

Ear damage caused by *Cryptococcus* spp. in guinea pigs: case report

Lesão auricular por *Cryptococcus* spp. em porquinho-da-índia: relato de caso

Daño al oído por *Cryptococcus* spp. en cobayo: reporte de caso

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Abstract

Cryptococcus spp affects mainly dogs and cats, however, there are reports in other animal species, such as guinea pigs. The objective of this study is to report a case of a lesion by cryptococcosis in a guinea pig's auricles. The animal had firm nodules under the touch in both auricles, being one of them with a granulomatous aspect, both ulcerated, with serosanguineous secretion, pain, and associated itching. For the diagnosis, a biopsy was performed for histopathological examination and after a result suggestive of fungal dermatitis by *Cryptococcus* spp., treatment with itraconazole and adjuvant therapy with *Echinacea angustifolia* 6CH and *Carduus marianus* 6CH was initiated, which demonstrated to be effective. Furthermore, we suggest the inclusion of cryptococcosis as a differential diagnosis in cases of auricular lesions in this species.

Keywords: Cryptococcosis; *Cavia porcellus*; Diagnosis; Treatment.

Resumo

Cryptococcus spp acomete principalmente cães e gatos, contudo existem relatos em outras espécies animais, como porquinhos-da-índia. Objetiva-se com este estudo relatar um caso de lesão por criptococose em aurículas de porquinho-da-índia. O animal apresentava nódulos firmes à palpação nas duas aurículas, sendo um deles com aspecto granulomatoso, ambos ulcerados, com secreção serosanguinolenta, dor e prurido associado. Para o diagnóstico foi realizada biópsia para exame histopatológico e após resultado sugestivo de dermatite fúngica por *Cryptococcus* spp., instituiu-se tratamento com itraconazol e terapia adjuvante com *Echinacea angustifolia* 6CH e *Carduus marianus* 6CH, o qual demonstrou ser efetivo. Além disso, sugere-se a inclusão da criptococose como diagnóstico diferencial em casos de lesões auriculares nesta espécie.

Palavras-chave: Criptococose; *Cavia porcellus*; Diagnóstico; Tratamento.

Resumen

Cryptococcus spp afecta principalmente a perros y gatos, sin embargo existen reportes en otras especies animales, como cobayas. El objetivo de este estudio es reportar un caso de lesión por criptococosis en las aurículas de un cobayo. El animal presentaba nódulos firmes a la palpación en ambas aurículas, uno de ellos de aspecto granulomatoso, ambos ulcerados, con secreción serosanguinolenta, dolor y prurito asociado. Para el diagnóstico se realizó biopsia para examen histopatológico y ante resultado sugestivo de dermatitis fúngica por *Cryptococcus* spp., se inició tratamiento con itraconazol y terapia adyuvante con *Echinacea angustifolia* 6CH y *Carduus marianus* 6CH, que resultó ser eficaz. Además, sugerimos la inclusión de la criptococosis como diagnóstico diferencial en los casos de lesiones auriculares en esta especie.

Palabras clave: Criptococosis; *Cavia porcellus*; Diagnóstico; Tratamiento.

1. Introduction

Cryptococcus are organisms found in the environment (Honsho et al., 2003) that can cause primary disease or act as an opportunistic pathogen (Malik & Sykes, 2014). This agent primarily affects dogs and cats, with cats being six to eight times more likely to be infected (Malik & Sykes, 2014). Cryptococcosis has also been reported in other animal species such as cheetahs, mice, foxes, sheep, marmosets, rats, goats, guinea pigs, and koalas (Jungerman & Schwartzman, 1972; Malik et al., 1995).

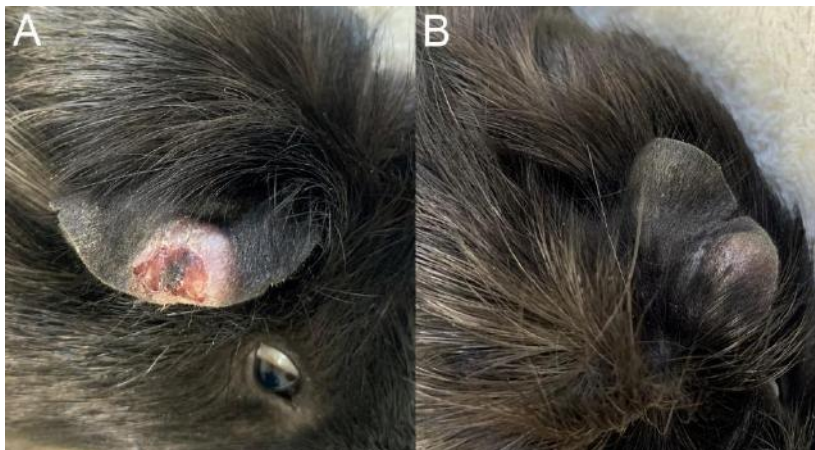
Skin lesions in guinea pigs manifest as nodules, ulcerated or not, in the nasal, eyelid, and ear regions (Van Herck et al., 1988; Lima, 2018; Fernandes, 2020). Other clinical signs found in studies are meningitis (Betty, 1977) and disseminated disease with pulmonary, brain, liver, and splenic involvement described by Riera et al. (1983) in an experimental study.

Given the lack of clinical reports in the literature due to sporadic cases of the disease, the objective of this study is to report a case of fungal dermatitis by *Cryptococcus* spp. in guinea pigs and describe an effective diagnostic and therapeutic method, encouraging veterinarians to include this disease in their differential diagnoses.

2. Case Report

A one year and two-month-old guinea pig was attended at a veterinary clinic in the city of Concórdia, west of Santa Catarina, Brazil, in October 2020. The animal had a lesion in both auricles for about 15 days. It lived in a region close to the forest, with access to the backyard. In the physical evaluation, there was development of nodules and moderate ulceration was noted in the right ear nodule (Figure 1). The biopsy was chosen for histopathological examination. For the procedure, the animal was submitted to anesthesia using 40 mg/kg of ketamine associated with 2 mg/kg of midazolam applied subcutaneously, with subsequent maintenance in an isoflurane mask. After the procedure, meloxicam 0.2 mg/kg was prescribed once a day for 3 days, dipyron 25 mg/kg twice a day for 5 days, both orally, and topical ointment based on chloramphenicol, retinol, amino acids, and methionine (Regencil®). Ten days after the biopsy, the nodules increased, the ulceration of the right auricle aggravated and became a granulomatous appearance, and the nodule in the left auricle ulcerated moderately, both of which began to drain serosanguineous secretion (figure 2), with pain and itching reported by the tutor. Faced with this condition, enrofloxacin was prescribed at a dose of 10 mg/kg every 12 hours for 7 days, meloxicam 0.2 mg/kg once a day for 5 days, and vitamin C 100 mg/kg a day for an undetermined period until additional recommendations. Such medications were prescribed orally.

Figure 1. A: Right auricle with ulcerated nodule. B: Nodule in left auricle.



Source: Authors.

Figure 2. A: Right auricle with ulceration aggravation and granulomatous formation. B: Left auricle with increase in size and ulceration.

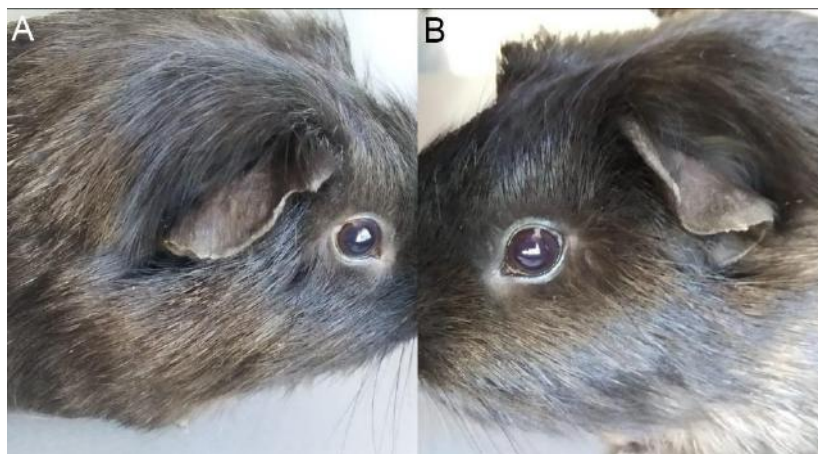


Source: Authors.

In the histomorphological analysis, superficial and deep dermis were observed with a marked infiltrate composed predominantly of macrophages, forming nodules outlined by epithelioid macrophages and sometimes associated with discrete multinucleated giant cells. Macrophages had ample vacuolar cytoplasm and sometimes contained rounded yeast-like structures measuring 2 to 4 micrometers with a peripheral pale-colored halo and nuclei with loose chromatin. The epidermis revealed moderate acanthosis, intraepidermal pustules and superficial serosanguineous content. Thus, the report indicated fungal granulomatous dermatitis, suggestive of *Cryptococcus* spp.

Upon the diagnosis, a protocol was started with itraconazole at a dose of 10 mg/kg orally, once a day, during a period of 6 months, with monthly reassessments. As an adjuvant therapy, oral homeopathics based on *Echinacea angustifolia* at 6CH potency were prescribed for 10 days as an immunity stimulant, and *Carduus marianus* at 6CH potency throughout the treatment with itraconazole, acting as a hepatic protector. Furthermore, the use of vitamin C was maintained during the treatment period. The lesions completely reduced, with successful treatment. Figure 3 shows the animal at the end of the treatment.

Figure 3. A and B: Right and left auricles at the end of the treatment, after 180 days.



Source: Authors.

3. Discussion

The occurrence of cryptococcosis in guinea pigs is rare since there are few clinical descriptions, such as those made by Betty (1977), Van Herck et al. (1988), Lima (2018), and Pastor et al. (2021), who reported meningitis, nodules in the nose and eyelid, respectively. In a report made by Fernandes (2020), the animal had a lesion in the nose, conjunctiva, auricle, and another lesion located between the auricle and eye. Carvalho, Paula, and Kanayama (2017), in addition to skin lesions, reported respiratory complications that led to the animal's death. Another systemic description of the species was made by Brandes et al. (2003), in which the animal presented neurological symptoms in the form of opisthotonos and ataxia, and after it died.

In cats, the most common species, cryptococcosis has different clinical forms (Pennisi et al., 2013). Comparing the species, the nasal form, which is more common in cats, presents as nodules that follow with deep ulceration and a mucopurulent or bloody appearance (Pennisi et al., 2013), like reports made in guinea pigs (Van Herck et al., 1988; Fernandes, 2020). Furthermore, they may present neurological symptoms such as convulsions (Pennisi et al., 2013, Vercelli et al., 2021), as described by Brandes et al. (2013), and the cutaneous form is characterized by non-pruritic and non-painful nodules (Pennisi et al., 2013), different from what we found in the present report and in the description made by Lima (2018), in which the animals presented itching and painful sensitivity.

In humans, cryptococcosis is one of the most common opportunistic diseases in immunosuppressed patients (Shourian & Qureshi, 2019) and patients who have experienced organ transplantation or who are affected by lupus, cancer, and diabetes (Maziarz & Perfect, 2016; Ponzio & Chen, 2019; Yehia & Eberlein, 2009). Thus, due to the importance in human medicine, studies in guinea pigs with the purpose of the experimental model are also developed, such as the studies carried out by Riera, Masih, and Nobile (1983), Van Cutsem et al., (1987), Kirkpatrick et al. (2007) and Diamond (1977).

The evolution of the lesion in the present report was followed by firm nodules under the touch, one of them with a granulomatous appearance, ulcerated, draining serosanguineous secretion, with associated pain and itching. In the report made by Lima (2018), the eyelid lesion did not have ulceration, but it also had a nodular and firm appearance. In the report made by Van Herck et al. (1988), the lesion had severe granulomatous proliferation and ulceration in the dorsal region of the nose, and Fernandes (2020) reported a prominent and hyperemic lesion without secretion in the nasal region, and an ulcerated nodule at the base of the auricle. By comparing the different works, it is possible to observe that the aspects of the lesions caused by *Cryptococcus* spp. have some similarities, regardless of the affected site.

As for the diagnosis, the method chosen for the case was biopsy for histopathological examination. In the report described by Van Herck et al. (1988), the authors also used this technique, but the material collection was performed only during necropsy. Fernandes used cytopathological and histopathological examination. In the report by Lima (2018), cytopathology, fungal culture, Polymerase Chain Reaction (PCR) were used to confirm the species and sequencing from a tissue biopsy. Thus, it is demonstrated that several techniques can be used for the diagnosis of cryptococcosis in the species and the histopathological examination is a precise methodology for the diagnosis, as demonstrated by Van Herck et al. (1988), Fernandes (2020), and in the present report.

The animal treatment reported in this study, using itraconazole at a dose of 10 mg/kg, proved to be effective. This active ingredient was also used in the case described by Lima (2018), however at a dose of 15 mg/kg, which also obtained excellent results. Van Herck et al. (1988) used griseofulvin at a dose of 50 mg/kg, but even with this therapy, the lesions aggravated and entered the nose, thus suggesting that itraconazole should be the chosen medication for the treatment of cryptococcosis in guinea pigs.

Due to the long period of use of the antifungal, it was decided to administer *Carduus marianus* in 6CH potency together as a liver protector. Lima (2018) used silymarin as a liver protector, which is the main component of *Carduus marianus* (Souza et al., 2012) used in this work. According to Rambaldi et al. (2005), this compound has been used since

ancient times to treat several liver diseases and to protect the organ against chemical toxins. Although no specific exams were performed for liver evaluation during treatment, it was possible to verify that the animal did not present clinical symptoms that indicated liver alterations, demonstrating the effectiveness of the homeopathic compound.

Due to the lesion being in the auricle, the first clinical suspicion was leishmaniasis, in which *Leishmania enriettii* is the species that affect guinea pigs (Paranaíba et al., 2017). Lesions in the auricles caused by leishmaniasis are nodular and ulcerated (Thomaz-Soccol et al., 1996; Ecco et al., 2000), as in the animal in the present report. The histopathological examination can be used both for the diagnosis of cryptococcosis and for leishmaniasis and, therefore, effective for use against auricular lesions in guinea pigs, thus excluding differential diagnoses. Another way of diagnosing for both diseases is the cytology, which is a simple, low-cost technique that provides quick results. If cytology does not provide accurate results, the histopathological examination should be used for a definitive diagnosis.

4. Conclusion

Through this report, it is possible to affirm that the histopathological examination was effective for the cryptococcosis diagnosis and the use of itraconazole for 180 days was effective for the treatment in this case. Furthermore, we propose the inclusion of cryptococcosis as a differential diagnosis in cases of ear lesions in guinea pigs, mainly in the southern region of Brazil, where leishmaniasis occurs in the species, demonstrating that it is essential to carry out complementary exams in the clinical routine previously to the establishment of therapy.

It is suggested that in future reports, molecular tests are carried out to confirm the species of *Cryptococcus*. This is because *Cryptococcus neoformans* is an opportunistic pathogen and *Cryptococcus gattii* is a primary pathogen, thus having a direct influence on aggressiveness and treatment time.

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