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NEUROINVASIVE *MYCOPLASMA PNEUMONIAE* INFECTION WITHOUT INTRATHECAL ANTIBODY RESPONSE

Patrick M. Meyer Sauteur, MD, Benedikt M. Huber, MD,† and Philippe Goetschel, MD†*

Abstract: The pathogenesis of extrapulmonary *Mycoplasma pneumoniae*–associated neurologic disease is unclear. We present a case of acute meningoencephalitis in a 15-year-old girl with central nervous system invasion of the bacterium but without intrathecal antibody synthesis. Our observations suggest that in this setting *M. pneumoniae* infection can be self-limiting and mild despite invasion of the central nervous system.

Key Words: Mycoplasma pneumoniae, meningoencephalitis, cerebrospinal fluid, polymerase chain reaction, intrathecal antibody synthesis

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From the *Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital; and †Department of Pediatrics, Triemli Hospital, Zurich, Switzerland.
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Address for Correspondence: Patrick M. Meyer Sauteur, MD, Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital of Zurich, Steinwiesstrasse 75, CH-8032 Zürich, Switzerland. E-mail: patrick.meyer@kispi.uzh.ch.
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Mycoplasma pneumoniae is a cause of encephalitis in children,[1] but it remains controversial because causation is difficult to prove. The paucity of reports on isolation of *M. pneumoniae* from the central nervous system (CNS) favors the hypothesis of an immune-mediated inflammation in most cases. We report on a 15-year-old girl manifesting a few signs and symptoms of meningoencephalitis with CNS invasion of *M. pneumoniae* but without intrathecal antibody detection.

CASE REPORT

A 15-year-old girl was admitted with fever and complaining of neck pain, headache and diplopic images. She was completely oriented (Glasgow Coma Scale score 15) and had no nuchal rigidity. Diplopia was the only abnormal finding on neurologic examination. Her personal and family history was unremarkable.

Prodromal symptoms had started 12 days earlier with fever and a nonproductive cough. On day 10, a chest radiograph showed a pulmonary infiltrate on the right side. Amoxicillin (50 mg/kg in 3 doses daily) was started by the general practitioner. On day 11, she had morning vomiting.

At admission on day 13, a lumbar puncture revealed a pleocytosis (39 cells/mm^3 with 95% lymphocytes) and normal protein and glucose values. Polymerase chain reaction (PCR) for *M. pneumoniae* in the cerebrospinal fluid (CSF) was positive, but negative in a pharyngeal swab (Institute for Medical & Molecular Diagnostics Ltd., Zurich, Switzerland; PCR method as described by Tjhie et al[2] using specific primers for the *M. pneumoniae* 16S rDNA gene). Serum *M. pneumoniae* antibodies were increased by complement fixation test at 1:>640 (cutoff 1:<15) and by enzyme-linked immunosorbent assay (ELISA; Virotech ELISA, *M. pneumoniae* IgM/IgG/IgA, Genzyme, Virotech GmbH, Rüsselsheim, Germany; cutoff for IgM/IgG/IgA antibodies: 1.5 Virotech Units, VU): IgM 31.7 VU, IgG 15.5 VU and IgA 40.7 VU (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B276). Blood tests showed a normal C-reactive protein and a white blood cell count of 11.7×10^9/L with 80% neutrophils. Blood and CSF cultures were negative for conventional bacterial pathogens. Electroencephalography and cranial magnetic resonance imaging revealed no abnormality.

Azithromycin was administered orally for 5 days (30 mg/kg once daily). The patient improved significantly within 24 hours and was discharged home after 5 days on day 17. Complete recovery was noticed on a follow-up consultation on day 20 with persistently high immunoglobulin titers against *M. pneumoniae* in blood, but no more CSF pleocytosis and no *M. pneumoniae* detected in the CSF by PCR (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B276). Intrathecal antibodies measured in the CSF (Virotech ELISA) of lumbar punctures on days 13 and 20 were far below cutoff.

DISCUSSION

Neuroinvasive *M. pneumoniae* infection is rare[3,4] and together with no intrathecal antibody response it has been reported only once in a child.[5,6] Although *M. pneumoniae* is known mainly as a mucosal pathogen residing extracellularly on epithelial surfaces, it has been detected in extrapulmonary organs, suggesting dissemination.[1,7] The way by which *M. pneumoniae* disseminates in the bloodstream to produce extrapulmonary disease is unclear. *M. pneumoniae* infection in our patient was based on detection of the bacterium by PCR in CSF and a strongly positive serology in blood (complement fixation test and ELISA).

The main laboratory sign of acute CNS disease was the increased CSF cell count.[8] The inflammatory process leading to CNS disease caused by *M. pneumoniae* is induced by interleukin-18, interleukin-8 and interleukin-6, but without elevated interferon-γ and tumor necrosis factor-α.[7,9] This suggests a distinct mechanism that distinguishes *M. pneumoniae* from other bacterial or viral CNS infections in which tumor necrosis factor-α, interferon-γ or both are highly elevated.[7] The absence of an intrathecal antibody response in our case is also remarkable because it differs from other infectious CNS diseases in which the demonstration of intrathecal antibody production is, in most instances, specific for an ongoing infection of the CNS.[8] Additionally, an autoimmune mechanism due to cross-reacting *M. pneumoniae* antibodies seems unlikely.

Of note, our patient had a few signs and symptoms of meningoencephalitis and recovered without sequelae. Nevertheless, *Mycoplasma* species invading the CNS have been shown to cause neurologic injuries in animals and humans.[4] The excellent clinical course supported by the normal neuroimaging in our patient makes a direct damage of neural cells improbable. This is in agreement with the treatment regimen including azithromycin that might have not contributed to the clinical improvement within 24 hours, because it was administered orally and appeared to be distributed into brain tissue but not into the CSF.[4] Thus, resolution of neurologic signs and symptoms and clearance of *M. pneumoniae* from the CSF at least until day 20 was rather spontaneous.

The case presented here differs from a few reports on severe and life-threatening courses with neurologic sequelae.[1,7] The degree of intrathecal antibody response in relation to the severity of disease is not known because it is rarely measured. Nevertheless, one might speculate that clinically more severe cases of *M. pneumoniae*–associated neurologic disease could be accompanied by some degree of intrathecal antibody response consistent with immunologic sequelae. Thus, our report may influence the choice of diagnostic methods by adding serologic testing of CSF to serologic testing of blood and PCR of specimens from the throat and CSF, to elucidate the mechanism of *M. pneumoniae* neurologic disease.

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HYPERACUTE INFECTIOUS KERATITIS WITH *PLESIOMONAS SHIGELLOIDES* FOLLOWING TRAUMATIC LAMELLAR CORNEAL LACERATION

J. Michael Klatte, MD, Mohammad H. Dastjerdi, MD,†‡ Kylie Clark, MD,§ Christopher J. Harrison, MD,* Florin Grigorian, MD,‡ and Erin D. Stahl, MD†‡*

Abstract: *Plesiomonas shigelloides* rarely causes extraintestinal human disease, and infection of ocular tissues is even rarer, never having been reported as the sole pathogen of posttraumatic ocular infection. We report the first case of infectious keratitis due solely to *P. shigelloides* following traumatic corneal laceration and a literature review with regard to *P. shigelloides* ocular disease.

Key Words: *Plesiomonas shigelloides*, keratitis, corneal laceration

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From *Children's Mercy Hospitals and Clinics, Pediatric Infectious Diseases Section, Kansas City, MO; †University of Kansas, Department of Ophthalmology, Kansas City, KS; and Departments of ‡Ophthalmology and §Pediatrics, Children's Mercy Hospitals and Clinics, Kansas City, MO.

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Address for Correspondence: J. Michael Klatte, MD, Children's Mercy Hospitals and Clinics, Infectious Diseases Section, 2401 Gillham Road, Kansas City, MO 64108. E-mail: mklatte@cmh.edu.

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Plesiomonas shigelloides is a facultative anaerobic, Gram-negative rod, recently recategorized into the Enterobacteriaceae family. Epidemiologically, *P. shigelloides* is indigenous to marine and brackish water, primarily in temperate climates.[1] This pathogen can be food-borne and is associated with acute gastroenteritis. Shellfish ingestion and contact with contaminated fresh water have been implicated as infectious sources. Reports of extraintestinal infection include sepsis, meningoencephalitis, cellulitis and osteomyelitis.[2,3] Four case reports exist with respect to *P. shigelloides* disease with ocular involvement. Two describe congenital endophthalmitis.[4,5] Two describe polymicrobial posttraumatic endophthalmitis and resolution-required enucleation.[6,7] Here, we describe a case of infectious keratitis following traumatic lamellar corneal laceration, caused solely by *P. shigelloides*, for which prolonged antimicrobials and multiple debridements allowed preservation of the involved eye.

CASE REPORT

A 13-year-old otherwise healthy Caucasian girl presented to Children's Mercy Hospital 1 day after sustaining a traumatic right eye injury, secondary to being struck by a rock. The rock's source was the creek bed of a river in central Missouri. She complained of pain and blurred vision of the affected eye immediately after the injury. She later developed eyelid swelling and progressively decreased vision. On the morning after the injury, she was seen at a local emergency department, where concern for a ruptured globe led to referral.

Upon presentation to Children's Mercy Hospital, right eye visual acuity was 20/400, with the left eye 20/20. On examination, both pupils were round and reactive, without afferent pupillary defects. Extraocular movements were intact bilaterally. A small abrasion with tenderness to palpation over the right maxillary bone was present. Gross right eye examination demonstrated mucopurulent discharge in the lashes and diffuse conjunctival injection. Slit-lamp examination revealed a triangular, opacified, flap-like corneal wound starting paracentrally and extending to the temporal limbus. Seidel testing, however, was negative for aqueous leakage. The anterior chamber revealed 3+ cells and flare, along with a 1 mm hypopyon. The lens was clear.

Within 18 hours of the original trauma, she underwent operative evaluation. The laceration was a nonpenetrating wound, with a 5 × 4 mm^2 triangular flap. The area surrounding the flap was edematous and opaque, with fluffy white infiltration into the corneal stroma. The laceration was not sutured intraoperatively. Corneal cultures were obtained, and the patient was treated with hourly ophthalmic fortified tobramycin (14 mg/mL) solution and moxifloxacin 0.5% solution. Initial dilated funduscopic examination showed a 3-disk diameter macular hemorrhage. She was discharged home postoperatively and continued solely on topical tobramycin and moxifloxacin solutions at hourly dosing intervals, with scheduled daily outpatient ophthalmology clinic follow-up.

For 2 days after discharge, no notable corneal ulcer or hypopyon changes occurred, but on the third day she developed increased facial swelling, erythema, induration and tenderness extending from the right cheek infraorbitally to the right tragus. She complained of chills and sharp left upper quadrant abdominal pain, but denied fever, emesis or diarrhea. She was afebrile when hospitalized for concern for cellulitis and/or systemic infection. Blood cultures were obtained, and oral clindamycin was started. Ophthalmic tobramycin and moxifloxacin were continued.

Corneal cultures from her initial surgical encounter grew *P. shigelloides.* Based on antimicrobial susceptibilities for tobramycin (minimum inhibitory concentration [MIC] = 8

