Case Report: Spinal Meningitis Associated with *Streptococcus suis* Infection in a Cat

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ABSTRACT

A 7-year-old, castrated male, Persian cat was presented to the hospital with acute onset of extreme reluctance to move. The cat lived strictly indoors, with no contact with other animals. It was fed exclusively a commercial kibble. Severe mid lumbar back pain and extreme reluctance to move were the only abnormalities on physical and neurological examinations. Blood test abnormalities included mild lymphopenia and mildly increased serum creatinine kinase activity. Thoracic and lumbar survey radiography and magnetic resonance imaging (MRI) were unremarkable. Cerebrospinal fluid (CSF) analysis showed marked neutrophilic pleocytosis. CSF culture yielded pure growth of *Streptococcus sui*s, sensitive to all antibiotics tested, excluding azithromycin. Pending CSF culture results, the initial treatment included intravenous clindamycin and ceftriaxone. After four days, the cat showed hypersalivation, vomiting and inappetence. Based on bacterial culture and sensitivity results, oral amoxicillin-clavulanic acid and cefpodoxime were prescribed. Three weeks after presentation, the cat had only mild inappetence, but was neurologically normal. A repeat CSF analysis two months post-discharge was normal. At that point antibiotic treatment was discontinued. *S. suis* is an uncommon causative infective agent of meningitis in cats, however, it should be considered as such, even when there is no historical evidence of exposure to pork or swine-related remains. The favorable outcome of this case was probably due to the very short lag of time from onset of clinical signs to the administration of aggressive antibiotic treatment, the overall good health status of this cat, and possibly low bacterial virulence.

Keywords: Feline; Cerebrospinal fluid; Spinal cord; Zoonosis; Neutrophilic pleocytosis.

INTRODUCTION

Streptococcus suis infection is a major disease in pigs, causing meningitis, septicemia, arthritis, pneumonia, and endocarditis (1, 2). Although historically considered an important pathogen exclusive to pigs, over the last decades, it has been increasingly isolated from a wide range of other mammalian species, including lambs, horses, dogs, cats and humans, as well as from birds (3-9). A single case of *S. suis* meningoencephalitis, manifested by neurological signs, and diagnosed at necropsy, was previously described in a cat (10).

This report describes a case diagnosed *ante mortem* of spinal meningitis associated with *S. suis* infection. To the authors' knowledge, this is the first report of such a case, which has been successfully treated.

CASE REPORT

A 7-year old, castrated male, Persian cat was presented to the hospital due to acute onset of reluctance to move that had started 24 hours prior to presentation. The cat lived exclusively indoors and had no contact with other animals. It was solely fed a dry feline commercial kibble. There was no history of trauma prior to the onset of the clinical sings.

Physical and neurological examinations revealed reluctance to move and severe mid lumbar spinal pain. Based on these findings, a lesion affecting the lumbar meninges and (or) the spinal cord was suspected.

Complete blood count (CBC; Advia 2120i, Siemens, Erfurt, Germany) showed mild lymphopenia ($0.94x10^3/\mu L$; reference interval [RI]: $2.0\text{-}7.2x10^3/\mu L$). Stained (modified Wright's staining solution) blood smear examination revealed mild neutrophilic left shift, mild neutrophil cytoplasmic toxicity (mild Döhle body formation) and some giant platelets. Serum chemistry (Cobas 6000, Roche, Manheim, Germany; at 37°C) showed mildly increased creatine kinase activity (340 IU/L; RI, 73-260 IU/L), mild hyponatremia (142 mmoL/L; RI, 145-158 mmoL/L) and mild hypochloridemia (107.3 mmoL/L; RI, 110-126 mmoL/L). Thoracic and lumbar survey radiographs were unramarkable.

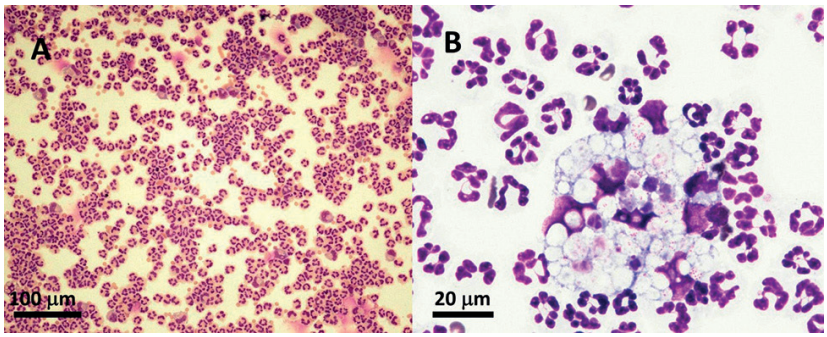

Figure 1: Cytology of cyto-centrifuged cerebrospinal fluid from a cat with spinal meningitis associated with *Streptococcus suis* infection. A. Note the severe suppurative inflammation, manifesting predominantly neutrophilc pleocytosis. Occasional monocytes may be seen as well (Modified Wright's stain; original magnification X200). B. Marked neutrophilic pleocytosis. A cluster of highly reactive macrophages phagocytizing neutrophils can be seen in the center of the image (Quick Romanowsky stain; original magnification X600).

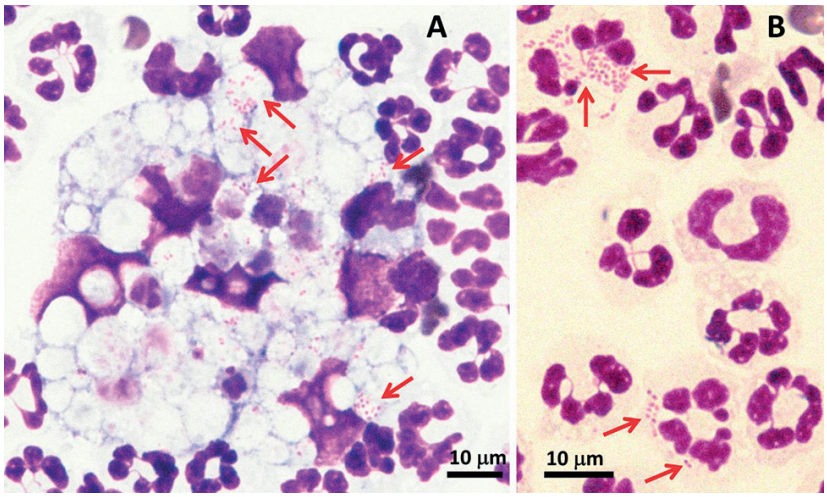

Figure 2: Cytology of cyto-centrifuged cerebrospinal fluid from a cat with spinal meningitis associated with *Streptococcus suis* infection. A. A cluster of highly reactive macrophages can be seen in the center of the image. The macrophages show phagocytosis of cellular elements, most probably neutrophils. Intracellular bacterial cocci can be seen (red arrows) (Quick Romanowsky stain; original magnification X600). B. Note the intracellular bacteria within neutrophils (red arrows) (Modified Wright's stain; original magnification X1000).

Magnetic resonance imaging (MRI; Siemens Magnetom C 0.35T, Siemens Medical Systems, Germany) was performed, from spinal vertebrae T3 to S3, with transverse, sagittal and dorsal planes, T1-weighted (pre- and post-contrast) and T2-weighted sequences. The images obtained did not show any abnormality.

Lumbar puncture cerebrospinal fluid (CSF) analysis revealed mild iatrogenic blood contamination, with marked pleocytosis (total cell count [TCC], 2880 cells/µL; RI, <5; Figure 1) and increased protein concentration (72 mg/dL; RI, ≤25). Cytological CSF examination showed marked neutrophilic pleocytosis (90% of nucleated cells), with some reactive macrophages (8%) and reactive monocytes (2%). Intracellular cocci within neutrophils and macrophages were occasionally observed (Figure 2). The CSF was sent for bacterial culture and sensitivity.

A CSF sample was injected into pediatric blood culture bottle (BACTEC™ Peds Plus™; Becton Dickinson, Sparks, NV) and incubated (BACTEC™ FX unit; Becton Dickinson, Sparks, NV). Positive growth was detected after two days, flagged positive by the BACTEC FX unit.

Table 1: Antimicrobial susceptibility of the *Streptococcus suis* strain isolated from the cerebrospinal fluid of cat with suppurative meningitis.

Antibiotic	Susceptibility	MIC (mcg/mL)
Ampicillin	S	0.016
Amoxicillin-Clavulanic Acid	S	
Cefuroxime	S	
Ceftriaxone	S	
Penicillin G	S	0.016
Erythromycin	S	
Clindamycin	S	
Vancomycin	S	
Sulfamethoxazole-Trimethoprim	S	
Tetracycline	S	
Azithromycin	R	1.5
Chloramphenicol	S	

MIC, minimal inhibitory concentration; S, sensitive; R, resistant.

Direct microscopic Gram staining showed presence of Gram-positive cocci. Samples were cultured on 5% sheep blood, Columbia CNA, CDC anaerobic blood (HyLab, Rehovot, Israel), chocolate, MacConkey and CDC anaerobic Blood+gentamycin (NOVAmed, Jerusalem, Israel) plates. After 24hr of incubation at 35˚C, in presence of 5% CO_2, small gray-white α-hemolytic, catalase-negative colonies were observed. Bacterial identification was performed directly from the colonies by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry (VITEK MS, BioMerieux, Marcy l'Etoile, France). The bacteria were identified as *S. suis*. Antimicrobial susceptibility testing was performed both directly on the positive blood culture, and on the next day, from colony suspension as well, according to Clinical and Laboratory Standards Institute (CLSI) guidelines (11). The *S. suis* isolate was sensitive to all antibiotics tested, excluding azithromycin (Table 1).

The history, clinical signs and CSF analysis results were consistent with bacterial meningitis. The cat was hospitalized (day 1), and intravenous lactated Ringer's solution (Teva Medical, Ashdod, Israel) was administered (at 10 ml/kg/h). Intravenous clindamycin (clindamycin Injection, Rafa Laboratories, Jerusalem, Israel; 15 mg/kg IV q12h) and ceftriaxone (Pan-ceftriaxone, Panpharm Laboratoires, Luitre, France; 7 mg/kg IV q12h) treatment was initiated, pending bacterial culture results. After 48 hours, IV clindamycin was switched to oral therapy (Dalacin C, Pfizer, Cisse-sur-Poce, France; 17 mg/kg PO q12hs) and ceftriaxone therapy was substituted with oral cefpodoxime-proxetil (Simplicef, Zoetis Inc., Sandoz Kundl, Austria; 17 mg/kg q24hs). On day 4, the cat showed hypersalivation, inappetence, one vomiting episode and moderate lumbar spinal pain. Abdominal ultrasonography was unremarkable. Repeat CBC showed marked absolute eosinophilia ($3.9x10^3$/μL; RI, 0.3-1.7 $x10^3$/μL) that was confirmed by blood smear examination.

When the above-mentioned bacterial culture and sensitivity results became available, clindamycin was then discontinued, and substituted with amoxicillin-clavulanic acid (Synulox, Zoetis, Latina, Italy; 17 mg/kg PO q12h) while cefpodoxime-proxetil was continued. Mirtazapine (generic, Teva, Petach-Tikva, Israel; 1.25 mg q24h PO for 3 days) and omeprazole (generic, Teva, Petach-Tikva, Israel; 1 mg/kg PO q24h for 3 days), were also administered. The cat markedly improved clinically, and showed moderate appetite and mild back pain and was discharged on day 6.

The cat was rechecked three weeks post discharge. Although it has not regained normal appetite, it was bright, alert and responsive, with no back pain signs. The above-mentioned antibiotic treatment was continued for four additional weeks. Upon reexamination, two months post presentation, the cat appeared completely normal. Physical and neurological examinations were both unremarkable. A second lumbar CSF tap was performed. The cytological examination was suggestive of a moderate iatrogenic blood contamination (TCC, 1000 cells/μL), but infection and inflammation were ruled out based on presence of very few mononuclear cells and absence of neutrophils, while the CSF protein concentration was only marginally increased (31 mg/dL). The antibiotic treatment was then discontinued. On reexamination two weeks later, the cat was neurologically normal. One year after its first presentation to the hospital, on a telephone interview, the owner had reported that the cat was completely healthy.

DISCUSSION

Streptococcus suis is an important pathogen in the swine industry, and is prevalent worldwide (12). Nevertheless, reported infections in other mammals and birds are limited to few isolated case reports (3-5, 8, 9). *S. suis* is transmitted among pigs both vertically and horizontally (13). Vertically, *S. suis* infections may be transferred from sow to piglets during parturition colonizing the piglet's tonsils. Horizontal transmission among pigs is presumed to occur mainly via

the respiratory (oro-nasal) route, by contact between infected and uninfected pigs (13, 14). Nevertheless, other infection routes, such as gastrointestinal, are suspected, but have yet to be proven (12, 13, 15).

S. suis has been isolated from tonsillar swabs of clinically healthy cats, dogs and horses, and in cats with pleuropneumonia and moist dermatitis (3, 4). One previous report has described the potential central nervous system pathogenicity of *S. suis* in cats. Severe *S. suis* meningoencephalitis was described in a Carthusian cat that was submitted for necropsy after 15 days of fever, anorexia, weakness and ataxia (10).

This case, to the best of the authors' knowledge, is the first report of spinal meningitis associated with *S. suis* infection in a cat. Previously, myelitis has been reported in pigs, sheep and humans, following septicemia (2, 16, 17). However, septicemia seemed highly unlikely in the present cat, because the only clinical signs that it had presented were reluctance to ambulate and lumbar spinal pain, however without significant signs of severe systemic illness. The leukocyte count was unremarkable, although mild neutrophilic cytoplasmic toxicity was noted at presentation. The absence of other neurological abnormalities suggested that the infection involved mainly the meninges. Although the presence of an additional infective agent that could not be cultured from the CSF cannot be entirely ruled out, the pure CSF culture of *S. suis* obtained, with absence of other infectious agents in the cytological examination of the CSF, were highly suggestive that this bacterium was the chief, and very likely, the sole causative agent of the meningitis and clinical signs in this cat.

In humans, MRI is considered the modality of choice for the radiological diagnosis of spinal meningitis or empyema, with 91% sensitivity (18, 19). The characteristic MRI findings include hyperintense extradural lesion on T2-weighted images, contrast enhancement after intravenous injection of gadolinium-based agent on T1-weighted images, and changes in adjacent tissues (e.g., discospondylitis, epaxial muscle changes and sinus tracts) (18-21). Similar MRI changes have been described in empyema cases in dogs and cats (22-27). In our case, the very short disease course, from the onset of the initial clinical signs to the time the MRI imaging was performed, likely accounted for the lack of MRI abnormalities. Furthermore, the small size of our patient likely contributed to suboptimal images on our low-field MRI, so that subtle, undetectable radiological changes might have been present.

The CSF analysis results in this case were indicative of severe bacterial suppurative meningitis. Clindamycin and ceftriaxone were selected as the initial antibiotics because of their wide volume of distribution and ability to penetrate the blood-brain barrier (28). This was considered important for preventing further dissemination of the infection to other spinal cord segments. Anorexia, hypersalivation and vomiting that were noted in this cat were assumed to be adverse effects of clindamycin therapy in cats (29, 30). Indeed, once oral clindamycin was discontinued, the cat's appetite had improved, and hypersalivation and vomiting did not recur. Clindamycin, which was an empirical choice, was replaced later on with amoxicillin-clavulanic acid, and the third generation cephalosporin therapy that has been administered as well has been maintained (through cefpodoxime therapy). This empirical choice of antibiotics proved to be appropriate based on the bacterial sensitivity results, and therefore, this therapy was administered.

Interestingly, a repeat CBC, performed on day 4, showed marked absolute eosinophilia, which was not present upon admission. Eosinophilia is most commonly associated with parasitic, hypersensitivity and neoplastic disorders, while in acute bacterial infections, eosinopenia is more commonly observed. Nevertheless, eosinophilia has already been described in bacterial infections, particularly, in cases of infections with *Streptococcus* spp. and *Staphylococcus* spp. (31).

In this case, it was impossible to characterize the precise *S. suis* strain and examine its virulence characteristics, but it is reasonable to assume that it had moderate virulence, which possibly played part in the overall favorable response to therapy. Other factors that may have played roles in this favorable outcome are the short disease course from onset of clinical signs to the initiation of aggressive, broad-spectrum intravenous antibiotic therapy and the good overall general condition of this cat.

This particular cat and its owners had no apparent history of exposure to pigs, a farm environment, or swine-based diet (e.g., raw pork). Its diet was exclusively a feline commercial one, and the cat lived strictly indoors. Although in most *S. suis* infections in humans, patients were either exposed to pigs through their occupation or had consumed raw pork (32-34), while in few cases, such exposures were absent, and the infection source remained unclear (35-37). Similarly, in two young lambs with polyserositis, arthritis and endocarditis due to *S. suis*, the infection source remained unknown (7). The transmission routes of *S. suis* vary (14). While among pigs

its transmission is considered mostly through the oro-nasal route, in humans, several exposure routes are considered possible, including oral and respiratory routes, as well as through cutaneous contact with infected lesions (35, 38). We therefore postulate that similarly to what is now assumed in human medicine (13, 14, 38), it is reasonable that some animals, including cats, may be healthy *S. suis* carriers, and potentially develop clinical infection only under special circumstances (e.g., stress, immunosuppression and comorbidities), and if so, such carrier animals might serve as reservoirs, posing health risks for other animals and humans.

In conclusion, *S. suis* is an uncommon infective cause of meningitis in cats. CSF cytological analysis and bacterial culture were useful in the *ante mortem* diagnosis of the infection. The relatively short disease course prior to presentation, the general good condition of this particular cat, the prompt, aggressive intravenous antimicrobial treatment and possibly, a moderate virulence of this specific *S. suis* strain, all contributed to the observed favorable outcome. *S. suis* should be considered among the potential infective agents in cases of meningitis and encephalomyelitis in cats, even when proven contact with pigs or swine meat products or remains, is absent in the history. The zoonotic potential of such infection of cats should not be overlooked.

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