

Case Report



Chronic Submandibular Lymphadenopathy due to Cryptococcosis in Cat

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Abstract | Cryptococcosis is one of the systemic mycosis in cats. Although it was considered a potential zoonotic disease, the transmission from cats to humans remains uncertain. This report observes the clinical and histopathological features of cryptococcosis in a cat exhibiting chronic submandibular lymphadenopathy. A five-year-old female cat showed lethargy, partial anorexia, weight loss, and intermittent sneezing for several months before being examined. Clinical examination demonstrated mucopurulent discharge from both nostrils, swollen on the nasal bridge and maxillary sinus. Subsequently, the cat was diagnosed infected by cryptococcosis based on cytology, fungal culture, serology, and hematology. Lymphadenopathy and the spreading of infection to the lungs were identified based on histopathological examination. Owing to potential zoonotic, a high index of suspicion was needed to identify mimickers like *Cryptococcus* spp. which in this case had initially presented as bilateral submandibular lymphadenopathy. The proper diagnosis and early treatment were needed to increase the chances of successful therapy.

Keywords | Cryptococcosis, Feline, Clinical signs, Histopathology, *Cryptococcus* spp.

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INTRODUCTION

Cryptococcosis is the most common systemic mycosis of cats worldwide caused by *Cryptococcus neoformans* and *Cryptococcus gattii*. Cryptococcosis affects more common in cats than dogs (Refai et al., 2017). Feline cryptococcosis is usually sporadic and commonly isolated from immunocompromised individual animals (Sykes et al., 2010). Evans et al. (2017) reported that environmental exposure and asymptomatic colonization of the respiratory tract are more common than clinical cases. Feline cryptococcosis infection is either subacute or chronic and it may infect cats through inhalation of spores from the environment. The initial site of colonization is suspected in

the nasal cavity. The nasal form of infection contributed to approximately 70% of cases, whereas 30% of cats with cutaneous cryptococcosis (Sykes et al., 2010).

Feline cryptococcosis was reported prevalent in several countries including Australia, United States, and South America (Firacative et al., 2018). Nevertheless, feline cryptococcosis reports in Indonesia was limited. Therefore, the potential of cryptococcosis as a zoonotic has not been a major concern. In several neighbour countries, cases of feline cryptococcosis have been reported in Malaysia (Habibahl et al., 2009) and Thailand (Worasilchai et al., 2017). This case report aims to provide information on feline cryptococcosis with the predominant clinical symptom

CASE DESCRIPTION

HISTORY

A five-year-old female cat was examined in the Veterinary Clinic, Faculty of Veterinary Medicine, Universitas Gadjah Mada, Indonesia. The cat was freely outdoors. The owner reported that the cat showed respiratory disorders including sneezing, and snoring, or grunting. These symptoms appeared for more than one year and no treatment was given. The condition of the cat got worse one month before it was examined in the animal clinic by showing lethargy, partial anorexia, and loss of body weight.

CLINICAL EXAMINATION

Clinical examination demonstrated that body condition score was poor (score 2), tachypnoea (respiration rate 64 breath per minute), and hyperthermia (body temperature 39.4°C). Conjunctiva and gingiva color were pale pinks, with capillary refill time (CRT) more than 2 seconds. Nasal deformity, swollen nasal bridge, and maxillary sinus, and mucopurulent discharge were observed from both nostrils (Fig.1A and 1B). Chronic bilateral enlargement of submandibular lymph nodes was found (Fig.1C). The conspicuous symptom was bilateral lymphadenopathy causing the facial appearance to be asymmetrical. Based on the owner's information, bilateral lymphadenopathy was persistent and occurs for about 1 year.



Figure 1: Nasal deformity, swollen nasal bridge and maxillary sinus (A). Mucopurulent discharge were observed from both nostrils (B). Bilateral enlargement of submandibular lymph nodes (arrow) (C).

CYTOLOGY EXAMINATION AND FUNGAL CULTURE

A nasal swab was stained with Giemsa for cytology examination. Cytology examination demonstrated *Cryptococcus* spp. on the nasal epithelium. *Cryptococcus* spp. were rounded to oval with a variably thick non-staining capsule and pale

in the center with a diameter varied about 3-5 μm (Fig.2). Fungal culture was performed to distinguish *Cryptococcus* and another dimorphic microorganism. The isolation and identification of fungi were performed on Sabouraud Dextrose Agar (SDA) (Himedia, India). A nasal swab was added with ampicillin 50 mg/L, macerated, plated on SDA, and incubated at 37°C. After 72 hours of incubation, creamy mucoid or milky colonies were observed. The colonies were then stained with lactophenol cotton blue for examination and demonstrated budding cell shape. The possibility of cryptococcal infection was considered based on the above findings.

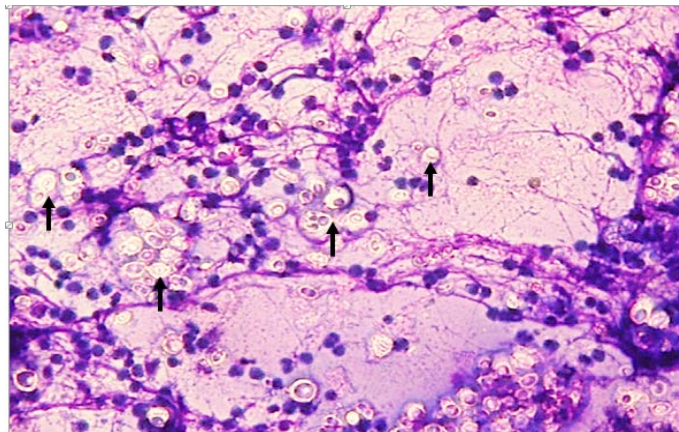


Figure 2: The nasal swab stained with Giemsa showed *Cryptococcus* spp. intracellular in the nasal epithelium. Fungi were rounded with a variably thick non-staining capsule and pale on center (arrow) (Giemsa stain 400 X).

SEROLOGY TEST

The rapid test was performed using StrongStep (Liming Bio, China) lateral flow immunoassay to detect the polysaccharide antigen of *C. neoformans* and *C. gattii* revealed a positive result. Serology examination using Feline leukemia virus (FeLV) and Feline immunodeficiency virus (FIV) test kit (Anigen Rapid, Bionote, South Korea) showed negative results. This result indicates there was no correlation between the immunocompromised condition in this case with FIV and FeLV infection.

HEMATOLOGY EXAMINATION

Complete blood count showed leukocytosis, neutrophilia, lymphopenia, hyperproteinemia, and hyperglobulinemia. The level of total plasma protein and fibrinogen were 10.9 g/dL and 600 mg/dL respectively. The increase in leucocyte ($32.9 \times 10^6/\mu\text{L}$) and neutrophils ($31.9 \times 10^6/\mu\text{L}$) indicated an inflammation reaction. Lymphopenia were indicated in this case as the absolute value of lymphocytes were $0.65 \times 10^6/\mu\text{L}$, much lower than normal range. Other blood parameters showed normal results (Table 1).

Table 1: Hematology examination result

Parameter	Unit	Normal range	Result
PCV	%	24-45	40
Hemoglobin	g/dL	8-15.9	8.8
Erythrocyte	10 ⁶ /μL	5-11.16	4.13
Leucocyte	10 ⁶ /μL	5.5-19.5	32.9
Neutrophils	10 ⁶ /μL	2.5-12.5	31.913
Lymphocyte	10 ⁶ /μL	1.4-7	0.658
Total plasma protein	g/dL	6-8	10.9
Fibrinogen	mg/dL	0-300	600

HISTOPATHOLOGICAL FINDINGS

Post-mortem examinations present a severe swollen nose and submandibular lymph nodes. Focal consolidation extending over several lobes was observed in the lung (Fig. 3A). Histopathological examination exhibit inflammation reaction markedly by neutrophils infiltration both in bronchioles and interstitial area of the lung (Fig. 3B).

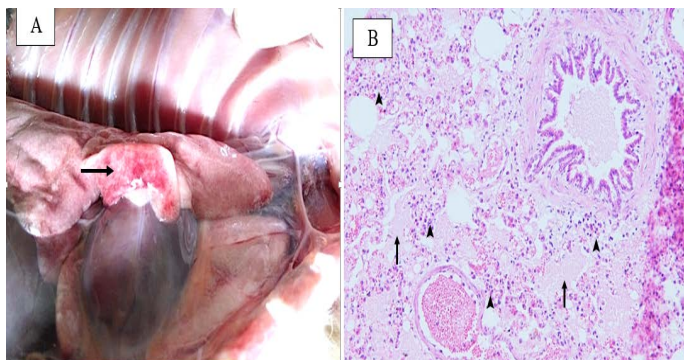


Figure 3: Postmortem findings on lung show focal consolidation (A). Histopathological examination showed neutrophils infiltration in bronchioles and interstitial area of the lungs (arrow). Also, mild edema as homogen eosinophilic mass in alveoli (arrow) (B).

Diagnosis and differential diagnosis: The cat was diagnosed with cryptococcosis with a poor prognosis.

Treatment: The cat was treated with itraconazole at a dose of 10 mg/kg q24h PO

DISCUSSION

Several investigators in Indonesia have reported cryptococcosis cases in immunocompromised humans. Unfortunately, based on the author’s knowledge, feline cryptococcosis in Indonesia has limited reports. It was likely cryptococcosis may be underdiagnosed due to the absence of pathognomonic symptoms or lack of modalities for diagnosis. Based on the results of clinical and laboratory examinations, this cat was diagnosed with cryptococcosis with a poor prognosis. Definitive diagnosis is based on the finding of the or-

ganism by cytological or fungal culture and characteristics on histopathological examination. Detection of antigens in body fluids by using polymerase chain reaction gives the opportunity to identify the specific genotype of *Cryptococcus* spp. (Pennisi et al., 2013).

The limitations of molecular tools and the weakness of rapid tests make the diagnosis of feline cryptococcosis more challenging. Further, the absence of pathognomonic symptoms complicates the diagnosis approach. Disease recognition based on existing clinical symptoms is important as an initial step in the diagnosis. Bilateral lymphadenopathy and persistent sneezing should be suspected as one of the manifestations of cryptococcosis (Pennisi et al., 2013). Furthermore, ‘nasal form’ as the most common cryptococcosis exhibited chronic sino-nasal disease, either alone or together with local spread to the skin, subcutis, and regional lymph nodes (McGill et al., 2009). According to Pennisi et al. (2013), this condition will induce naso-facial swelling followed by submandibular lymphadenopathy, chronic nasal discharge (monolateral or bilateral) with serous, mucopurulent or bloody aspect, stertor, and inspiratory dyspnoea, sneezing or snuffling.

This case was a poor prognosis. Early diagnosis will improve long term outcome in cryptococcosis (Pennisi et al., 2013). Among the drugs used to treat cryptococcosis are the anti-fungal such as amphotericin B, ketoconazole, fluconazole, and itraconazole (Pennisi et al., 2013; Vorathavorn et al., 2013). In this case, the cat was treated using itraconazole 10 mg/kg q24h orally. The treatment regimen in this case failed to cure the cat. No clinical response and the cat died ten days after treatment. Swollen submandibular lymph nodes and depletion of lymphoid tissues in this case have proven the dissemination of the infection. Severe disseminated cryptococcosis, diffuse pulmonary infiltrates, and/or dissemination to other sites including the CNS, requiring prolonged treatment regimens (Howard-Jones et al., 2022).

Currently, clinicopathological data from veterinary medicine in Indonesia was limited, suggesting that cryptococcosis may be infrequent or underdiagnosed. Nonetheless, tropical climates with high humidity are optimal for fungal growth. Moreover, the method of keeping cats mostly freely outdoors increases the risk of cryptococcosis infected from the environment. The ability of rapid diagnosis will increase the success of treatment and reduce the potential for transmission in immunocompetent animals.

This case report should raise awareness of cryptococcosis as a potential zoonotic disease in veterinary medicine. Diagnostic alertness for cryptococcosis should be advocated in cats presenting chronic bilateral lymphadenopathy. Enlargement of superficial lymph glands in chronic condi-

tions needs to be included as a differential diagnosis for cryptococcosis. *Cryptococcus* spp. is initially inhaled through the nostrils of animals and then replicate at the paranasal sinuses and lungs, then spread to lymph nodes and other organs (Trivendi et al, 2011). Because the submandibular lymph nodes cover the sinus and nostril areas, lymphadenopathy in these areas is most likely related to the inhalation of pathogenic microorganisms.

In conclusion, a high index of suspicion was needed to identify mimickers like *Cryptococcus* spp. which in this case had initially presented as bilateral submandibular lymphadenopathy. Early treatment should be started after diagnosis through cytology and fungal culture.

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CONFLICT OF INTEREST

The authors declare no competing interest.

NOVELTY STATEMENT

This case study provides preliminary information on submandibular lymphadenopathy as one of the clinical manifestations of cryptococcosis. Further investigation with a more significant number of samples was required to provide complete information about this case.

AUTHORS CONTRIBUTION

SI: Designing studies. SI, AN, and Y examined and treated the cat. SW and DR performed an autopsy, and histopathological examination; SI, AN, and DR collected data and literature and prepared manuscripts. All authors have read and approved the final manuscript.

- Brito-Santos F, Reis RR, Coelho RA, et al (2019). Cryptococcosis due to *Cryptococcus gatii* VGII in southeast Brazil: The One Health approach revealing a possible role for domestic cats. *Med. Mycol. Case Rep.* 24: 61–64. <https://doi.org/10.1016/j.mmcr.2019.04.004>
- Evans SJM, Jones K, Moore AR (2017). Atypical morphology and disparate speciation in a case of feline cryptococcosis. *Mycopathologia.* 183(2): 479–484. <https://doi.org/10.1007/s11046-017-0183-z>
- Firacative C, Lizarazo J, Illnait-Zaragozi MT, et al (2018). The status of cryptococcosis in latin america. *Mem. Inst. Oswaldo Cruz.* 113 (7). <https://doi.org/10.1590/0074-02760170554>
- Habibahl A, Mutalib AR, Bejo MH, et al (2009). Feline cryptococcosis in Malaysia: a first report. *J. Vet. Malaysia.* 21(1): 35 – 38.
- Howard-Jones AR, Sparks R, Pham D, et al (2022). Pulmonary Cryptococcosis. *J. Fungi.* 8: 1156–1175. <https://doi.org/10.3390/jof8111156>
- McGill S, Malik R, Saul N, et al (2009). Cryptococcosis in domestic animals in Western Australia: a retrospective study from 1995–2006. *Med. Mycol.* 47: 625–639. <https://doi.org/10.1080/13693780802512519>
- Pennisi MG, Hartmann K, Lloret A, et al (2013). Cryptococcosis in cats: ABCD guidelines on prevention and management. *J. Feline Med. Surg.* 15:611–8. <https://doi.org/10.1177/1098612X13489224>
- Refai MK, El-Hariri M, Alaoursy R (2017). Cryptococcosis in animal and birds: a review. *European J. Acad. Essay.* 4 (8) : 202–223
- Sykes JE, Sturges BK, Cannon MS, et al (2010). Clinical signs, imaging features, neuropathology, and outcome in cats and dogs with central nervous system cryptococcosis from California. *J. Vet. Intern Med.* 24(6):1427–1438. <https://doi.org/10.1111/j.1939-1676.2010.0633.x>
- Trivedi SR, Malik R, Meyer W, Sykes JE (2011). Feline Cryptococcosis Impact of current research on clinical management. *J. Feline Med. Surg.* 13(3): 163–172. <https://doi.org/10.1016/j.jfms.2011.01.009>
- Vorathavorn VL, Sykes JE, Feldman DG (2013). Cryptococcosis as an emerging systemic mycosis in dogs. *J. Vet. Emerg. Crit. Care.* 23(5): 489–497. <https://doi.org/10.1111/vec.12087>
- Worasilchai N, Tangwattanachuleeporn M, Meesilpavikkai K, et al (2017). Diversity and antifungal drug susceptibility of *Cryptococcus* isolates in Thailand. *Med. Mycol.* 55 (6): 680–685.