

## *Streptococcus equi* subspecies *zooepidemicus* meningitis—a case report and review of the literature

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**Abstract** A case is described of a 79-year-old man, trampled by his horses, who subsequently developed a wound infection and, later, meningitis. *Streptococcus equi* subsp. *zooepidemicus* was isolated as the causative organism. *S. equi* subsp. *zooepidemicus*, which carries the Lancefield Group C antigen, is an uncommon human pathogen but is commonly isolated from bacterial infections in animals, particularly horses. It is most commonly acquired by humans following animal contact. A review of the literature identified 20 previously described cases of *S. equi* subsp. *zooepidemicus* meningitis. Crude mortality following infection was 24%. All of the patients who died were over 70 years of age and the ingestion of unpasteurised dairy products was associated with all but one of the fatal cases. Hearing loss was a frequent complication, occurring in 19% of cases. Only 38% of patients made a complete recovery. Treatment regimes commonly included benzylpenicillin or a third-generation cephalosporin, with a mean treatment duration in survivors of 23 days.

### Case presentation

A 79-year-old man presented to his local hospital with confusion and pyrexia one week after being trampled by horses at the animal sanctuary which he managed. During the initial injury, he sustained a large haematoma over his right knee and a deep occipital scalp laceration; he was

found to have no neurological deficit. The occipital wound was cleaned and sutured, and the patient discharged.

One week later, several hours after the removal of his scalp wound sutures, he re-presented to his local hospital confused and drowsy, complaining of a severe occipital headache. He was febrile at 38.7°C with a pulse of 134/min in atrial fibrillation. His blood pressure was 111/68, oxygen saturation 98% on air, capillary blood glucose 5.5 mmol/L and his Glasgow Coma Scale (GCS) score was 14/15, although this rapidly dropped to 10/15. His head wound appeared to be infected with a malodourous discharge. Cardiac, respiratory and abdominal examinations were normal. Neurological examination was hindered by the patient's inability to follow commands; however, he was able to move all four limbs and his tone and reflexes were normal and symmetrical. Blood cultures were obtained.

Computed tomography (CT) of the head showed no fracture, bleed, infarct or features of raised intracranial pressure. Cerebrospinal fluid (CSF) obtained via lumbar puncture was cloudy, with an elevated opening pressure of 29 cm H<sub>2</sub>O. The CSF white blood cell count was 360 × 10<sup>6</sup>/L (70% lymphocytes and 30% neutrophils), protein 4 g/dl and glucose 0.2 mmol/l. No organisms were seen on Gram stain. The patient was treated with intravenous ceftriaxone and aciclovir.

The following day, the patient was noted to have left-sided neglect, agitation, profound hearing loss and a GCS of 11/15. He was transferred to the John Radcliffe Hospital, Oxford, UK, for neurological assessment. On arrival, amoxicillin was added to his treatment regimen to cover the possibility of listeriosis. His admission blood cultures became positive, growing Gram-positive cocci resembling streptococci. The streptococcus was identified as Lancefield Group C, and further testing undertaken using API 20 Strep (bioMérieux Vitek Inc., Hazelwood, MI, USA) identified

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**Table 1** Review of the literature

Demographics				Probable source		Treatment		Outcome	Reference
Age (years)	Sex	Past medical history	Location	Animal contact	Route	Notes	Agents	Duration	
59	M		Minnesota, USA	Farm animals	Ingestion	Farm hand, drank unpasteurised goat's milk, no unwell animals	Ampicillin, gentamicin, benzylpenicillin	16 days	Positional vertigo, unilateral hearing loss, improved at 2 months follow-up [5]
66	M	Nil	Leeds, UK	Dogs	Inhalation	Contact with unwell dogs	Benzylpenicillin, dexamethasone	Not stated	Not stated [6]
24	F	Nil	Manitoba, Canada	Horse	Inhalation	Pet horse	Chloramphenicol, ampicillin, benzylpenicillin	14 days	No neurological sequelae, "more garrulous and gregarious" than her usual self [7]
73	M		West Yorkshire, UK	Cows' milk	Ingestion	Unpasteurised milk from dairy herd with mastitis	Cefotaxime, benzylpenicillin	Died at 48 h	Died at 48 h [8]
73	M	Concurrent leaking aortic aneurysm	West Yorkshire, UK	Cows' milk	Ingestion	Unpasteurised milk from dairy herd with mastitis	Cefotaxime, benzylpenicillin	Died	Died, ruptured abdominal aortic aneurysm [8]
71	M	Concurrent deep vein thrombosis	West Yorkshire, UK	Cows' milk	Ingestion	Unpasteurised milk from dairy herd with mastitis	Cefotaxime, benzylpenicillin	6 weeks	Discharged [8]
80	F		West Yorkshire, UK	Cows' milk	Ingestion	Unpasteurised milk from dairy herd with mastitis	Cefotaxime, benzylpenicillin	Died at day 14	Died at day 14 [8]
24	M	Nil	Kentucky, USA	Horses	Inhalation	Employed at horse farm	Benzylpenicillin	14 days	Full recovery [9]
33	M		Créteil, France	Not recorded	Not recorded	Not recorded	Ampicillin, gentamicin	Not recorded	Recovered with mild bilateral deafness [10]
67	F		Bilbao, Spain	Cattle	Inoculation	Boiled milk, exposure to cattle, ear thought to be portal of entry	Cefotaxime, benzylpenicillin, tobramycin	23 days	Full recovery [11]
66	F	Chronic lymphocytic leukaemia recent chemotherapy	France	Horse	Inoculation	Horse with conjunctivitis, case had conjunctivitis at presentation	Amoxicillin, cefotaxime, fosfomycin	Not recorded	Complicated by unilateral endophthalmitis with associated visual loss [12]
74	M	Nil	Tours, France	Horses	Inhalation	Horse trainer, contact with unwell horses	Ampicillin, gentamicin	15 days	Discharged, no adverse outcome noted [13]
13	F	Asthma, allergic rhinitis	Philadelphia, USA	Horses	Inhalation	Close horse contact, equestrian competition	Cefotaxime, ceftriaxone, vancomycin	14 days	Residual unilateral sided hearing loss, otherwise well [14]
49	F	Nil	Toronto, Canada	Horses, donkeys	Inoculation/inhalation	Close contact with eight horses and a donkey ( <i>S. zooepidemicus</i> isolated from two horses and a donkey), kick to the face 2 weeks prior to infection, no break in skin	Cefotaxime, benzylpenicillin	10 days	Discharged after 11 days with diplopia [15]
74	M		Konya, Turkey	Horses	Inhalation	Frequent contact with horses, including one with upper respiratory tract infection	Ceftriaxone	Died on day 7	Died on day 7 [16]
79	M	Nil	Bedford	Indirect:	Inhalation	Gardener with daily	Benzylpenicillin, vancomycin	6 weeks	Associated endocarditis, [17]

83	F	Hypertension	Park, Australia	Indirect: horse manure	Ingestion	exposure to manure	Inadequately pasteurised cheese	Beta-lactam	Died	good recovery	[18]
41	M		Canaria	Indirect: cheese	Inhalation	Farmer, also had contact with animal manure while gardening	Ceftriaxone		14 days	Minimal neurological sequelae	[19]
30	F	Cocaine and Cannabis use	Stoke-on-Trent, UK	Indirect: animal manure	Inhalation	Horse contact		Cefotaxime, vancomycin, ampicillin	4 weeks	Initial tetraparesis, global aphasia, subsequently improved	[20]
72	F	Myocardial infarction	Salamanca, Spain	Horses	Ingestion	Unpasteurised milk, son had close contact with horses		Ampicillin, gentamicin, rifampicin	3 weeks	Good recovery	[21]
79	M	Atrial fibrillation, chronic obstructive pulmonary disease	Belgrade, Serbia	Indirect: horses and cattle	Inoculation	Owner of an animal sanctuary		Ceftriaxone, gentamicin, amoxicillin, benzylpenicillin	6 weeks	Good recovery, high-frequency hearing loss	Present case

the isolate as *Streptococcus equi* subsp. *zoepidemicus* (probability >99%). On the basis of this result, aciclovir and amoxicillin were discontinued.

The next day, the patient suffered two self-terminating tonic–clonic seizures. Phenytoin was prescribed, and no further seizures occurred. A magnetic resonance imaging (MRI) brain scan revealed multiple acute right middle cerebral artery territory infarcts, with normal neck, head and cranial vessels. A small subdural/subarachnoid bleed was identified. Transthoracic echocardiography was unremarkable. As it was possible that the subdural/subarachnoid blood seen on MRI had been infected during the patient’s bacteraemia, 6 weeks of therapy with intravenous ceftriaxone was planned. The patient improved rapidly with antibiotic treatment, with his GCS returning to 15/15 within 3 days and the left-sided inattention resolving completely.

The treatment was, unfortunately, complicated by severe *Clostridium difficile* infection. This was managed with enteral vancomycin and intravenous metronidazole, and in an attempt to reduce the risk of relapse, his meningitis treatment was changed to intravenous benzylpenicillin. The patient continued to recover well and was discharged after 6 weeks of therapy. However, profound high-frequency hearing loss remained. The horses involved in the original incident remained well throughout, with no features of *S. equi* subsp. *zoepidemicus* infection. Erratic behaviour noted in one of the horses following the original incident was felt to be related to it being in season.

### Review of the literature

*S. equi* subsp. *zoepidemicus* is an uncommon human pathogen but is commonly isolated from bacterial infections in animals, particularly horses [1]. It carries the Lancefield Group C antigen and is most commonly acquired by humans following animal contact. It shares 80% sequence homology with *S. pyogenes*, with many virulence factors in common [2]. Lancefield Group C streptococci cause human skin and soft tissue infections and pharyngitis, but bacteraemia is uncommon [3]. They have also been reported to cause numerous other infections in humans, including lower respiratory tract infection, endocarditis, septic arthritis, peritonitis, aortitis and pericarditis [3, 4]. They are a rare cause of meningitis in humans.

A literature review revealed only 20 previously reported cases of *S. equi* subsp. *zoepidemicus* meningitis. The demographics, animal exposure details, treatment and outcome data for published cases, including our case, are presented in Table 1 [5–21]. The median age of patients was 67 years (range 13–83 years). Just over half of the patients (12/21, 57%) were male, with nine cases occurring in females. In contrast to some reports of other types of invasive Group C

streptococcal disease [22], only a minority of patients (8/21, 38%) had recorded co-morbidities. The majority (13/21, 62%) of reported cases were located in the United Kingdom/Europe, with the majority of the remaining cases (5/21, 24%) occurring in North America.

Contact with animals or the ingestion of animal products was noted in all but one of the cases. While horse contact was the most prevalent, contact with cattle and dogs was also reported. The postulated route of infection varied significantly between cases. Inhalation of the organism was proposed in ten cases as the probable route of acquisition, whilst the ingestion of unpasteurised dairy products was found to account for one third (7/21) of cases. Inoculation was the postulated route in four cases, including the case presented in this article.

Treatment regimes for affected patients included benzylpenicillin (13 patients) and/or a third-generation cephalosporin (12 patients). The treatment duration varied. Amongst patients who survived and for whom the treatment duration was reported, the mean treatment duration was 23 days of antibiotics.

The crude mortality associated with *S. equi* subsp. *zooepidemicus* meningitis was 24% (5/21), although one of the patients who died also had a ruptured abdominal aortic aneurysm and it is unclear whether this was related to infection or pre-existing disease. All of the patients who died were over 70 years old, and all but one of the fatal cases was thought to have acquired their infection by ingesting unpasteurised dairy products. Other authors have reported rates of mortality with Group C streptococcal bacteraemia of 25–40%, with the highest rates in the elderly [3, 22]. Persistent hearing loss was the most common complication reported, occurring in 19% (4/21) of patients, although 3 of the 4 patients affected received aminoglycosides as part of their treatment. Other complications reported included endocarditis, endophthalmitis, tetraparesis and aphasia. Only 38% (8/21) of patients made a complete recovery.

## Conclusion

*Streptococcus equi* subsp. *zooepidemicus* meningitis is a rare but severe zoonotic infection, usually presenting in patients who have contact with horses or cattle. It is associated with high mortality and, in those who survive, significant complications, particularly hearing loss. The elderly and those who acquire infection by the ingestion of contaminated unpasteurised dairy products are at the greatest risk of death.

**Declarations** The patient described herein has given his full consent for inclusion in this review.

**Conflict of interest** The authors declare that they have no conflict of interest.

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