Journal of the Pediatric Infectious Diseases Society

CASE REPORT

Canine-to-Human Transmission of *Mycoplasma canis* in the Central Nervous System

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Dog bites remain a common occurrence in our society, particularly in toddlers and small children under the age of 2. Injuries to the head and face, more common in younger children, can often lead to significant morbidity. Additionally, there continues to be considerable clinical equipoise for standardized post-dog bite injury management. Here, we present the only reported pediatric case in the literature of *Mycoplasma canis*-associated central nervous system (CNS) infection in an 11-month-old infant who sustained a dog bite to the calvarium. The prevalence of dog bites during the SARS-CoV-2 pandemic had interestingly tripled in number after stay-at-home orders in 1 particular pediatric emergency department in Colorado. This observation paired with advances in microbiological identification like MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight mass spectrometer) may lead to the identification of future cases of uniquely canine pathogens that play a role in human infection.

Key words. central nervous system infection; dog bite; *Mycoplasma canis*; trauma.

BRIEF DESCRIPTION

Dog bites remain a frequent problem in pediatric populations with incidence of bites peaking in the spring and summer months. The worst outcomes occur most frequently in children younger than 2 years of age who sustain bites to the head, face, and neck. Significant trauma is most commonly influenced by breed-related behaviors of dogs and is associated with unprovoked behaviors, caused by a family dog that is familiar to the child.

CASE REPORT

An 11-month-old developmentally appropriate female presented to the emergency department (ED) after a traumatic dog bite by a Boxer breed dog that grasped her head, penetrated the cranium, and dragged the child about 2 feet before separation. The infant's parents detached her from the dog's jaws and brought her to the ED within 10 minutes of the incident. The bite resulted in a large left frontoparietal skull defect with exposed, herniating brain tissue. The patient did not lose consciousness and was crying and moving all extremities upon arrival. A CT (computed tomography) scan under general anesthesia demonstrated a 4.4-cm cranial defect with extruding brain parenchyma, subarachnoid hemorrhage within the Sylvian fissures, and a 2 mm subdural hemorrhage along the boundary of the superior left temporal lobe and Sylvian fissure (Figure 1). A 1 cm × 1 cm skull fragment was noted within the left parietal lobe deep to the calvarial defect's inferior portion. Within 1 hour of arrival to the ED, the patient was taken to the operating room (OR) by pediatric neurosurgery and plastic surgery for wound exploration, debridement, and washout. Intravenous (IV) cefazolin and vancomycin powder were used intraoperatively; however, no cultures were obtained during the initial procedure. Due to the high risk of intracranial infection with foreign bodies and dog bite flora complications, antimicrobial coverage with IV ceftriaxone, vancomycin, and metronidazole was initiated.

After her initial operation, she remained intubated and sedated with hyperosmolar therapies for neuroprotection in the pediatric intensive care unit (PICU). Pediatric infectious disease (ID) was consulted for antimicrobial management of her complex wound and assessing risk for rabies and tetanus. The family's dog showed no signs of rabies while being held by local animal control for 10 days. Rabies prophylaxis was deemed unnecessary as the dog was up to date on rabies vaccinations. The patient had received 3 appropriate doses of DTaP (Diphtheria, Tetanus, acellular Pertussis) vaccine at 2, 4, and 6 months of life; therefore, additional tetanus toxoid was not given.

On hospital day 7, the patient was taken back to the OR for repeat debridement and washout of the wound. While on broad-spectrum antimicrobials, 4 samples from the epidural space and 1 specimen of brain tissue were obtained for culture. The specimens were cultivated on 5% sheep's blood, chocolate,

Received 1 March 2021; editorial decision 1 June 2021; accepted 7 June 2021; Published online August 4, 2021.

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Journal of the Pediatric Infectious Diseases Society 2021;XX(XX):1–3

https://doi.org/10.1093/jpids/piab049

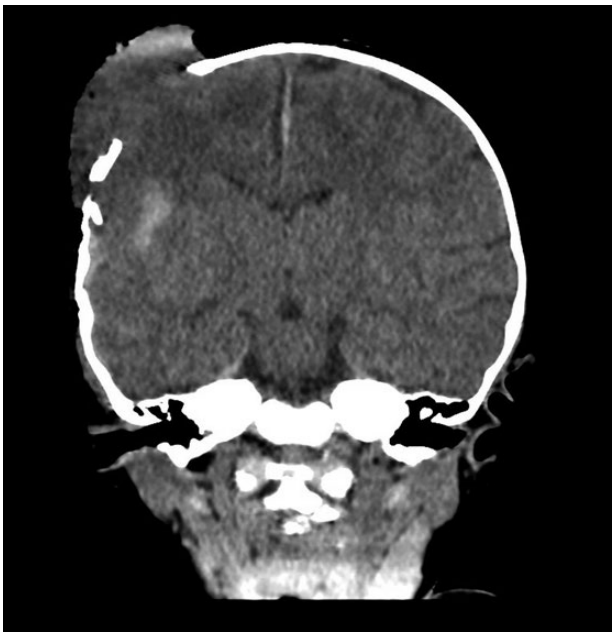

Figure 1. Coronal view of CT (computed tomography) brain without contrast showing extruded brain matter, subarachnoid and subdural hemorrhages.

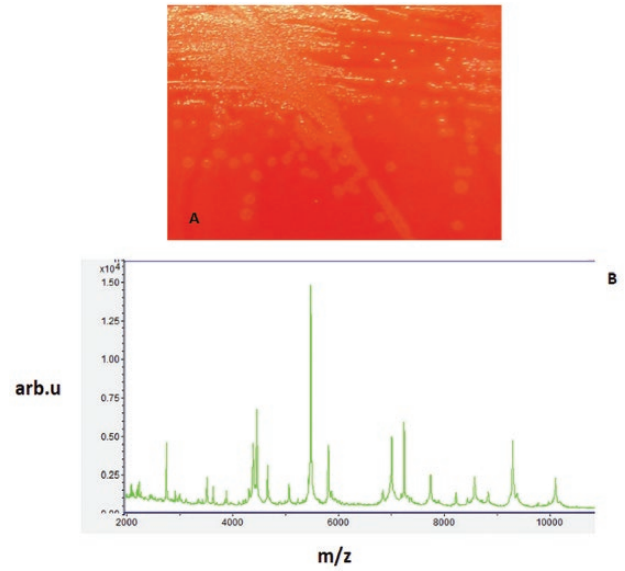

Figure 2. (A) Pinpoint-like colonies of *Mycoplasma canis* on sheep's blood agar. Adapted from Klein et al [1]. (B) Matrix-associated desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry spectrum identification of *Mycoplasma canis*. The x-axis represents mass-to-charge ratio values (m/z) and the y-axis represents intensities of the peaks expressed as arb.u or "arbitrary intensity units."

and CDC blood agar. The plates were incubated at 35°C in an atmosphere containing 5% carbon dioxide for 72 hours and the CDC blood agar in anaerobic conditions for 5 days. After 48 hours of incubation, a green haze was observed at the inoculation site on the blood and chocolate agar plates (Figure 2A) for all 5 specimens and after an additional 24 hours alpha-hemolytic, pinpoint colonies became visible. No bacterial structures were observed on Gram-stained material. Colonies from each specimen were analyzed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MALDI-TOF) and identified as *M. canis* (Figure 2B). The best growth of *M. canis* was noted in the epidural fluid collection (obtained after irrigation).

Following the second procedure, the infant remained afebrile and was extubated 2 days later. Vancomycin was discontinued as there was no concern for MRSA (methicillin-resistant *Staphylococcus aureus*) infection. Mild leukocytosis was noted at 14.7 × 1000/μL, platelets were elevated at 768 × 1000/μL, and C-reactive protein was elevated at 34.2 mg/L (reference <5 mg/L). MRI revealed new restricted diffusion within the left globus pallidus, putamen, and thalamus, indicating ischemic changes. No evidence of fluid collection or abscess surrounding the retained skull fragment was seen. IV ceftriaxone was stopped, and IV levofloxacin at 10mg/kg IV q12 was added to treat potential polymicrobial infection, including *M. canis*. This isolate's susceptibilities are not routinely performed either by California Public Health or by the Centers for Disease Control and Prevention (CDC).

On hospital day 14, a free flap procedure and washout were performed after the infant received 48 hours of levofloxacin. Additional epidural tissue cultures were obtained during this third surgery that did not reveal any further growth of *M. canis*. Free flap failure required its removal 2 days postoperatively, during which additional epidural tissue cultures were obtained. Cultures obtained during flap removal were again negative for growth. The patient was transferred to a nearby hospital for further management and skin graft procedure. She concurrently needed a gastrostomy tube for nutrition optimization. She ultimately completed a 6-week course of IV levofloxacin with additional culture samples continuing to remain negative.

Though her traumatic brain injury led to clinically significant neurologic deficits (right-sided hypertonicity and weakness, expressive language impairment, and oral motor dysfunction), she underwent intense rehabilitation and physical/occupational therapies with improvement. After 191 days in the hospital, she was discharged able to feed herself with her right hand (with moderate assist), use right finger extension/fine motor skills (though preferentially utilizes the left hand), perform sit to stand transitions, and ambulate up to 450 feet wearing a right custom solid ankle-foot orthosis.

DISCUSSION

Dog bites are a frequent infection source, with an estimated 4.5 million dog bites occurring each year. Younger children account for about one-half to three-quarters of dog bites, and about 20%

of these bites become infected [2]. One study suggested that the prevalence of dog bite injuries decreased within the time frame of 2010-2014 from 953 hospitals in 34 states and the District of Columbia [3]. Interestingly, in a more recent study, it has been noted that during the COVID-19 pandemic and subsequent stay-at-home orders, there was a recent tripling of the number of dog bite-related visits to a pediatric ED in Colorado [4].

Medical management of bite wounds requires cleansing and debridement with ample irrigation and closure if needed. Cultures are not routinely obtained, though this depends on the complexity of the injury [3]. Organisms routinely responsible for infection include a mix of aerobic and anaerobic species found in a dog's oral flora. The most commonly isolated organisms in these infections belong to the *Pasteurella* species, which colonize dogs' upper respiratory tracts. Other organisms responsible for infection include *Capnocytophaga canimorsus*, *Streptococcus*, *Staphylococcus*, and anaerobes like *Fusobacterium* and *Bacteroides* species [2]. Before cultures and susceptibility results are available, prophylactic antibiotic therapy with oral amoxicillin-clavulanate or parenteral ampicillin-sulbactam is indicated in dog bites with a high risk of infection. Extended-spectrum cephalosporins or trimethoprim-sulfamethoxazole plus clindamycin are an alternative in cases of penicillin allergy [2]. High-risk dog bite wounds include wounds that have undergone primary closure, presence of devitalized tissue or edema, full-thickness or puncture wounds, bites to the hand, face, foot, or genital area, and bites in immunocompromised and asplenic patients. There remains a lack of expert consensus on the duration of prophylactic treatment after an animal bite.

Mycoplasma canis is an opportunistic organism found in the urogenital and respiratory tract of dogs [5]. It is also a common organism implicated in canine kennel cough or infectious tracheobronchitis and typically transmitted via droplets. Only one prior report shows *M. canis* isolated from human tissue after a finger amputation following a dog bite in an adult [1].

Mycoplasma species are unique because they lack a cell wall; therefore, beta-lactams and other antibiotics that target cell wall synthesis are deemed ineffective. Tetracyclines, macrolides, and fluoroquinolones are effective against most *Mycoplasma* species as they target bacterial protein synthesis. Fluoroquinolones have been shown to exhibit superior CNS penetration compared to macrolides and were the antibiotic of choice in this case. Levofloxacin demonstrates superior activity against many unique causes of CNS infections, including *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Rhodococcus equi*. Though not licensed in children less than 6 months of age, quinolones (particularly levofloxacin) were the superior solution given the best CSF (cerebrospinal fluid) penetration capacity. Further data on dosing, duration, and efficacy of this drug in complicated CNS infections, as in this case, are necessary.

Antimicrobial susceptibility profile from the only other reported human case of *M. canis* revealed ciprofloxacin to be effective [1]. The lack of growth in subsequent cultures of epidural tissue in our case patient is also likely a result of appropriate antimicrobial susceptibility and successful eradication with levofloxacin.

The complex calvarial wound and potential for long-term sequelae given retained bone fragment associated with *Mycoplasma* species was a clear indication for treatment in this case. The neurological manifestations of *M. pneumoniae* infections are from 3 different mechanisms: (1) direct damage from local activity, (2) indirect damage due to host immune response, and (3) vascular type in which local vasculitis or thrombotic vascular occlusion occurs. *Mycoplasma* isolates have been noted to cause meningitis or brain abscesses in post-head trauma cases. *M. pneumoniae* has also been implicated in neurological conditions like meningoencephalitis and other postinfectious states like Guillain-Barré syndrome (GBS), mediated by the host immune response. Some patients have also been noted to have CNS cerebrovascular thrombosis associated with *Mycoplasma* infections.

Ultimately, prompt microbiological identification of *M. canis* through MALDI-TOF was instrumental in targeted therapy in this case, mitigating the risk of further infectious complications given retained bone fragments in brain parenchyma. MALDI-TOF has been shown to be a reliable tool for the identification of *Mycoplasma* [6].

Notes

Financial support. The authors have no financial relationships relevant to this article to disclose.

Potential conflicts of interest. The authors have no conflicts of interest relevant to this article to disclose. All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Klein S, Klotz M, Eigenbrod T. First isolation of *Mycoplasma canis* from human tissue samples after a dog bite. New Microbes New Infect **2018**; 25:14–5.
2. Bula-Rudas FJ, Olcott JL. Human and animal bites. Pediatr Rev **2018**; 39:490–500.
3. Holzer KJ, Vaughn MG, Murugan V. Dog bite injuries in the USA: prevalence, correlates and recent trends. Inj Prev **2019**; 25(3):187–90.
4. Dixon CA, Mistry RD. Dog bites in children surge during coronavirus disease-2019: a case for enhanced prevention. J Pediatr **2020**; 225:231–2.
5. Chalker VJ. Canine mycoplasmas. Res Vet Sci **2005**; 79:1–8.
6. Pereyre S, Tardy F, Renaudin H, et al. Identification and subtyping of clinically relevant human and ruminant mycoplasmas by use of matrix-assisted laser desorption ionization-time of flight mass spectrometry. J Clin Microbiol. **2013**; 51(10):3314–23.