

Brain magnetic resonance imaging findings suggestive of widespread white matter involvement in children with *Streptococcus mitis* meningitis

Uluç Yiş¹, Kürşat Bora Çarman¹, Reyhan Yiş², Ümit Derundere³

Departments of ¹Pediatric Neurology and ²Microbiology and Clinical Microbiology, Gaziantep Children's Hospital, and ³Radyotek Imaging Center, Gaziantep, Turkey. E-mail: ulyis@yahoo.com

SUMMARY: Yiş U, Çarman KB, Yiş R, Derundere Ü. Brain magnetic resonance imaging findings suggestive of widespread white matter involvement in children with *Streptococcus mitis* meningitis. Turk J Pediatr 2012; 54: 425-428.

Streptococcus mitis (*S. mitis*) is a rare cause of meningitis in immunocompetent children. It has been described in patients with neurosurgical procedure, previous spinal anesthesia and immunodeficiency. We report two childhood cases of *S. mitis* meningitis. The children were previously healthy. One of the patients had poor oral hygiene and the other had a history of sinusitis. Both of them had encephalopathy and signs of meningeal irritation at presentation. Widespread cerebral white matter lesions were found on brain magnetic resonance imaging. The lesions disappeared and encephalopathy recovered with antibiotic and immunomodulatory treatment.

Key words: *Streptococcus mitis*, meningitis, cerebral white matter.

Streptococcus mitis (*S. mitis*) belongs to the family of viridans streptococci and is a normal component of the oropharynx, skin, gastrointestinal system, and genital system floras¹. The pathogenicity and virulence of the bacteria are very low. *S. mitis* as a cause of meningitis has been described in patients with previous spinal anesthesia, neurosurgical procedure, malignancy, alcoholism, poor oral hygiene, and maxillary sinusitis, and in newborns²⁻⁵. Cerebral white matter involvement during the course of *S. mitis* meningitis has been described rarely⁶. We report two cases with widespread cerebral white matter lesions that were detected by magnetic resonance imaging (MRI) during the course of *S. mitis* meningitis.

Case Reports

Case 1

A six-year-old boy was referred with a three-day history of fever, generalized convulsions and altered state of consciousness. The child's previous medical history was unremarkable. His vaccinations, which were included in the Turkish Health Ministry program, were complete according to his age group. He was not immunized for *Hib* and *Streptococcus*

pneumoniae. On admission, he was confused, and the physical examination revealed poor oral hygiene, nuchal rigidity and fever (Fig. 1). Deep tendon reflexes were hyperactive. A computed tomography (CT) examination of the brain was normal. A complete blood count revealed 16.6×10^3 /uL white blood cells (reference value $4.5-11.0 \times 10^3$ /uL) and a C-reactive protein serum level of 3.53 mg/dl (reference value 0.0-0.8 mg/dl). A lumbar puncture was performed, which showed 20 white blood cells/mm³, total protein content



Figure 1. Poor oral hygiene of Case 1.

of 91.3 mg/dl (reference value 15-60 mg/dl) and normo-glycorrhachia of 76 mg/dl (reference values 75-106 mg/dl; concomitant blood glucose: 120 mg/dl). Therapy with ceftriaxone (100 mg/kg/day) and vancomycin (60 mg/kg/day) was started. Two days after the admission, cerebrospinal fluid culture yielded growth of penicillin-sensitive *S. mitis*. On the fourth day of admission, brain MRI was performed because of ongoing altered state of consciousness and revealed brain swelling and diffuse periventricular and white matter hyperintensity on T2 FLAIR sequence (Fig. 2).

Intravenous immunoglobulin was given for five days (total 2 g/kg) for widespread cerebral white matter lesions and altered state of consciousness. The patient benefited well from immunoglobulin treatment and antibiotics were continuously administered for 14 days. A follow-up brain MRI at the end of treatment revealed mostly reduced hyperintensities on the affected sides (Fig. 3). Serum immunoglobulin levels, which were obtained before intravenous immunoglobulin treatment, and peripheral blood smear were normal. At discharge, the neurologic examination was normal and he had no neurologic or psychiatric disabilities like epilepsy, mental retardation or behavioral disorder. The patient was referred to pediatric dentistry for his poor oral hygiene.

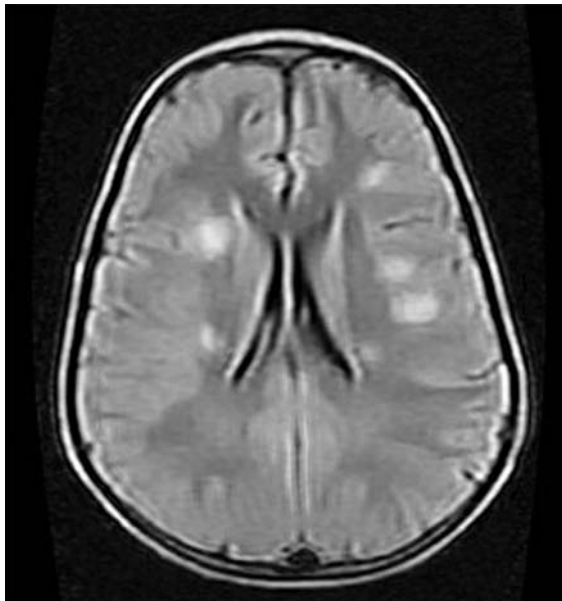


Figure 2. Brain swelling, diffuse periventricular and white matter hyperintensity on T2 FLAIR sequence before treatment.

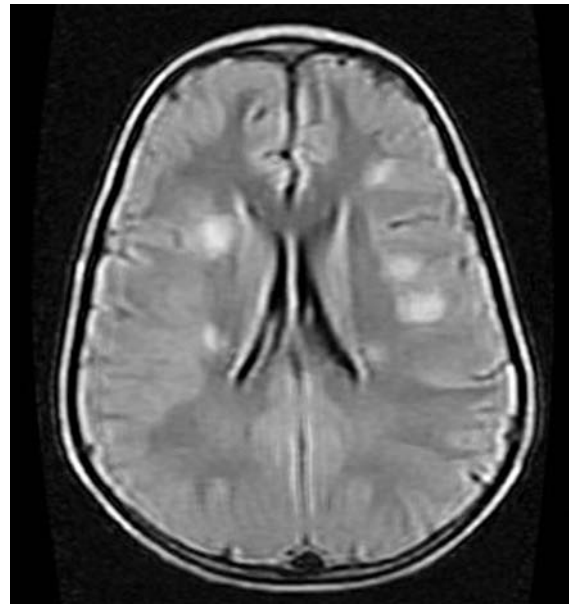


Figure 3. Reduced hyperintensities on the affected sides after treatment.

Case 2

This patient was previously described by us⁶. She was an eight-year-old girl who was admitted to the pediatric intensive care unit with a five-day history of drowsiness, fever, headache, and vomiting. The child's previous medical history was unremarkable. Her vaccinations, which were included in the Turkish Health Ministry program, were complete according to her age group. She was not immunized for *Hib* or *S. pneumoniae*. Two weeks before admission, she was treated for sinusitis with amoxicillin-clavulanate for 10 days. On admission, Glasgow coma scale score was 10, and she had nuchal rigidity and purulent postnasal discharge. A complete blood count revealed 18.6×10^3 /uL white blood cells (reference value $4.5-11.0 \times 10^3$ /uL) and a C-reactive protein serum level of 5.36 mg/dl (reference value 0.0-0.8 mg/dl). Brain MRI at admission revealed diffuse brain swelling with significant white matter hyperintensities on T2 FLAIR sequences (Fig. 4).

A lumbar puncture was performed and showed 150 white blood cells/mm³, total protein content of 80 mg/dl (reference value 15-60 mg/dl) and hypoglycorrhachia of 40 mg/dl (reference values 75-106 mg/dl; concomitant blood glucose: 112 mg/dl). Therapy with ceftriaxone (100 mg/kg/day) was started. Two

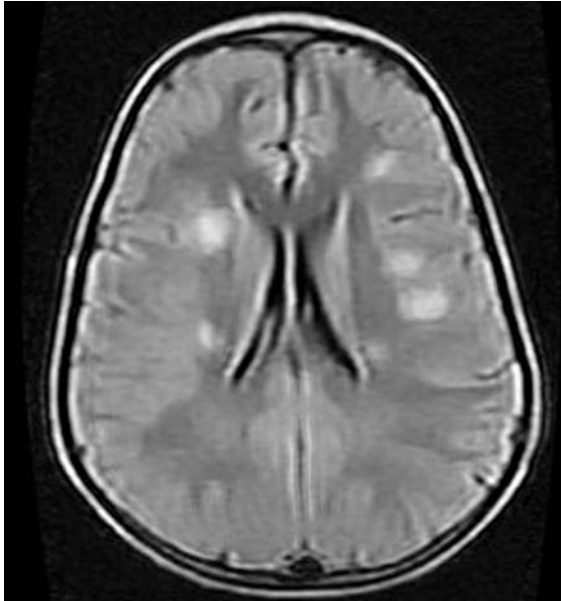


Figure 4. Diffuse brain swelling with significant white matter hyperintensities on T2 FLAIR sequences before treatment.

days after the admission, cerebrospinal fluid culture yielded growth of penicillin-sensitive *S. mitis*. Dexamethasone (0.6 mg/kg/day) was administered for widespread white matter lesions and ongoing neurological symptoms. Dexamethasone treatment was continued for 10 days and antibiotics were administered until day 14. Serum immunoglobulin levels and peripheral blood smear were normal. At discharge, the neurologic examination was normal and she had no neurologic or psychiatric disabilities like epilepsy, mental retardation or behavioral disorder.

Discussion

Streptococcus mitis is primarily responsible for subacute bacterial endocarditis in patients with poor oral hygiene and a previous history of dental treatment¹. Meningitis caused by *S. mitis* has been described rarely. Patients with *S. mitis* meningitis usually have underlying factors. Most of the *S. mitis* meningitis occurs after invasive procedures like spinal anesthesia or neurosurgical interventions². Newborns and patients with primary and second immunodeficiency are also predisposed to *S. mitis* meningitis^{3,4}. Poor oral hygiene, maxillary sinusitis, alcoholism, and endocarditis caused by *S. mitis* had also been described as risk factors⁵. In our cases, there was no history

of spinal anesthesia or lumbar puncture, and serum immunoglobulins were normal. We suggest poor oral hygiene in the first patient and sinusitis in the second patient as the respective sources of meningitis.

Although focal parenchymal abnormalities and cerebral white matter lesions have been described in *S. pneumoniae* meningitis, there is only one report describing radiological features during *S. mitis* meningitis⁶⁻⁸. Streptococcal cell wall components induce release of cytokines by the endothelium, epithelium and leukocytes⁹. They also induce permeability of the blood brain barrier and are cytotoxic to neurons. Accumulation of inflammatory cells among the small arteries and arterioles may cause inflammation and thrombosis, or organisms may directly invade blood vessels⁹. The resulting vasculitis and thrombosis may result in widespread white matter lesions that reflect local areas of ischemia with cytotoxic edema^{8,10}.

Early antibiotic therapy is the key point in the management of meningitis. When widespread white matter lesions and encephalopathy are present, corticosteroids or immunoglobulins are used to suppress the inflammatory cascade, brain edema and demyelination, all of which cause neuronal injury. We did not use high-dose pulse methylprednisolone treatment because of adverse effects including hepatopathy and cardiotoxicity. Because of their fewer side effects, immunoglobulin and standard dexamethasone treatments were chosen in the first and second case, respectively. These treatments resulted in disappearance of white matter lesions and clinical recovery.

Acute disseminated encephalomyelitis, neurodegenerative disorders like mitochondrial encephalopathies, metachromatic leukodystrophy, vanishing white matter disease, and Krabbe disease should be considered in the differential diagnosis of neurological deterioration and widespread white matter lesions. Acute disseminated encephalomyelitis was not considered because it is a demyelinating disorder that is usually observed a few weeks after a previous infection or vaccination. Growth of bacteria in the cerebrospinal fluid, improvement after antibiotic and immunomodulatory treatments, and nonprogressive neurological symptoms also did not suggest a neurodegenerative disorder.

In conclusion, although *S. mitis* has a low virulence and pathogenicity, it may cause meningitis in children with poor oral hygiene and sinusitis. Widespread white matter lesions may be observed during the course of meningitis probably as a result of vasculitis and thrombosis. Short-term dexamethasone and immunoglobulin treatments should be used in patients with ongoing encephalopathy to suppress the inflammatory cascade.

REFERENCES

1. The Gram-positive cocci part II: streptococci, enterococci and the 'Streptococcus-like' bacteria. In: Koneman EW, Allen SD, Janda WM, Schreckenberger PC, Tenover FC, Tenover FC (eds). Color Atlas and Textbook of Diagnostic Microbiology (5th ed). New York, USA: Lippincott; 1997: 577–649.
2. Villevieille T, Vincenti-Rouquette I, Petitjeans F, et al. Streptococcus mitis-induced meningitis after spinal anesthesia. Anesth Analg 2000; 90: 500-501.
3. Bignardi GE, Isaacs D. Neonatal meningitis due to Streptococcus mitis. Rev Infect Dis 1989; 11: 86-88.
4. Balkundi DR, Murray DL, Patterson MJ, Gera R, Scott-Emuakpor A, Kulkarni R. Penicillin-resistant Streptococcus mitis as a cause of septicemia with meningitis in febrile neutropenic children. J Pediatr Hematol Oncol 1997; 19: 82-85.
5. Kutlu SS, Sacar S, Cevahir N, Turgut H. Community-acquired Streptococcus mitis meningitis: a case report. Int J Infect Dis 2008; 12: 107-109.
6. Yiş R, Yüksel ÇN, Derundere Ü, Yiş U. [Meningitis and white matter lesions due to Streptococcus mitis in a previously healthy child]. Mikrobiyol Bul 2011; 45: 741-746.
7. Cabral DA, Flodmark O, Farrell K, Speert DP. Prospective study of computed tomography in acute bacterial meningitis. J Pediatr 1987; 111: 201-205.
8. Jorens PG, Parizel PM, Wojciechowski M, et al. Streptococcus pneumoniae meningoencephalitis with unusual and widespread white matter lesions. Eur J Pediatr Neurol 2008; 12: 127-132.
9. Tuomanen EI. Molecular and cellular mechanisms of pneumococcal meningitis. Ann NY Acad Sci 1996; 797: 42-52.
10. Jorens PG, Parizel PM, Demey HE, et al. Meningoencephalitis caused by Streptococcus pneumoniae: a diagnostic and therapeutic challenge. Diagnosis with diffusion-weighted MRI leading to treatment with corticosteroids. Neuroradiology 2005; 47: 758-764.