP), and renal panel tests (BUN and creatinine) were within normal limits. On day 0, the cat was treated with oral antibiotic (amoxicillin and clavulinic acid) at a dose of 20 mg/kg orally twice a day, and topical treatment with 3% chlorhexidine and climbazole mousse pending histopathology result. On day 3, the results of histopathology revealed severe chronic multifocal to coalescing granulomatous dermatitis and panniculitis, with intralesional budding yeasts, consistent with blastomycosis and intralesional fungal hyphae, consistent with dermatophyte pseudomycetoma (Fig. 2A and 2B). The diagnosis of concurrent blastomycosis and dermatophyte pseudomycetoma was made. The sample of the chin biopsy was sent for PCR analysis. The treatment was changed to oral itraconazole 10 mg/kg daily. On day 7, the cat died at home. Necropsy was performed (Fig. 3A). There were multiple ulcerated and proliferative cutaneous nodules, estimated from 2 to 5 cm, on the face, chin, neck, and body. Superficial cervical lymph nodes were enlarged. Visceral organs were grossly unremarkable. Microscopic examination of the proliferative skin nodules was consistent with the biopsy results (Figs. 3B and 3C). Histopathology of liver cells revealed severe, acute diffuse centrilobular hepatocyte degeneration. Histopathology of lung tissues revealed alveolar collapse with presence of minimal to moderate fluid in alveolar lumen. Granulomatous inflammation and budding yeasts were not found in the lung parenchyma.

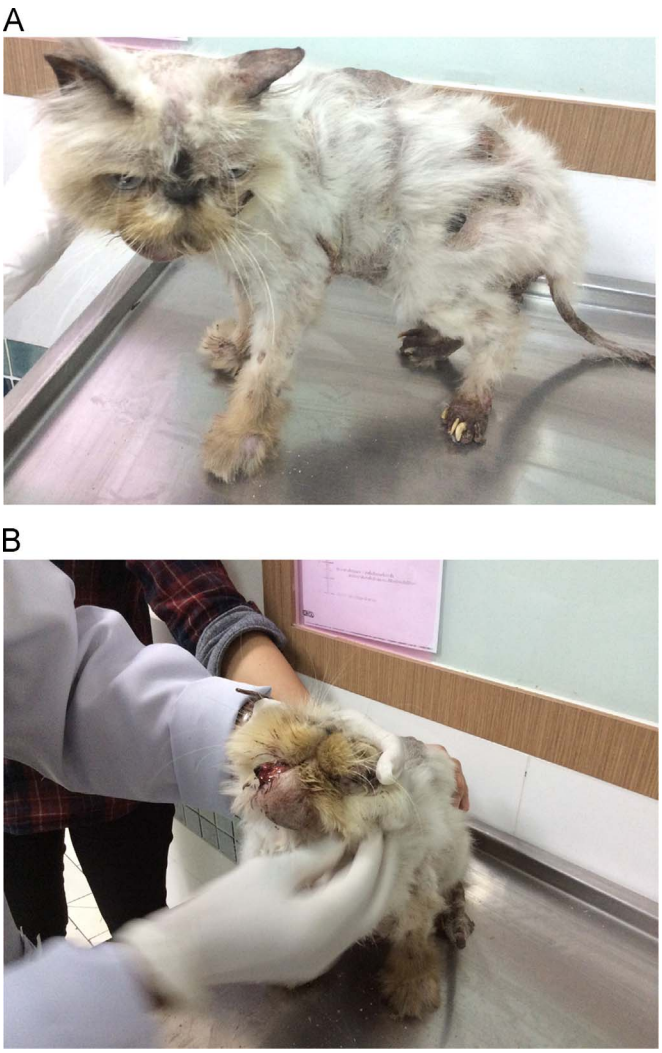

Fig. 1. A: Photograph of the cat showing alopecic, hyperpigmented and scaling skin. There were multifocal ulcerated nodules throughout the body. B: Photograph of the skin nodules at chin area with draining tract and bloody discharge.

3. PCR analysis

In order to confirm the histopathological result, a polymerase chain reaction (PCR) was performed twice from Formalin-fixed, paraffin-embedded (FFPE) tissue from the chin area. In brief, the 10 FFPE Section (5 μm thickness) were deparaffinized with 1 ml xylene and washed with absolute alcohol. The samples were subjected to DNA preparation using the conventional method: glass beads and phenol extraction protocol [12]. These genomic DNAs were amplified in the inter-transcribed spacer region by universal ITS1 and ITS4 primers

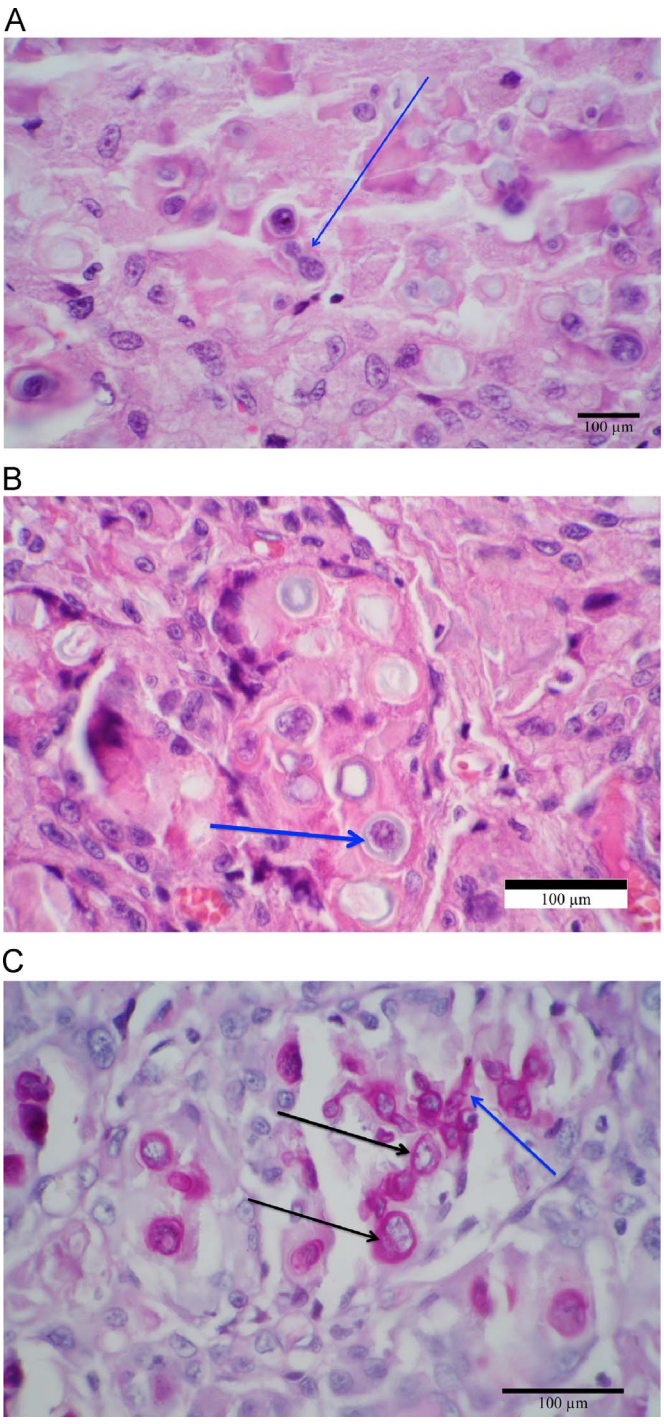

Fig. 2. A: Photomicrograph of broad-based budding yeasts of *Blastomyces* sp. (blue arrow): H & E). B: Photomicrograph of intralesional yeasts with thick, refractile, and double contoured cell wall (blue arrow): H & E). C: Photomicrograph of broad-based budding yeasts and thick, refractile, and double contoured cell wall (Black arrow) and branching septate hyphae (blue arrow), PAS. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

(ITS1 5'-TCC GTA GGT GAA CCT GCG G-3' and ITS4 5'-TCC TCC GCT TAT TGA TAT GC-3'). The amplicons were purified by a PCR purification kit (Qiagen, USA) and sent for sequencing (1st BASE Laboratory, Malaysia). The sequences were blasted with the data in GenBank BLAST searching tool. The sequences from the first collected specimen at chin area revealed 98% homology to *Ajellomyces dermatitidis* (*Blastomyces dermatitidis*, anamorph) and sequences from pseudomycetoma area were 98% homology to *Microsporum canis*.

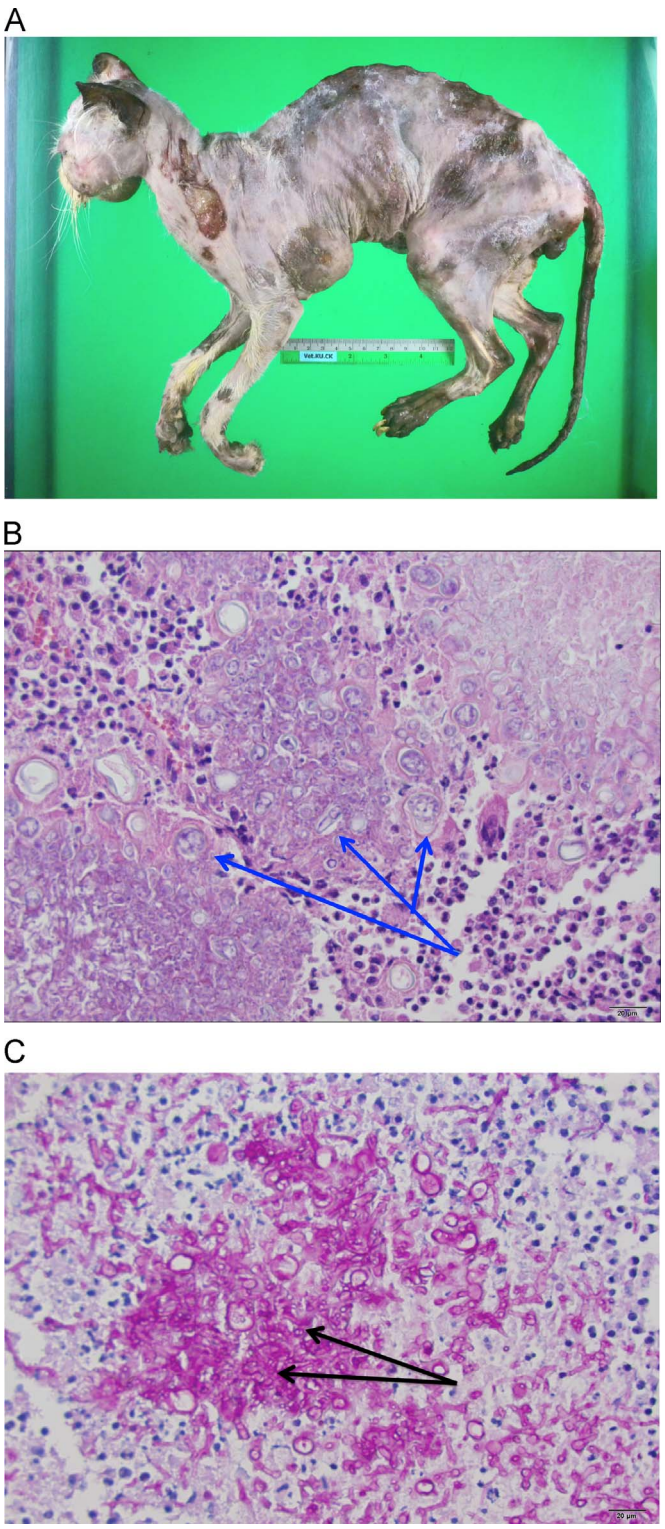

Fig. 3. A: Photograph of the cat (hair-clipped) with multiple ulcerated and proliferative skin nodules. B and C: Photomicrograph of the granulomatous lesion collected from the skin mass. B: Photomicrograph of the granuloma showing multifocal to coalescing granulomatous panniculitis containing numerous septate hyphae (blue arrow), epithelioid macrophages, plasma cells, neutrophils, and multinucleated giant cell. H & E. C: Photomicrograph of the septate hyphae in the granulomatous lesion (black arrow), PAS. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

4. Discussion

This is the first case report of blastomycosis and concurrent dermatophyte pseudomycetoma in a Persian cat from the central part of Thailand. The initial diagnosis was made from histopathology of the antemortem lesion from nodules at the chin. Since South-East Asia is not an endemic area of blastomycosis, PCR analysis of formalin embedded tissues from the same ante-mortem lesion was performed. Molecular analysis confirmed the infection of *Blastomyces dermatitidis* and pseudomycetoma caused by *Microsporum canis*. The infected cat died within one week and histopathology of necropsy samples supported the diagnosis.

According to the owner, the infected cat was bought from a breeder in Bangkok, Thailand at the age of 3 months, and was always in poor body condition. At the age of 6 months, the cat was suspected to have a dermatophyte infection, and was treated periodically with oral itraconazole and medicated shampoo containing 2% chlorhexidine and 2% miconazole, which resulted in some improvement. This cat might have a defective cell mediated immune system leading to susceptibility for dermatophyte infection when it was a kitten. Dermatophyte pseudomycetoma (DPM) is associated with breed related immunodeficiency or an aberrant immune response to dermatophytes [6]. With the weak cell mediated immune system, this Persian cat was infected by DPM followed by blastomycosis.

The reservoir for the blastomycosis was suspected to be soil, where the organism grows in a saprophytic mycelial form. This Persian cat was an indoor cat, but liked to sit by the window where the owner placed a flowerpot. The owner always brought the potting soil from different flower shops and changed the soil at least three times per year. The potting soil for indoor plants might be a source to grow the organism. There are reports about blastomycosis in indoor cats [4,9]. Gilor et al. published the retrospective report of clinical aspects of natural infection with *Blastomyces dermatitidis* in 8 cases of cats [4]. Five cats were reported to be indoor-outdoor cats, and one was an indoor only cat, and the status of the remaining two cats was unknown. All cats had negative test results for FIV and FelV infection. Respiratory tract signs were evident in six of the eight cats, skin lesions were evident in seven cats, and five cats had one or more non-ulcerated dermal nodules. Blondin et al. investigated the environment of five urban, indoor cats diagnosed at three veterinary clinics between March 3-July 13, 2005 in suburban Chicago, Illinois, by owner interviews, site visits, and environmental cultures for *Blastomyces dermatitidis*. The study could not isolate the organism from any of 60 environmental samples. There were no environmental exposures common to the five cats. The study suggested that the acquisition of *Blastomyces dermatitidis* was from the home site environment. It was assumed that the fungus had been growing in the nearby environment and possibly spread into close proximity to the home by windborne dust [9].

The mode of transmission for this Persian cat was suspected to be from inhalation of aerosols containing infective spores. The spores entered the terminal airways and disseminated via the blood or lymphatic system to skin. There was no abnormality detected from chest radiographs. Necropsy of the lung tissue both gross and histopathology samples did not show evidence of granulomatous inflammation or yeast organism. Fisher et al. reported a case of feline histoplasmosis limited to the skin [11]. The author suspected that the rapid dissemination of the infectious agents to other organs, such as skin after inhalation, might make it difficult to detect lung lesions on radiographs. For this Persian cat, we assumed the same reason, or that there was not enough time to develop lesions in the lung tissue.

The cause of death in this cat was still inconclusive. Histopathology of liver cells revealed diffuse hepatocyte degeneration. The change of hepatocytes might be from the prolonged treatment of itraconazole when the cat had a recurrent dermatophyte infection.

Due to the indoor status of the cat, an autochthonous blastomycosis in Thailand is suspected [10]. The owner of this cat was educated about how the reservoir of the mycelial form of the organism might be from the potting soil. The yeast phase of the organism cannot be transmitted through aerosols between humans, between animals, or from animals to humans. Therefore, this disease is not considered contagious or zoonotic [1,4,10].

According to the author's knowledge, this is the first case report of *Blastomyces dermatitidis* concurrent with dermatophyte pseudomycetoma infection in a Persian cat from Thailand and South-East Asia.

Conflict of interest

There are none.

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