

**Diagnosis of nasal cryptococcosis with cutaneous and respiratory involvement in a domestic feline**

Diagnóstico de criptococose nasal com comprometimento cutâneo e respiratório em um felino doméstico

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ABSTRACT: This paper describes a case of *Cryptococcus* sp. infection in a domestic feline with cutaneous and respiratory alterations. The 4-year-old male animal, of no defined breed, presented with an increase in volume in the nasal region, with multifocal ulcers and a reddish surface. After careful clinical assessment, samples were taken for a screening cytopathological examination, which revealed yeast-like structures compatible with *Cryptococcus* sp., which was confirmed with a biopsy followed by a histopathological examination which showed the presence of yeasts of the fungus and a fungal culture obtained by swabbing the lesion and exudates which confirmed the presence of yeasts. Different diagnostic techniques were decisive in instituting treatment, based on using oral antifungals for 90 days.

Keywords: fungal culture; itraconazole; *Cryptococcus* sp.

RESUMO: Este trabalho descreve um caso de infecção por *Cryptococcus* sp. em um felino doméstico apresentando alterações cutâneas e respiratórias. O animal macho, sem raça definida, 4 anos de idade, apresentava aumento de volume na região nasal, com úlceras multifocais e de superfície avermelhada. Após criteriosa avaliação clínica, foi realizada colheita de amostras para exame citopatológico de triagem, que revelou estruturas leveduriformes compatíveis com *Cryptococcus* sp., em que foi confirmado com a biópsia seguida de exame histopatológico que evidenciou a presença de leveduras do fungo e cultura fúngica obtida por swab da lesão e exsudatos que confirmou a presença de leveduras. O uso de técnicas diferentes de diagnóstico foi decisivo para a instituição do tratamento que foi baseado no uso de antifúngico por via oral, durante 90 dias.

Palavras-chave: cultura fúngica; itraconazol; *Cryptococcus* sp.

INTRODUCTION

Cryptococcosis, also known as Torulosis, European Blastomycosis and Busse-Buschke Disease, is a systemic mycosis caused by an opportunistic pathogen (Müller; Nishizawa, 2017). It affects humans, domestic animals, and wild animals (Rondelli *et al.*, 2010). Its incidence is higher in cats than in other domestic animals. It may be associated with their grooming behavior, which involves frequent licking, facilitating transmission of the fungus to the nasal passages (Pimenta *et al.*, 2015).

It is caused by yeasts of the genus *Cryptococcus*, with *Cryptococcus neoformans* and *Cryptococcus gatti* being the two species most commonly involved in the disease (Kon *et al.*, 2008). The fungus can be found in a variety of environments, such as soil, wood trunks and decaying organic matter. It is common in soils containing bird droppings and can remain viable for over two years (Qüeiroz *et al.*, 2008).

The clinical manifestations can be isolated or combined: respiratory syndrome, neurological syndrome, ocular syndrome, and cutaneous syndrome (Müller; Nishizawa, 2017). It is predominant in immunosuppressed organisms, given the reduced immune response capacity to pathogens (Nelson; Couto, 2010).

In fungal infections, the absence of specific

clinical signs and characteristic macroscopic lesions makes an accurate presumptive diagnosis impossible (Galiza *et al.*, 2014). Diagnosis is established by cytological examination, antibody serology, fungal culture, histopathological examination, and PCR (Pimenta *et al.*, 2015).

The prognosis of cryptococcosis in cats is considered favorable when the diagnosis is made in the early stages. However, the presence of central nervous system (CNS) involvement is associated with a significantly worse prognosis (Pimenta *et al.*, 2015).

This paper aims to report a case of nasal cryptococcosis with cutaneous and respiratory involvement in a semi-domiciled feline in the Alto Sertão region of Paraíba, emphasizing the accuracy of the diagnostic process.

CASE REPORT

A 4-year-old male SRD feline was seen at the Adílio Santos de Azevedo Veterinary Hospital in Alto Sertão Paraíba with a history of an ulcerated lesion on the nasal planum draining exudate with a firm subcutaneous increase in volume on the nasal bridge. The clinical signs began approximately 10 days before the consultation, with a gradual progression of the

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condition. The guardian attempted home treatment with anti-inflammatory drugs (SID for 5 days), healing ointment and essential oil, but the condition did not improve. It was also reported that the feline had access to the street and had not been immunized with multiple feline and rabies vaccines, as well as not being tested for FIV (Feline Immunodeficiency Virus) and FELV (Feline Leukemia Virus).

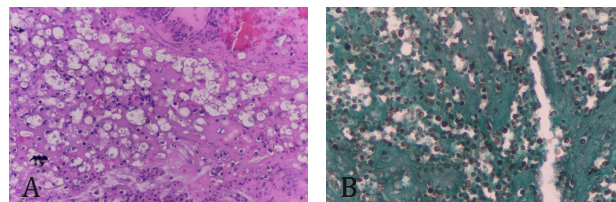
On general and specific physical examination, there was an increase in volume in the nasal plane, with multifocal ulcers with a reddish surface on the skin (Figure 1.A). Physiological parameters were within normal limits: heart rate (HR) 120 bpm, respiratory rate (RR) 30 bpm, rectal temperature (RT) 38.8 °C, capillary refill time (CRT) 2 seconds, hydrated, strong peripheral pulse, no alterations in lymph nodes or on cardiac and pulmonary auscultation.

For the diagnosis, a cytopathological examination was carried out through scarification and fine needle aspiration puncture (FNAP) of the lesion and exudates. During this procedure, yeast-like structures compatible with *Cryptococcus* sp. were observed stained with rapid panopticon and India ink (Figures 1.B and 1.C).

To aid in the diagnosis, a histopathological

LTDA, Sa o Paulo, Brazil), Amoxicillin + Clavulanate Potassium (10 mg/kg, VO, BID, for 10 days) (Vansil LTDA, São Paulo, Brazil) and Omega 3 (1 capsule/kg, VO, SID, for 30 days) (Avert - Biolab LTDA, São Paulo, Brazil).

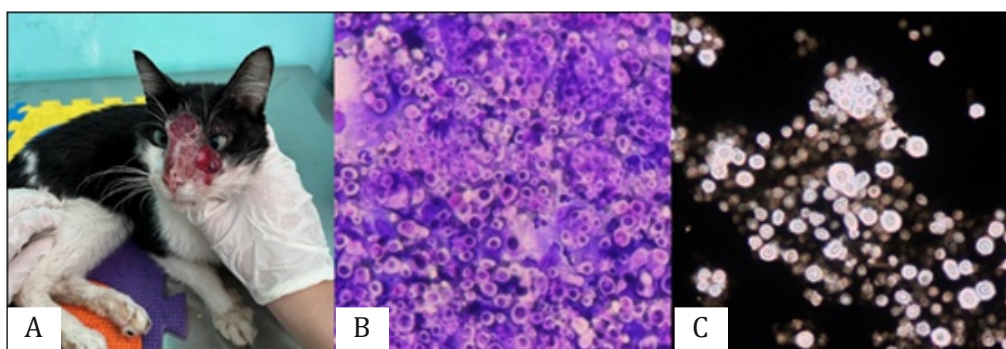
Figure 2 – Morphological diagnosis of nasal cryptococcosis in a feline. A- Yeasts suggestive of *Cryptococcus* spp. oval-shaped and rounded with a central cell surrounded by a capsule that does not stain, using the Hematoxylin and Eosin (HE) staining method, 40x objective. B- Yeasts strongly stained with Grocott-Gomori Silver Methenamine (GMS), 40x objective.



Source: A and B - IFPB Animal Pathology Laboratory (Sousa Campus), 2024.

On returning to the veterinary hospital after 30 days of initial care, the patient showed signs of apathy

Figure 1 – *Cryptococcus* spp. infection in a feline. A - Adult male SRD feline with increased volume in the nasal plane and multifocal skin ulcers. B - Slide stained with rapid panotype showing yeast-like structures compatible with *Cryptococcus* spp. (red arrow) - obj.40x. C- Slide stained with India ink showing yeast-like structures compatible with *Cryptococcus* spp. (red arrow) obj.40x.



Source: A - HV-ASA, 2024. B and C - IFPB Animal Pathology Laboratory (Sousa Campus), 2024.

examination was carried out using a punch skin biopsy, which was submitted to the Hematoxylin and Eosin (HE), periodic acid Schiff (PAS), and Grocott-Gomori Silver Methenamine (GMS) staining methods for histopathological evaluation of the affected tissue. The results revealed moderate, focally extensive mononuclear dermatitis associated with yeasts suggestive of *Cryptococcus* sp. (Figure 2).

The definitive diagnosis was obtained by fungal culture on Dicloran Rose Bengal Chloramphenicol Agar (DRBC) of swab samples by printing the tissue in the nasal region, with growth in 7 days at room temperature of around 25°C, in which it was possible to observe the presence of yeast-like structures (Figure 3).

Antifungal and supportive therapy was started with Itraconazole (10 mg/kg, VO, SID, for 90 days) (CEPAV - Vetrico LTDA, Rio de Janeiro, Brazil), Dipyrone (25 mg/kg, VO, BID, for 3 days) (EMS LTDA, São Paulo, Brazil), Ketoprofen (1 mg/kg, VO, SID, for 3 days) (Syntec 107 LTDA, São Paulo, Brazil), Amoxicillin + Clavulanate Potassium (10 mg/kg, VO, BID, for 10 days) (Vansil LTDA, Sa o Paulo, Brazil), for 3 days) (Syntec

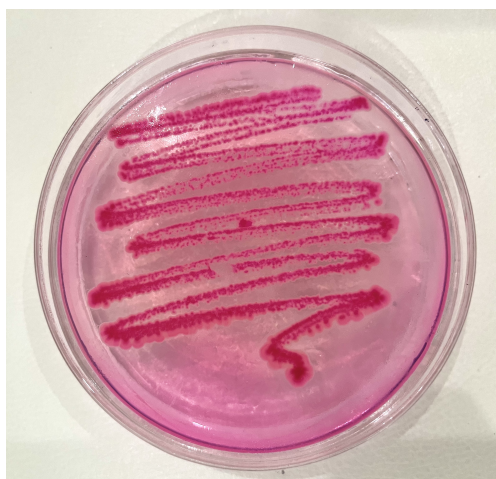
and weight loss, although his physiological standards were within the normal range. During the consultation, the guardian reported that he had only administered the antibiotic as instructed due to the difficulty in administering the medication to the animal. Still, the antifungal therapy with itraconazole had only been carried out once.

The guardian was told to leave the animal in the hospital for further tests, since at the previous appointment he had not authorized the hematological, biochemical and imaging tests to be carried out, and to restart the treatment instituted to improve the patient's clinical condition. A complete blood count, biochemical tests (urea, creatinine, ALT - alanine aminotransferase and FA - alkaline phosphatase), a rapid screening test for retroviruses (FIV and FELV), and skull and chest X-rays were requested. However, the animal's guardian did not authorize all the tests requested, only allowing the blood count and blood biochemistry to be carried out.

The blood count results showed intense leukocytosis, and the patient was then given

antimicrobial therapy which included the administration of Ceftriaxone 1g (25 mg/kg)

Figure 3 – Yeast growth on Dichloran Rose Bengal Chloramphenicol Agar (DRBC).



Source: IFPB Animal Microbiology Laboratory (Sousa Campus), 2024.

(Eurofarma LTDA, São Paulo, Brazil), IV, every 12 hours, for 10 days, together with Metronidazole 5 mg/ml (15 mg/kg), IV, also administered every 12 hours, for 10 days.

After the change in biochemical values was detected, the animal was referred for abdominal ultrasound to identify a possible hepatocellular lesion, but no change was observed on the imaging test.

After 16 days in the hospital, complementary tests and the start of treatment with Itraconazole under veterinary medical supervision, the patient was discharged from the hospital for home treatment. The patient was recommended to return to the hospital every 30 days, along with guidelines to ensure a good recovery and specific instructions for the guardian. However, 20 days after discharge, it was reported that the animal had died due to the difficulty of administering the medication at home.

DISCUSSION

The animal in this report showed increased volume in the nasal plane with multifocal 147 ulcers on the skin, which according to Giordano *et al.* (2010), is commonly observed in 148 cases of feline cryptococcosis. Facial deformities are observed in the nasal region. In 149 cases, the granulomatous tissue can protrude outside the nostrils, which was not observed in the patient, possibly due to the short duration of the disease. According to the same author, the fungus can invade the cribriform plate, reaching the olfactory bulbs and even the optic nerve, hardly involving the orbit, however, no ocular lesions were observed in the animal.

During the hospitalization period, it was possible to notice that the animal sneezed and wheezed, a characteristic respiratory manifestation common in cats. According to Faria (2015) and Müller and Nishizawa (2017), the main clinical manifestations observed in the respiratory tract include nasal secretions, which can be unilateral or bilateral, with mucopurulent or bloody serous characteristics. Other manifestations include sneezing, abnormal breath sounds, firm subcutaneous volume increase in the nasal bridge, and nasal granulomas that can cause airway obstruction.

Franco *et al.* (2019) report that the classic symptoms of cryptococcosis, which usually affect the front of the nasal cavity, can include nasal deformities such as the well-known "ottoman nose" or "clown nose." These signs are the most commonly observed by guardians and were the reason for seeking clinical care for the patient.

The diagnosis was obtained by screening cytopathology from ulcerated lesions, which according to Calesso *et al.* (2019) and Fernandes *et al.* (2021), is an excellent screening technique for detecting *Cryptococcus* infections. The material collected was stained with rapid panopticon and India ink, showing yeast-like structures compatible with the agent. According to these authors, cytopathology is an excellent and effective diagnostic technique when fungal culture is unavailable.

Histopathological examination using stains such as Periodic Acid Schiff (PAS), Hematoxylin and Eosin (HE), and Grocott-Gomori Silver Methanamine (GMS) was also used for diagnosis, showing moderate, focally extensive mononuclear dermatitis associated with yeasts suggestive of *Cryptococcus* sp. In addition to these stains, Queiroz *et al.* (2008) also describe that special histological stains can be used, such as Alcian Blue, Methenamine Arsenic, Masson-Fontana and the elective Mayer's Mucicarmin.

The definitive diagnosis was obtained from the fungal culture, because, according to Galiza *et al.* (2014), this method is considered the gold standard. Although most of the time the mycological examination is carried out using Sabouraud agar (Kon *et al.*, 2008), in this study, we used Rose Bengal agar with Chloramphenicol at a temperature of around 25 °C 186 for the isolation of yeasts, as this medium inhibits the growth of bacteria, making it possible to isolate the fungal agent individually. Considering that the fungal culture can take several days to produce results, antifungal therapy was started based on the diagnosis obtained through the screening cytopathological examination to increase the patient's chances of a cure.

Although the blood count results showed intense leukocytosis, the hematological and biochemical tests are not indicators of this disease (Queiroz *et al.*, 2008). According to Trivedi *et al.* (2011), abdominal ultrasound changes are generally not observed in animals with cryptococcosis, as described in this case.

In their research, Müller and Nishizawa (2017) described a variety of systemic antifungals that can be used to treat felines with cryptococcosis, such as amphotericin B, ketoconazole, itraconazole and fluconazole. Itraconazole was the antifungal of choice for the treatment of this case, which, according to Faria (2015), is commonly used when there is no central nervous system (CNS) involvement, due to its safety, efficacy and fewer side effects with shorter treatment duration when compared to other antifungals. Also, according to Faria (2015), the dose described is 10 mg/kg, administered orally once a day. As described, the dose and frequency follow the same protocol used in this study, demonstrating consistency in therapeutic practice.

It was possible to observe an increase in ALT levels in the biochemical test results carried out after 15 days of treatment with itraconazole, indicating a possible hepatocellular lesion. This result is in line with the recommendations of Fernandes *et al.* (2021), who highlight the importance of considering the severity of the infection and the patient's condition when using

antifungal drugs, since toxicity to the kidneys and liver should be monitored during the administration of itraconazole.

No central nervous system involvement in the patient was reported, which contributes to a more favorable prognosis; when the CNS is involved, the prognosis for cryptococcosis is usually guarded. Faria (2015) describes that the patient's condition, involvement of the central nervous system (CNS), the existence of immunosuppressive diseases and the guardian's commitment to treatment, which can be long and expensive, determine the prognosis for cryptococcosis.

The cryptococcosis pathogen is not spread by aerosolization from contaminated tissues or secretions. However, the increase in the number of cases in urban environments indicates a risk for people and animals with a healthy immune system and those with immunosuppression (Faria, 2015; Müller; Nishizawa, 2017). Therefore, the guardian was made aware of the importance of this disease in pets and the risk that some mycoses can cause for humans, as well as receiving guidance on hygiene habits and the importance of keeping environments clean to avoid continuous exposure to the fungus.

The distribution of this infection in the national territory gives cryptococcosis considerable importance for single health, given its impact on patients with compromised immune systems. Cryptococcosis is a disease with high morbidity, commonly fatal, with zoonotic characteristics (Müller; Nishizawa, 2017). Considering the important contribution regarding diagnosing *Cryptococcus* sp. infection, identifying the infection early allows for effective treatment, avoiding serious complications such as respiratory and neurological damage.

CONCLUSION

The diagnosis of cryptococcosis based on the screening cytopathology test was decisive for starting antifungal therapy. In addition, confirmation was obtained by culturing the pathogen from infected tissues, considered the gold standard method for diagnosis and histopathology. It is, therefore, important that complementary tests are carried out for effective therapy. Early diagnosis increases the patient's chances of a cure.

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