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Disseminated *Scytalidium* infection in a German shepherd dog

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ABSTRACT

We report a systemic mycosis in a German shepherd dog caused by *Scytalidium* spp. The patient presented for progressive cervical pain and forelimb hemiparesis. Cervical computed tomography revealed lysis associated with multiple vertebrae and a soft tissue mass adjacent to the spinal cord, as well as prescapular lymphadenopathy. Fine needle aspirates of the lymph nodes yielded hyphae, and a subsequent culture obtained a *Scytalidium* spp. Itraconazole therapy was initiated, but the subject was euthanized three months later due to progressive neurologic disease and discomfort. This appears to be the first report of disseminated disease by this species in veterinary medicine.

1. Introduction

In veterinary medicine, numerous mycotic agents have been reported to cause systemic infections, often affecting the central nervous system [1–6]. German shepherd dogs appear to over-represented in this subset of veterinary literature, and are reportedly predisposed to opportunistic fungal infections [2]. In current literature, a case of systemic infection cause by *Scytalidium* species has not been reported in veterinary medicine.

In humans, several subspecies of *Scytalidium* including *Scytalidium hyalinum* and *Neoscytalidium dimidiatum,* have been documented as responsible for human cases of dermatomycosis, infections that mimic dermatophytosis [7]. *Scytalidium* infections occur in the feet and nails of people walking barefooted in contaminated soil in tropical countries such as Thailand, Nigeria, Australia, and Jamaica. Rare systemic infections have been reported involving central nervous system abscesses, endopthalmitis, sinusitis, osteomyelitis, mycetoma, subcutaneous lesions, and disseminated infections, usually in immunocompromised or immunosuppressed patients [7]. These fungi show a high resistance to antifungal drugs used most commonly in human and veterinary medicine [8].

We describe a case of disseminated mycosis leading to progressive cervical pain and forelimb hemiparesis in a German shepherd dog caused by *Scytalidium* spp.

2. Case

A four-year-old intact female German shepherd dog was referred to the surgery center for a month long history of cervical pain and progressive forelimb hemiparesis. On initial physical exam (day 0), she was found to have mildly delayed proprioceptive placing in her right pelvic limb. No cervical or spinal pain was elicited. The remainder of her physical exam was unremarkable. She had been treated with steroids by the primary veterinarian, and was initially responsive, but had begun to exhibit mild neurologic dysfunction in her forelimbs (stumbling and mild toe scuffing) in the week prior to presentation. She was hospitalized for diagnostics performed under general anesthesia. Pre-anesthetic blood work was within normal limits.

Computed tomography (CT) of the patient's cervical spine showed lysis of the endplate with active periosteal reaction of the ventral aspect of the fourth vertebral body (*C*4) (Fig. 1). Similar lysis was noted in the end plates of the fifth and sixth vertebral bodies (*C*5 and *C*6). A soft tissue mass was noted along the left lateral aspect of the vertebral canal through the body of *C*5 (Fig. 2). The soft tissue did not overlie an intervertebral disc space, but did cause dorsal and lateral deviation of the spinal cord. No other areas of compression were noted. Severe symmetrical bilateral pre-scapular lymphadenopathy and moderate bilateral retropharyngeal lymphadenopathy were also present (Fig.3).

Following imaging, the initial primary differential diagnosis for the patient's condition was metastatic neoplasia, based on the combination of the soft tissue mass adjacent to the spinal cord and the generalized lymphadenopathy. Secondary consideration was

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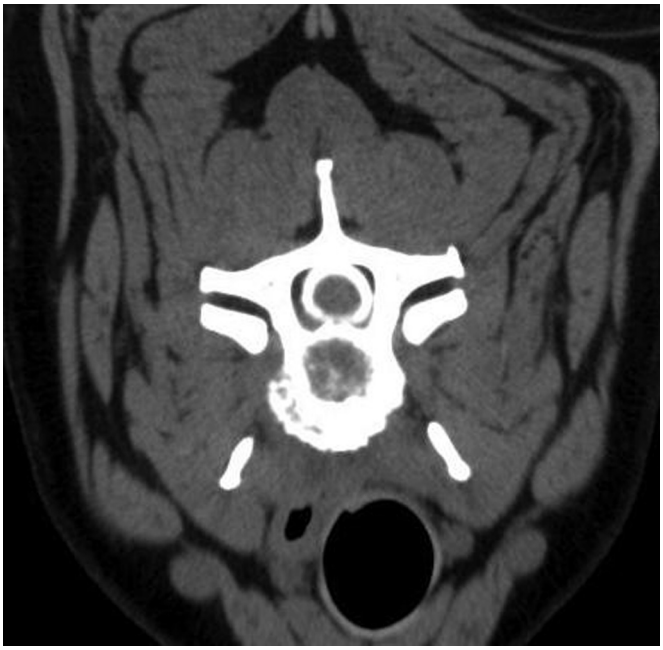

Fig. 1. CT image showing lysis associated with the endplate of the fourth cervical vertebra.

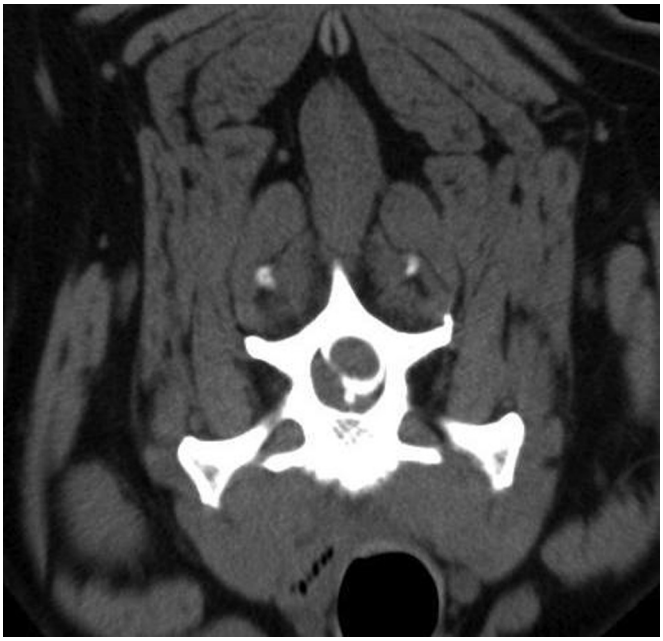

Fig. 2. CT image showing a soft tissue mass effect in the vertebral canal along the body of the fifth cervical vertebra.

given to discospondylitis with associated reactive lymph nodes, though the presence of a soft tissue mass is not a typical finding in patients with discospondylitis. All CT and myelogram images were submitted for review by a board certified radiologist. Cerebral spinal fluid (CSF) and aspirates from the pre-scapular lymph nodes were sent for cytologic evaluation. The patient was discharged the following day (day +1) with carprofen 2.2 mg/kg PO twice daily (BID) and tramadol 3 mg/kg PO three times daily (TID) for palliative care pending cytology results.

CSF analysis was cytologically unremarkable. The pre-scapular lymph node aspirates were indicative of systemic fungal infection, yielding moderate reactive lymphoid hyperplasia with mild to moderate pyogranulomatous inflammation containing

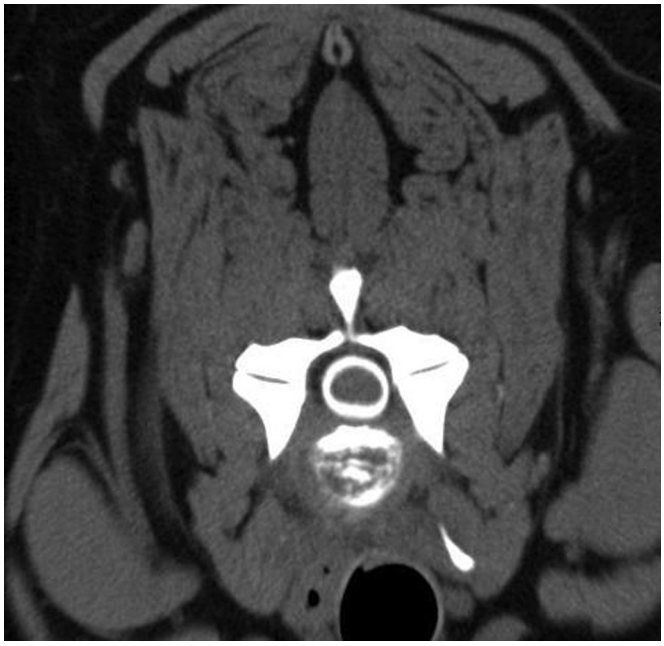

Fig. 3. CT image showing enlarged pre-scapular lymph nodes and lysis associated with the endplate of the sixth cervical vertebra.

intralesional fungal hyphae (Fig. 4). Based on cytology results, a second lymph node aspirate sample was submitted for fungal culture. Itraconazole therapy was initiated at 5 mg/kg PO BID, and gabapentin 5 mg/kg PO TID was added for additional pain control (day +5).

The lymph node aspirate was plated on four different fungal culture media: Sabouraud's dextrose agar, potato dextrose agar, mycobiotic agar, and trypticase soy agar with 5% sheep blood. Plates were incubated at 25 °C. After 7 days of incubation, a pure culture of fine, filamentous fungal growth was observed on the Sabouraud's dextrose, potato dextrose, and blood agars, while no growth was observed on the mycobiotic agar. By the sixteenth day of incubation, the three agars on which the fungal isolate grew were covered with dark gray to black wooly growth. The isolate was completely inhibited by the mycobiotic agar. Microscopic examination of a wet mount of the fungal hyphae revealed the formation of chains of arthroconidia.

DNA sequencing was performed on an approximately 475-base

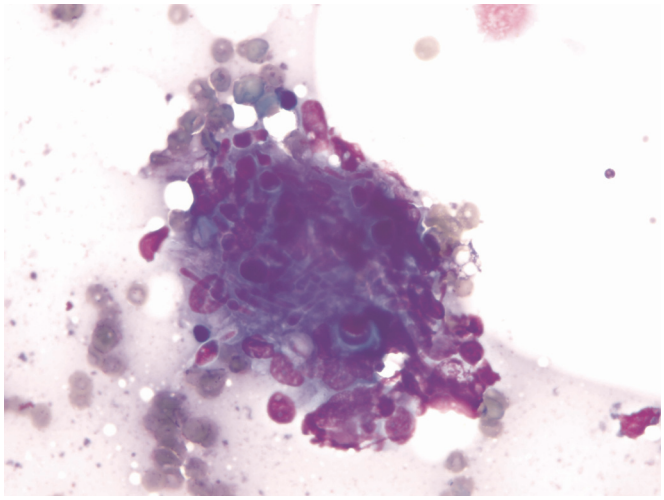

Fig. 4. Large, multinucleated macrophages containing hyphal structures. Hemophyllin and eosin (100x).

pair fragment of the intergenic transcribed spacer (ITS) region of the 18S ribosomal subunit. 5.0 μl of extracted DNA was amplified in a 25 μl reaction volume with 20 μl of PCR master mix containing ITS forward primer 5′-tccgta ggt gaa cct gcg g-3′ and ITS reverse primer 5'-tcc tcc gct tat tga tat gc-3′. Reactions were performed on a 9700 Thermocycler GeneAmp PCR System (Applied Biosystems, Carlsbad, California 92008, USA). Cycle sequencing on purified products was performed on a 3130 Genetic Analyzer (Applied Biosystems). Sequence data analysis was performed with the use of Geneious Pro software (Biomatters Ltd., Auckland 1010, New Zealand). A BLAST search of the ITS sequence data in Genebank at the NCBI website (http://www.ncbi.nlm.nih.gov/BLAST/) revealed 95% identical sites with *Scytalidium lignicola*; the next closest match was 88.4% identity with *Scytalidium cuboideum*. The morphologic evaluation combined with the molecular analysis led to the conclusion that an undetermined species of *Scytalidium* had been isolated from the lymph node aspirate.

Three weeks after starting itraconazole and gabapentin therapy (day +21), the owner reported that the patient was comfortable, and seemed improved neurologically. Regrettably, three months (approximately day +60) after initiating antifungal therapy, the patient was euthanized due to declining neurologic status and comfort.

3. Discussion

There are more than 15 species of *Scytalidium* listed, though only two are significantly associated with human pathology – *S. hyalinum* and *N. dimidiatum* [7]. The pathogen generally causes superficial infections similar to dermatophytosis in the nail beds and skin of people living in tropical regions (Africa, South America, the Caribbean, and parts of Asia) who come in contact with contaminated soil. Recently, more cases of scytalidiosis have occurred in humans living in temperate countries, likely secondary to increased travel and immigration [7]. Prevalence in endemic areas ranges from 9 to 24% [8]. Deep or systemic infections are rarely reported in human literature, but can occur in immunocompromised patients. Manifestations of systemic disease include central nervous system abscesses, endophthalmitis, sinusitis, and osteomyelitis [7]. Diagnosis is achieved via fungal culture of the affected area. According to Machouart et al. (2013), there is not a standardized therapy for treatment of *Scytalidium* spp. since the organism is resistant to most topical or systemic antifungal agents used in human dermatology [7,8].

In the case presented, the patient had no known travel history to an endemic, or tropical, region. She was not considered immunocompromised prior to diagnosis, though she was a breed considered predisposed to opportunistic fungal infection. Her clinical signs and diagnostic imaging results were consistent with other case reports of dogs with vertebral osteomyelitis, spinal cord compression, and lymphadenopathy secondary to systemic fungal infection [1–6]. Unsurprisingly, considering the reported resistance of *Scytalidium* to antifungals, itraconazole therapy was not successful.

In conclusion, the case report describes *Scytalidium* spp infection causing vertebral lysis and spinal cord deviation leading to progressive cervical pain and forelimb hemiparesis. Treatment was not successful; leading to the suggestion that further diagnostics involving antifungal therapy targeted at *Scytalidium* is warranted. To the author's knowledge, this is the first report of systemic mycotic infection caused by *Scytalidium* spp. in veterinary medicine.

4. Conflict of interest

None of the authors declare conflict of interest pertaining to this case report.

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