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Successful medical management of a domestic longhair cat with subdural intracranial empyema and multifocal pneumonia

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Running title: Medical management of subdural empyema in a cat
Abstract

Objective: To describe a case of successful medical management of subdural intracranial empyema and multifocal pneumonia in a domestic longhaired cat.

Case Summary: A 7-year-8-month-old male neutered domestic longhair cat presented with tachypnea, respiratory compromise, vestibular ataxia, obtundation, left-sided head tilt and multiple cranial nerve deficits. Neuroanatomical localisation was multifocal with central vestibular involvement. Magnetic resonance imaging (MRI) of the head indicated diffuse subdural empyema, mainly affecting the middle cranial fossa and the right cerebrum. Analysis of cerebrospinal fluid revealed degenerate neutrophils with a mixed population of intracellular bacilli. Computed tomography (CT) of the thorax was suggestive for multifocal pneumonia. Aggressive medical management with IV fluids, oxygen supplementation, mannitol boluses, dexamethasone, and broad-spectrum antibiotics was started. The cat demonstrated gradual improvement within 24 hours of starting treatment. General physical and neurological examinations nine weeks after initiating treatment did not reveal any abnormalities. A CT examination performed at this time revealed resolution of the cat’s pulmonary lesions. The cat was still free of clinical signs nine months after treatment was started.

New or unique information provided: Subdural empyema is infrequently reported in cats and has high mortality rates even following surgical treatment. This is the first reported case of successful medical management of a cat with subdural empyema and suggests that aggressive medical management should be attempted in cats that are not considered surgical candidates.

Key words: brain abscess, bacterial meningitis, MRI, CT, antibiotics, corticosteroids
Introduction

Bacterial infection of the central nervous system (CNS) in cats is rare and can arise from multiple sources including direct extension from adjacent structures, inoculation via bite wounds, trauma or iatrogenic means.\textsuperscript{1-5} Although haematogenous spread from distant foci and migration of foreign bodies can also occur, these routes of intracranial infection have not yet been reported in cats.\textsuperscript{6-10} Bacterial infection can result in diffuse meningoencephalomyelitis as well as focal parenchymal abscesses and empyema in epidural or subdural spaces.\textsuperscript{4,6} Reports of subdural empyema are limited with only six reports in cats.\textsuperscript{1,3,6} Prognosis is considered poor and even with aggressive surgical and medical treatment mortality rates are reported to be as high as 75\%.\textsuperscript{1,3,6} This report describes the first case of successful medical management of subdural empyema and multifocal pneumonia in a cat.

Case description

A seven-year and eight-month-old, 3.9 kg, male neutered domestic longhair cat presented following a three-week history of weight loss (0.8 kg) and a four-day history of progressive lethargy and inappetence. In the 48 hours before presentation the cat developed a worsening generalized ataxia and obtundation. General physical examination revealed the cat to be normothermic (38.3\(^\circ\)C) with a grade II/VI left apical systolic heart murmur. The cat was tachypnoeic with increased respiratory effort and right-sided serous ocular and nasal discharge. No lesions were noted in the oropharyngeal cavity and both ear canals were clear with visible intact tympanic membranes. Neurological examination revealed mild obtundation, vestibular ataxia with falling to the left, left-sided head tilt, vertical nystagmus of the left eye (oculus sinister), external ophthalmoplegia of the right eye (oculus dexter), anisocoria with a mydriatic right pupil,
absent right-sided palpebral and corneal reflexes, and decreased sensation of the right side of the face. A multifocal lesion with central vestibular involvement was suspected. The onset, progression, clinical examination findings and multifocal neuroanatomical localization were most suggestive of infectious/inflammatory disease (Intracranial empyema, FIP, mycotic granuloma, and toxoplasmosis) or neoplastic causes (lymphoma).

CBC revealed a mature neutrophilia (leukocytes: 21.74x10^9/l, Reference interval (RI): 5.5-19.5, neutrophils: 19.43x10^9/l, RI: 2.5-12.5) and mild anaemia with no evidence of regeneration (haematocrit 29%). Results of a biochemistry profile, venous blood gas and electrolytes and coagulation parameters were within normal limits. Feline immunodeficiency virus antibody and feline leukaemia virus antigen tests were negative as was Toxoplasma serum IgG/IgM antibody testing. The cat was up to date with routine vaccinations and parasite treatments. Magnetic resonance imaging (MRI) of the brain was performed under general anaesthesia using a 1.5 Tesla magnet, which included sagittal and transverse T2-weighted (T2W) sequences, transverse T2*-weighted and T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences. Transverse, sagittal, and dorsal plane T1-weighted (T1W) images were obtained before and after IV administration of gadolinium contrast. On T2W images there was marked thickening and hyperintensity of the meninges, mostly around the right cerebrum and extending to the ventral aspect of the brain and brainstem (Figure 1A, B). Ventral to the cerebrum and brainstem on the right side there was separation of the pachymeninges and leptomeninges with a hypointense fluid accumulation (Figure 1A, B). T1W images obtained after contrast administration showed marked enhancement of the meninges but no enhancement of the accumulated fluid within the meninges (Figure 1 C, D). There was swelling of the right cerebrum with a midline shift and mild
displacement of the cerebellum into the foramen magnum (Figure 1A, B). These MRI findings were most consistent with a diffuse meningitis and predominantly right-sided subdural empyema.\textsuperscript{2,4,12,13} No evidence of otitis media/interna or retrobulbar abscessation was identified. Computed tomography (CT) of the thorax and abdomen performed with a 16-slice scanner\textsuperscript{e} revealed 12 well-defined, rounded nodules in the left and right caudal and right middle lung lobes (Figure 2). All lesions demonstrated uniform contrast enhancement after IV administration of iohexol\textsuperscript{d} (Omnipaque, 240mg I/mL, GE Healthcare; Belgium). The abnormal thoracic CT findings were most consistent with a multifocal pneumonia. Abdominal CT findings were within normal limits.

Mannitol\textsuperscript{c} (0.5mg/kg, IV over 20 minutes) was administered before a cisternal cerebrospinal fluid (CSF) puncture was performed. Only a limited amount of CSF could be collected due to its abnormal viscous nature. Determination of total nucleated cell counts, protein concentration, and culture were therefore not possible. A direct smear was prepared, which demonstrated moderate numbers of degenerate neutrophils along with lesser numbers of macrophages and occasional lymphocytes, scant to moderate erythrocytes and smeared nuclear debris. Long filamentous beading rods and occasional thicker bacilli were present both extracellularly and within neutrophils (Figure 2). The cytological diagnosis was septic suppurative inflammation with multiple Gram-positive bacterial species. Urine collected by cystocentesis and blood samples taken from three different venous sites at hourly intervals did not identify any microorganisms after 72 hours of aerobic and anaerobic culture. The owner declined performing a bronchoalveolar lavage.
Subdural empyema is considered to be a neurosurgical emergency but due to the diffuse nature and challenging location of the lesion surgery was not felt to be a feasible treatment option in this case.\textsuperscript{3,4} Consequently intensive medical management and supportive care was initiated. For the first 24 hours following general anaesthesia the cat was placed on continuous ECG and oscillometric blood pressure monitoring with supplemental flow by oxygen.\textsuperscript{14,15,16} Respiration rate, oxygen saturation (pulse oximetry) and Modified Glasgow Coma Scale (MGCS) were measured every hour.\textsuperscript{14,15,16} Analyses of arterial blood gas, venous blood gas and electrolytes were performed every six hours. Throughout this period oxygen saturation and partial pressures of oxygen and carbon dioxide remained largely within normal limits meaning that respiratory support other than flow-by oxygen was not required.\textsuperscript{15,16} During the first 24 hours the cat received three boluses of mannitol\textsuperscript{e} (0.5g/kg, IV over 20 minutes) due to clinical signs suggestive of increases in intracranial pressure. These signs included a worsening vestibular ataxia, non-invasive blood pressure measurements between 180mmHg and 220mmHg, heart rate between 90 and 120 beats per minute and episodes of marked obtundation with a concurrent reduction in MGCS from 15 to 10. The cat further received IV fluids (compound sodium lactate at 3ml/kg/hr), clindamycin\textsuperscript{f} (20 mg/kg, IV, q24h), enrofloxacin\textsuperscript{g} (5mg/kg, IV, q24h) and dexamethasone\textsuperscript{h} (0.2mg/kg, IV, q24h).

The cat started to demonstrate gradual improvement from 24 hours after initiating treatment and continuous ECG and oscillometric blood pressure monitoring were stopped. After 48 hours of treatment corticosteroid administration was discontinued and the cat was started on oral antibiotics including clindamycin\textsuperscript{i} (11mg/kg, PO, q24h) and enrofloxacin\textsuperscript{j} (5mg/kg, PO, q24). At 48 hours the cat was grooming and feeding itself and respiratory rate and effort had returned to normal. After five days of hospitalisation the cat was discharged. The cat demonstrated mild vestibular
ataxia and head tilt at this time. Neurological examination three weeks after discharge demonstrated further improvement with only mild vestibular ataxia present. General physical and neurological examinations nine weeks after discharge were within normal limits. A CT examination performed at that time demonstrated resolution of the earlier observed pulmonary changes. Following discharge oral enrofloxacin was continued for one month and clindamycin was continued for three months due to its activity against Gram-positive bacteria and anaerobes. Telephone follow-up with the owner revealed that the cat was still free of clinical signs nine months after discharge from our hospital.

Discussion

This case report describes successful medical treatment of a cat with subdural intracranial empyema and concurrent multifocal pneumonia. This has not yet been reported to the best of the authors’ knowledge. Subdural empyema is considered a neurosurgical emergency.\textsuperscript{3,4} Because of the extensive nature of the infection, including the ventral aspects of the cerebrum and brainstem, the cat in this report was not considered a good surgical candidate.

Subdural empyema is a specific condition where empyema occurs within the boundaries of the dura mater and arachnoid.\textsuperscript{3,11,12} Six reports in cats have been documented with only one animal surviving following aggressive surgical and medical treatment.\textsuperscript{1,3,6} In agreement with the case presented here, all reported cats with intracranial empyema presented following initial periods of general systemic illness with lethargy, inappetence and weight loss.\textsuperscript{1-3,6} These cases invariably experienced subsequent acute neurological deterioration with evidence of increased intracranial pressure and brainstem compression. All cats were reported as being obtunded with evidence of
vestibular deficits and in the majority of cases ataxia and/or paresis. 1-3,6 Of note is that only one previously reported cat demonstrated pyrexia.3 These findings are in agreement with the clinical presentation of the case presented here in which an initial history of lethargy, inappetence and weight loss rapidly progressed to marked neurological signs.

MRI is considered the most effective diagnostic tool for empyema with characteristic imaging findings that are consistent across human and veterinary medicine: a crescent or lentiform-shaped extra-axial collection of fluid that is hyperintense relative to brain parenchyma on T2W images and hypointense on T1W images. The lesions have strong ring enhancement following contrast administration.2-4,11,12 This lentiform appearance is attributed to the purulent fluid conforming to the subdural space and in some cases, as seen in the present report, can extend over almost an entire cerebral hemisphere (Figure 1).2 In contrast to epidurally located lesions, subdural empyema can cross cranial suture lines. Extension is however limited by dural folds; such as the falx cerebri and tentorium cerebelli.13 This can explain why the infection was limited to only one cerebral hemisphere.

As with previous reports, blood and urine cultures were not found to be diagnostic and in half of cases haematological and biochemical changes are limited to an inflammatory leukogram and mild-regenerative anemia.1-3,6 Route of infection has been identified in 4/6 previously published cases: retrobulbar abscess (two cases), bite wound (one case), and extension from tympanic bulla (one case).1-3 In this case there was no evidence of otitis media/interna, oropharyngeal lesions, retrobulbar abscesses or bite wounds but a multifocal pneumonia was identified on CT images. Although bacterial pneumonia can be associated with haematogenous
spread it cannot be concluded that the subdural empyema and pneumonia in this case were associated as it was not possible to obtain bacterial culture from both sites. In previous reports bacterial cultures from the sub-dural space at necropsy most commonly identified a polymicrobial growth with at least one anaerobic bacteria (Fusobacterium spp., Bacterioides spp., and Actinomyces spp.). In this case the benefits of trying to obtain a definitive diagnosis with a cisternal CSF sample were felt to outweigh the potential risks of performing the procedure. MRI signs of increased intracranial pressure were considered relatively mild but as a precaution mannitol was administered prior to CSF sampling and the cat was intensively monitored post-sampling. Direct smears from CSF in the current case identified a polymicrobial infection with Gram-positive organisms. However there was insufficient sample to allow culture and it was therefore impossible to provide a definitive identification of the organisms involved.

Although subdural empyema is expected to disrupt the blood-brain barrier and facilitates drug penetration, the concentration of antimicrobials within the CSF can still be limited. Consequently clindamycin and enrofloxacin were chosen as antibiotic therapy because both drugs cross the blood-brain barrier and in combination provide excellent broad-spectrum bactericidal antimicrobial activity. It is currently unclear how long antibiotic treatment should be continued in cases of feline subdural empyema. The duration of treatment in this case was based on recommendations of medical management of subdural empyema in humans and spinal empyema in dogs. Dexamethasone was administered immediately after a diagnosis of subdural empyema was made. This was based on studies in people with bacterial meningitis, which support the use of short-term anti-inflammatory doses to lower intracranial pressure and reduce CNS inflammation.
Conclusions

This case report suggests that subdural empyema in cats can be effectively treated by aggressive medical management resulting in complete resolution of clinical signs. It also highlights that thorough examination for concurrent distant infections is warranted in a cat with subdural empyema.

Footnotes

a Gyroscan Intera; Philips Medical Systems, Surrey, UK
b Gadovist, 1mmol/mL gadobutrol; Bayer, Berkshire, UK.
c Mx8000 IDT; Philips Medical Systems, Surrey, UK
d Omnipaque, 240mg I/mL; GE Healthcare; Buckinghamshire, UK
e Polyfusor K; Fresenius Kabi, Cheshire, UK
f Dalacin C; Pharmacia, Kent, UK
g Baytril; MSD Animal Health, Buckinghamshire, UK
h Dexafort; MSD Animal Health, Buckinghamshire, UK
i Antirobe; Zoetis, London, UK
j Baytril; MSD Animal Health, Buckinghamshire, UK
References


Figure Legends:

Figure 1: T2-weighted sagittal (A) and transverse plane (B) MR images of cat brain. Sagittal (C) and dorsal (D) plane T1W images following IV administration of gadolinium contrast media. On T2W images there is marked thickening and hyperintensity of the meninges around the right cerebrum extending to the ventral aspect of the brain and brainstem (Figure 1A, B). Ventral to the right temporal lobe, adjacent to the right occipital lobe and ventral to the brainstem there is separation of the pachymeninges with T2W hyperintense and T1W hypointense material (Figure 1A, B). Meninges show marked contrast enhancement (White arrow heads, Figure 1C, D) whilst the T1W hypointense separation of the pachymeninges and leptomeninges did not enhance after contrast administration (Figure 1 C, D).
Figure 2: (A) variably degenerate neutrophils against a background of smeared nuclear debris and erythrocytes. Modified Wright's Giemsa, bar = 50μm. Inset: Neutrophil containing several beaded rods, bar = 10μm. (B): Transverse CT image of the thorax showing multiple pulmonary nodules in right and left lung lobes (White arrow heads)