



## Case report

Possible canine source of *Streptococcus equi* subspecies *zooepidemicus* causing meningitis in an infantYorgo Zahlanie<sup>a,\*</sup>, Mohammed Almatrafi<sup>a</sup>, Laura Filkins<sup>b</sup>, Michelle S. Hsiang<sup>a</sup><sup>a</sup> Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, USA<sup>b</sup> Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA

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## ABSTRACT

*Streptococcus equi* subspecies *zooepidemicus* (*S. zooepidemicus*) is a pathogen that colonizes and causes disease in horses, and less commonly, in other mammals. This zoonotic disease in humans is rare. In the reported human cases, it has caused bacteremia, endocarditis, arthritis and meningitis, and it has been linked to contact with horses or ingestion of unpasteurized dairy products.

We report a case of a six-month-old female patient who presented with a one-day history of fevers and neurological symptoms. Blood and cerebrospinal fluid cultures revealed *S. zooepidemicus*, and brain imaging showed a subdural fluid collection and diffuse brain infarcts. Exposure history suggested a canine source as patient had close contact with two dogs that had respiratory infections but no contact with other pets including horses. She had clinical and radiographic improvement after a four-week course of penicillin G and drainage of a subdural fluid collection but she had residual severe to profound hearing loss and mild neurocognitive deficits. This case report provides the third reported case of possible *S. zooepidemicus* transmission from dogs to humans, and the second such case that has led to meningitis. Clinicians and public health practitioners should recognize that *S. zooepidemicus* may be transmitted from dogs and can lead to severe disease in humans.

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## Introduction

*S. zooepidemicus* is a beta-hemolytic group C streptococcal bacterium that is closely related to *Streptococcus equi* subspecies *equi*, a pathogen that causes “strangles”, a severe respiratory infection in horses, and shares virulence factors with *Streptococcus pyogenes*, a major human pathogen [1]. In horses, *S. zooepidemicus* is a commensal organism of mucous membranes and is described to cause endometritis in mares [2]. Colonization and disease have also been reported in other animals including pigs, ruminants, monkeys, cats and dogs [3]. In humans, *S. zooepidemicus* is a rare zoonotic infection that has been associated with a wide variety of invasive infections including bacteremia, endocarditis, arthritis [4], meningitis [5], endophthalmitis [6], acute poststreptococcal glomerulonephritis [7], and toxic shock syndrome [8].

## Case presentation

A 6-month-old female patient presented to the emergency department with one day of fever, vomiting, fussiness, decreased energy, and imbalance during crawling. These symptoms were preceded by cough and rhinorrhea for two weeks. Her birth history was unremarkable. Her past medical history was notable only for constipation and gastroesophageal reflux. She had no previous surgeries, was up to date on her immunizations and had unremarkable history. She lived with her parents and two siblings in a suburb of north Texas. None of the other household members were ill. The family had two pet dogs that were coughing at the time without other animal exposures or no recent travel. Her diet consisted of elemental formula and some solid foods and had never consumed unpasteurized dairy products.

At presentation, vital signs were notable for low-grade fever (38.4 °C), tachypnea (respiratory rate 76/min) and tachycardia (pulse 208/min). She was well perfused throughout, looked pale and sleepy, and had a bulging fontanelle without nuchal rigidity. Pupils were four mm in size and briskly reactive to light. Her oropharynx was injected. The physical examination was otherwise unremarkable. Shortly after presentation, she was noted to have bilateral eye deviation and arm tremors and right arm stiffening,

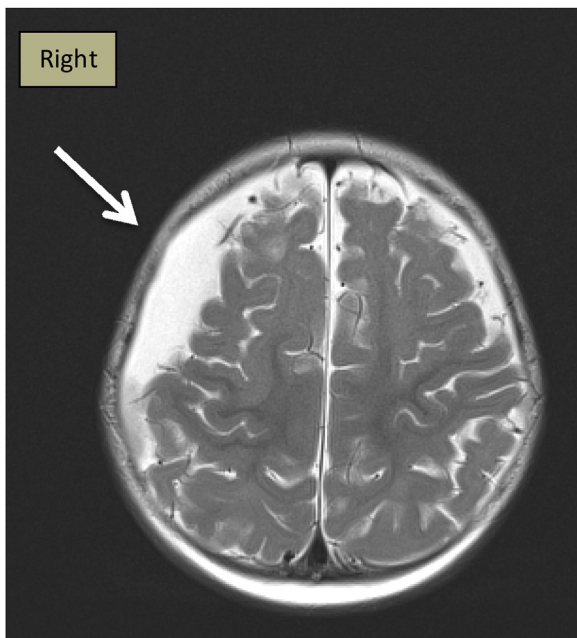
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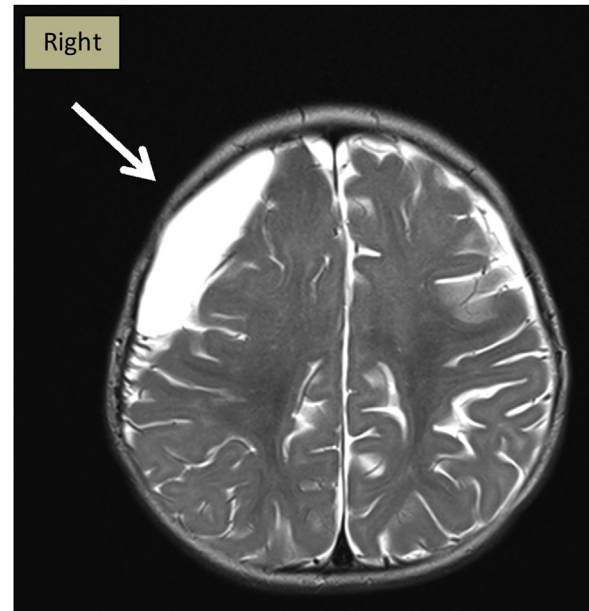
which were relieved with lorazepam and levetiracetam. Laboratory testing revealed mild leukopenia ( $4300$  white blood cells/ $\text{mm}^3$ ) with a left shift (neutrophils 69.8% and bands 10.1%). Cerebrospinal fluid (CSF) showed pleocytosis ( $57$  white blood cells/ $\text{mm}^3$ ) with neutrophilic predominance (95%), hypoglycorrhachia ( $4$  mg/dL), elevated protein ( $239$  mg/dL), and many Gram-positive cocci in pairs on Gram stain. CSF, blood, and urine were cultured. Multiplex respiratory polymerase chain reaction testing from a nasal swab (Biofire Filmarray Respiratory Panel, BioMérieux, Marcy l'Etoile, France) was positive for rhinovirus/enterovirus. The patient was empirically started on intravenous vancomycin and ceftriaxone and dexamethasone was added about two hours after antimicrobials for suspected bacterial meningitis. She was then transferred to the pediatric intensive care unit for further observation.

Magnetic resonance imaging (MRI) of brain on day 2 of hospitalization showed multifocal infarctions within the brain and a moderate subdural fluid collection along the right cerebral hemisphere (Fig. 1). CSF and blood cultures grew Group C *Streptococcus*. Both isolates were identified as *Streptococcus equi* by MALDI-TOF mass spectrometry (Bruker Daltonics, MA, USA) with best matches to reference spectra from *Streptococcus equi* subspecies *zooepidemicus*. *S. zooepidemicus* identification was later confirmed by phenotypic and biochemical testing using the API 20 Strep system (BioMérieux, Marcy l'Etoile, France). After the patient's *S. zooepidemicus* isolates tested susceptible to penicillin, antibacterial therapy was narrowed to aqueous penicillin G. Dexamethasone was administered for total of two days.

Although the patient continued to have clinical seizures, they resolved with the addition of phenobarbital and fosphenytoin, and neurosurgical intervention was not felt to be indicated as the patient was otherwise clinically stable and the fluid collection did not appear to be an empyema. The patient was transferred from the pediatric intensive care unit to a regular pediatric ward on day 9 of hospitalization as her neurological status was improving. On day 23 of hospitalization, hearing screen revealed severe to profound right sensorineural hearing loss. After four weeks of aqueous penicillin G, a repeat brain MRI showed progressive enlargement of the right subdural fluid collection and corresponding mass effect but the left subdural fluid collection looked smaller



**Fig. 1.** Axial T2-weighted image of MRI brain without contrast showing moderate subdural fluid collection along the right cerebral hemisphere (arrow).



**Fig. 2.** Axial T2-weighted image of MRI brain with contrast showing bilateral subdural fluid collections which are larger on the right side (arrow).

(Fig. 2). Due to the increased size of the right fluid collection, patient underwent a burr hole placement for drainage. After the subdural fluid cultures had returned negative, antimicrobials were discontinued, and the patient was discharged home three days after surgery. At ten months of age, she had normal follow-up brain MRI but she was diagnosed with mild language and motor delays as well as persistent right hearing loss.

## Discussion

There are 28 human cases of meningitis due to *S. zooepidemicus* in the literature [1,5,6,9–15]. These cases were mostly associated with contact with horses or ingestion of unpasteurized dairy products. The routes of exposure were through inhalation, inoculation or ingestion. Among the eleven patients who had reported outcomes, five died and six had hearing impairment. There are only three pediatric meningitis cases, including a one-day-old infant who died [14], a fourteen-week-old infant who recovered well without sequelae [13], and a thirteen-year-old patient who had hearing defect [15]. The majority of patients were treated with penicillin, ampicillin or third-generation cephalosporin, with a duration ranging between 10 days and 6 weeks. The role of steroids was unclear.

*S. zooepidemicus* in canines has been associated with toxic shock as well as respiratory infections that can progress into acute hemorrhagic pneumonia [16]. In Texas, outbreaks of *S. zooepidemicus* pneumonia were observed in greyhounds during 1992 and 1993 [17]. In the United Kingdom, there are two reported human cases of *S. zooepidemicus* infection with likely transmission from contact with dogs [18,19]. In one of these cases, both the dog handler and the dog developed respiratory infection [18]. *S. zooepidemicus* isolates from the dog and human were identical by phenotypic and molecular analysis. Although the dog was exposed to horses on a farm, none of these horses was found to be carrier of *S. zooepidemicus*. In the second case, the patient developed meningitis and bacteremia due to *S. zooepidemicus* and was exposed to four dogs that had diarrhea and rash [19]. Details of the dogs' exposure to other animals were not provided, and Group C *Streptococcus* was not isolated from the dogs. In our case, microbiological testing of the dogs was not performed but the

patient did not have any other exposures to explain an alternative source.

*S. zooepidemicus* is closely related genotypically to two other subspecies of *S. equi*, *S. equi* subspecies *equi* and *S. equi* subspecies *ruminatorum* [20]. These subspecies historically have been distinguished phenotypically based on biochemical reactions, including acid production from sorbitol and hippurate hydrolysis [20]. However, most clinical laboratories do not report bacterial identifications beyond the species level, with the exception of a few organisms for which knowing the higher level identification may change therapy and/or has public health implications (for example the identification of *Salmonella enterica* subspecies *enterica* Serotype Typhi). As in this patient's case, MALDI-TOF mass spectrometry analysis may provide suspicion for *S. zooepidemicus* based on strong spectral matches to reference sequences of *S. zooepidemicus*, but unless a clinical laboratory has validated the identification of this organism beyond the species level, the full identification will not be reported. Evaluation of the spectrum of potential disease and frequency of infection due to *S. zooepidemicus* in humans is challenged by the lack of subspecies reporting by clinical laboratories and by not being considered a reportable disease for public health surveillance.

In summary, we report a rare case of *S. zooepidemicus* meningitis in an infant. *S. zooepidemicus* should be considered in the differential diagnosis of patients who have severe infection and exposure to symptomatic dogs. Clinicians should be also aware of the potential of this organism to cause serious disease and death. As a large proportion of families with children have dogs, more epidemiological investigation and research on the pathogenesis of this zoonotic infection may be warranted.

#### Conflict of interest

None.

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#### Consent

Consent is not needed.

#### Author contribution

Yorgo Zahlanie, MD: Writing – Original draft (majority of writing).  
Mohammed Almatrafi, MD: Writing – Original draft (minority of writing).

Laura Filkins, PhD: Writing – Original draft (minority of writing).  
Michelle Hsaing, MD, MSc: Writing – Reviewing and Editing.

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