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# Streptococcus equi subsp. equi meningitis, septicemia and subdural empyema in a child

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## ABSTRACT

*Streptococcus equi* subsp. *equi* is a group C  $\beta$ -hemolytic streptococcus, and is an invasive pathogen with a very restricted host, causing the equine infection known as 'strangles'. It is a poor colonizer in horses, preferentially causing invasion and infection, compared with its ancestor *Streptococcus equi* subsp. *zooepidemicus*, which is considered an opportunistic commensal of the equine upper respiratory tract. In humans, *S. equi* subsp. *equi* causes invasive infections in immunocompromised hosts, often following close contact with horses. Such infections are associated with a high mortality, as well as a poor neurological outcome in survivors. Beta-lactam antimicrobials form the mainstay of treatment, while neurosurgical intervention is occasionally required. We present the case of a 13-year old boy with systemic lupus erythematosus being treated with hydroxychloroquine, who presented with *S. equi* subsp. *equi* meningitis and sepsis after contact with a sick pony. Although he recovered fully following eight weeks of intravenous ceftriaxone and oral rifampin, the clinical course was complicated by subdural empyema requiring neurosurgical evacuation.

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## Introduction

The group C  $\beta$ -hemolytic streptococcus (GCS) *Streptococcus equi* subsp. *equi* is an invasive pathogen with a very restricted host, causing the equine infection known as 'strangles' [1]. *S. equi* subsp. *equi* very rarely causes infections in humans but may be associated with bacteremia, sepsis, and meningitis in immunocompromised hosts. Such infections often follow close contact with horses, and are associated with significant mortality and morbidity, including long-term sensorineural deafness, amnesia, and visual loss [1]. We present a case of *S. equi* subsp. *equi* meningitis and sepsis in a 13 year old patient reporting recent contact with a sick pony. Although responding well to antimicrobial treatment, his clinical course was complicated by subdural empyema requiring surgical evacuation.

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## Case

A 13 year old boy with a history of systemic lupus erythematosus (SLE) being treated with regular ibuprofen and hydroxychloroquine, presented with a one-day history of lethargy and unresponsiveness. While previously treated with methotrexate, this was stopped 3 months prior as his SLE was in remission. He also complained of headache, photophobia, and neck stiffness, associated with 3 weeks of intermittent fever and worsening generalized joint pain and stiffness. His C-reactive protein (CRP) was mildly raised (22 mg/L), and he demonstrated a significant leukocytosis (35,800 cells/ $\mu$ L) and neutrophilia (31,940 cells/ $\mu$ L). He was admitted to hospital and commenced on intravenous rehydration and ceftriaxone (80 mg/kg/day). Initial magnetic resonance imaging (MRI) of the brain confirmed a small subdural hygroma at the right parietal vertex, and mild smooth meningeal thickening overlying the right parieto-occipital lobes suggestive of purulent meningitis. A lumbar puncture was therefore performed within 2–3 h of administration of antimicrobials: while cerebrospinal fluid (CSF) cultures and real-time PCR assay for common CSF pathogens were negative, the CSF was turbid, with a raised protein (4191 mg/L) and low glucose (18.5 mg/dL; random blood glucose = 155.9 mg/dL), and raised neutrophil content (936 cells/ $\mu$ L). With meningoencephalitis strongly

43 suspected, intravenous vancomycin, dexamethasone and aciclovir  
44 were added to his treatment.

45 Blood cultures taken on admission flagged positive (BD  
46 BACTEC™ FX, Becton Dickinson and Co., NJ, USA) after 48 h. In  
47 subculture, β-hemolytic streptococci (“*S. pyogenes*-like”) were  
48 observed on blood agar, which were Lancefield group C, and  
49 identified as *S. equi* subsp *equi* by Matrix-assisted laser desorption/  
50 ionization time-of-flight mass spectrometry (MALDI-TOF; VITEK®  
51 MS V3, bioMerieux, Marcy L'Etoile, France). Sensitivity testing was  
52 done using ETest® (bioMerieux, Marcy L'Etoile, France). The  
53 isolated *S. equi* subsp. *equi* was sensitive to beta-lactams  
54 (minimum inhibitory concentrations (MIC): penicillin = 0.016 μg/  
55 mL; ceftriaxone = 0.032 μg/mL; ampicillin 0.032 μg/mL), vanco-  
56 mycin (MIC = 0.05 μg/mL), levofloxacin (MIC = 1.5 μg/mL), and  
57 erythromycin (MIC = 0.064 μg/mL), and resistant only to clinda-  
58 mycin (MIC = 1 μg/mL). The patient's family subsequently revealed  
59 regular contact with horses, and that the index patient had a pet  
60 pony that was recently unwell and required antimicrobial  
61 treatment.

62 On day 21 of treatment, the patient complained of persistent  
63 headaches, neck stiffness, and recurrent fever. Repeat MRI of the  
64 brain showed persistence of the right-sided subdural fluid  
65 collection, with restricted diffusion and rim enhancement,  
66 consistent with a subdural abscess, as well as pachymeningeal  
67 dural enhancement along the right hemispheric cavity (Fig. 1). Oral  
68 rifampin was added to his treatment (10 mg/kg BD), but his fever  
69 persisted, so the subdural empyema was surgically evacuated on  
70 day 35. He subsequently recovered completely following 8 weeks  
71 of intravenous ceftriaxone and oral rifampin, and exhibited no  
72 long-term neurological sequelae on subsequent follow up.

## Discussion

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*Streptococcus equi* subsp. *equi* is a known pathogen in horses,  
causing the highly contagious and invasive upper respiratory tract  
infection known as ‘strangles’ [2]. *S. equi* subsp. *equi* is a poor  
colonizer in horses, preferentially causing invasion and infection,  
its ancestor *Streptococcus equi* subsp. *zooepidemicus* is considered  
an opportunistic commensal of the equine upper respiratory tract.  
Both these subspecies are classified as Lancefield Group C  
streptococci (GCS). While both *S. equi* subsp. *equi* and *S. equi*  
subsp. *zooepidemicus* share over 80% DNA sequence homology with  
*S. pyogenes*, sequence homology with *S. pyogenes* for the super-  
antigens SeeH, SeeI, SeeL and SeeM is much high for *S. equi* subsp.  
*equi*(96–99%) compared with *S. equi* subsp. *Zooepidemicus* (34–  
59%), which could explain the predilection for invasiveness in both  
*S. equi* subsp. *equi* and *S. Pyogenes* [2,3]. Proper species and  
subspecies identification of GCS by MALDI-TOF, however, has only  
been available for the last decade or so, and many laboratories still  
lack these facilities [4].

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A literature search using the terms ‘*Streptococcus equi*’, in  
combination with ‘meningitis’, yielded 34 cases of reported  
meningitis with this group of pathogens, 31 of which were caused  
by *S. equi* subsp. *zooepidemicus*, and only 2 confirmed to be of *S. equi*  
subsp. *equi*, as in our case (one report did not distinguish between  
the 2 subspecies) [1,5–7]. *S. equi* subsp. in children are especially  
uncommon: of the infections caused by *S. equi* subsp. *equi* or *S. equi*  
subsp. *zooepidemicus*, the majority were adult patients (>70 years:  
13 patients; 40–69: 10 patients; 20–39: 6 patients), and only 2  
cases (*S. equi* subsp. *zooepidemicus*: 1; *S. equi* subsp. *equi*: 1)  
involved patients aged between 10 and 19 years [5,6]. Two further

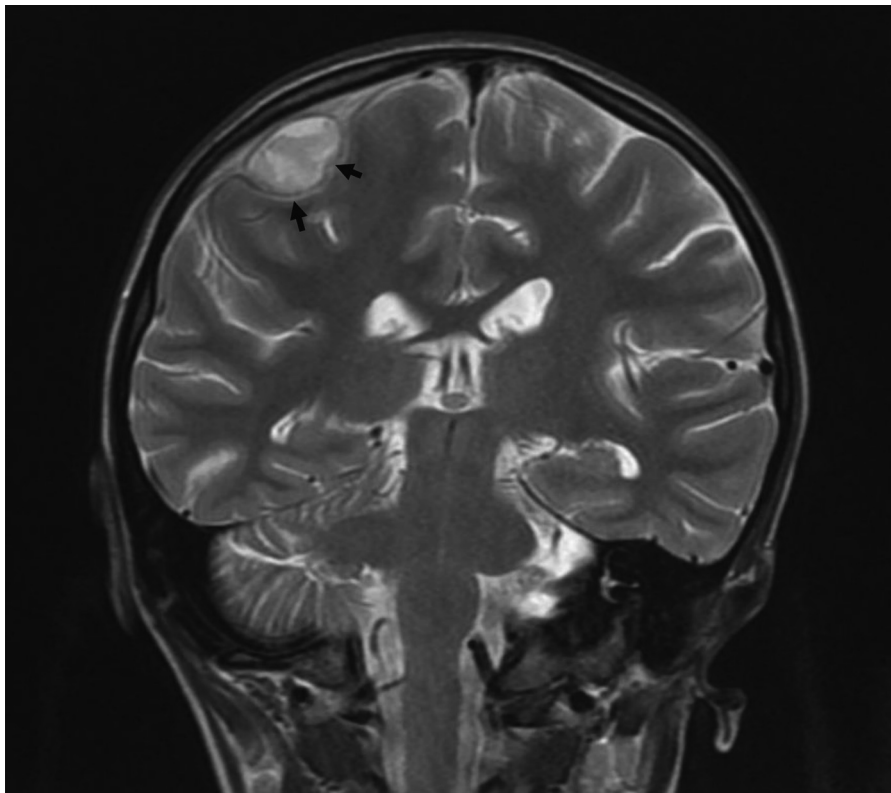


Fig. 1. Magnetic resonance imaging demonstratin right-sided subdural fluid collection with restricted diffusion and rim enhancement, and pachymeningeal dural enhancement along the right hemispheric cavity, consistent with a subdural abscess.

cases are reported in infancy, both with *S. equi* subsp. *zoepidemicus* [1,8]. The index patient is therefore only the second case of *S. equi* subsp. *equi* meningitis reported in a child.

Contact with horses or dogs, or ingestion of unpasteurized cheese or milk, are prerequisites for infection with *S. equi* subsp., with the nature of horse contact varying widely: eighteen patients reported direct contact with horses, 4 reported members of their immediate family who had direct contact with horses, and 3 reported being bitten by a horse [1,4,9–11]. One previous case of *S. equi* subsp. *zoepidemicus* meningitis involved a gardener reporting regular contact with horse manure [10]. Nine previous cases were associated with ingestion of unpasteurized milk or cheese, and two associated with canine contact [1,6,8,9,12]. This data is consistent with the history of regular close equine contact we report here, though only one previous case reported that the horse in contact with the patient had recently been unwell [13]. In our case, *S. equi* subsp. *zoepidemicus* was successfully isolated from a nasal swab performed on the sick horse, but the sample was only taken one month after the index horse had received a course of antimicrobials and fully recovered. Since *S. equi* subsp. *equi* is a poor colonizer of asymptomatic horses, the isolation of the equine commensal *S. equi* subsp. *zoepidemicus* rather than *S. equi* subsp. *equi* was not unexpected [2,3].

From a clinical perspective, 3 of the previously reported cases of *S. equi* subsp. *zoepidemicus* meningitis also presented with infective endocarditis, while mastoiditis, sinusitis, and acute otitis media were present in 2 patients each [4,6,12,14]. Complications are common following *S. equi* subsp. *equi* meningitis: 2 previous cases were complicated by one or more brain abscesses, and three patients developed endophthalmitis [4,10,11,13]. The case we report is only the second reporting the development of a subdural empyema (SDE) in the course of *S. equi* subsp. *equi* meningitis, and the first to require surgical evacuation of the SDE [8]. This may be because it was secondary to the rarer and more invasive *S. equi* subsp. *equi*, rather than the more commonly-reported *S. equi* subsp. *zoepidemicus*. In horses, *S. equi* subsp. *equi* causes 'strangles', an invasive upper respiratory tract infection associated with rapid dissemination to the lymph nodes, massive influx of neutrophils to the tonsils, and subsequent metastatic abscessation, often requiring drainage [2]. Including our case, reported cases of *S. equi* subsp. meningitis show an all-cause mortality of 20%, with permanent neurological morbidity reported in 31.4% (sensorineural deafness or neurocognitive impairment: 5 patients each, visual loss or diplopia: 4 patients, ataxia: 1 patient, hydrocephalus: 1 patient) [1,4,8,10,11,13]. Despite the initially complicated course, the case reported here did not exhibit any long-lasting neurological complications.

Being immunocompromised is a risk factor for *S. equi* subsp. *equi* infection [1]. In horses, the failure of an effective immune response allows the rapid multiplication of *S. equi* subsp. *equi*, followed by massive influx of neutrophils to the tonsil, causing abscess formation [2]. In our case, the child was known to have SLE, and while this was quiescent at the time of presentation, and he was not cytopenic, regular hydroxychloroquine treatment, as well as previous treatment with methotrexate (stopped 3 months prior), may have contributed to a state of relative immunosuppression. Previous *S. equi* subsp. meningitis are reported in patients with leukemia, diabetes mellitus, and receiving immunosuppressive therapies [4].

Beta-lactam antimicrobials form the mainstay of treatment of *S. equi* subsp. meningitis [1]. Our patient received 8 weeks of ceftriaxone and rifampin, with adjunctive dexamethasone in the early stages. Among previously-reported cases of *S. equi* subsp. meningitis, 4, 16 and 2 patients were treated with ampicillin, penicillin, and amoxicillin respectively. Fifteen patients received

ceftriaxone, and seven received cefotaxime. Five patients each received adjunctive vancomycin or aminglycoside (gentamicin, tobramycin) treatment respectively, while two were treated with additional rifampin, and another patient was given adjunctive fosfomycin therapy [1,6,10]. Adjunctive dexamethasone is reported in 5 previous patients with *S. equi* subsp. meningitis [1,4,11]. Of those patients who survived the illness, antimicrobial treatment duration ranged between 10 days and 8 weeks [1,6,10].

## Conclusion

We present a rare case of *S. equi* subsp. *equi* meningitis in a child reporting regular contact with horses. Although he recovered completely with 8 weeks of intravenous ceftriaxone and rifampin, his clinical course was complicated by a right-sided subdural empyema requiring neurosurgical evacuation. The case provides an important reminder of a rare, but potentially devastating infection by an invasive equine pathogen, amenable to treatment with a penicillin or cephalosporin if administered promptly, though occasionally requiring surgical drainage of purulent foci.

## CRediT authorship contribution statement

**Paul Torpiano:** Writing - original draft. **Nina Nestorova:** Writing - review & editing. **Cecil Vella:** Supervision.

## Declarations of competing interest

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