Neisseria Meningitidis Serogroup Z–Induced Meningitis: The First Case from Turkey

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Abstract

Neisseria meningitidis is a significant worldwide cause of bacterial meningitis and sepsis. High case-fatality rates and severe complications in survivors can occur. We present a 1-month 23-day-old case diagnosed with meningococcal meningitis and sepsis, in which serogroup Z of *N. meningitidis* was isolated from cerebrospinal fluid and blood cultures and treated with ceftriaxone for 7 days. Our patient is the first case of *N. meningitidis* serogroup Z–induced invasive meningococcal infection in Turkey. *N. meningitidis* serogroup Z is not included in the current meningococcal vaccines. It is concerning that a nonvaccine serogroup caused this invasive meningococcal disease and that even if the vaccine would cover this serogroup, it has happened before the usual age of administration. Therefore, meningococcal disease surveillance should continue, and an effective prevention and control strategy for nonvaccine serogroups should be implemented.

Keywords
- *Neisseria meningitidis*
- meningococcal infection
- meningitis
- serogroup Z

Introduction

Neisseria meningitidis is a significant worldwide cause of bacterial meningitis.[1] In the rare cases where invasive diseases occur, the clinical spectrum of the meningococcal disease varies widely, but the highest proportion of cases present with meningococcal meningitis (30–50%).[2] It can cause bacteremia without sepsis, meningococcal septicemia with or without meningitis, pneumonia, and focal infections such as arthritis, myocarditis, pericarditis, endophthalmitis, epiglottitis, otitis, and urethritis.[1,2]

The peak incidence of meningococcal disease occurs in the first year of life, with 35 to 40% of cases occurring in children younger than 5 years of age.[3] Invasive meningococcal disease often has a rapid and poor progression and should always be considered a medical emergency.[1] Early antibiotic treatment is the most important step to save lives and reduce complications.[1] Case-fatality rate ranges from 80% in untreated cases to 4 to 20% with appropriate treatment. More than one-third of survivors have severe complications, and 9% have a severe lifelong disability.[4]

The meningococcal polysaccharide capsule is the major virulence factor,[5] and the serogroups are the basis for the classification and nomenclature of the bacteria. There are 12 meningococcal serogroups: A, B, C, E, H, I, K, L, X, W, Y, and Z. Half of these (A, B, C, W, X, and Y) are responsible for almost all invasive meningococcal cases globally.[4]

We present the first case of meningococcal meningitis due to *N. meningitidis* serogroup Z in Turkey.

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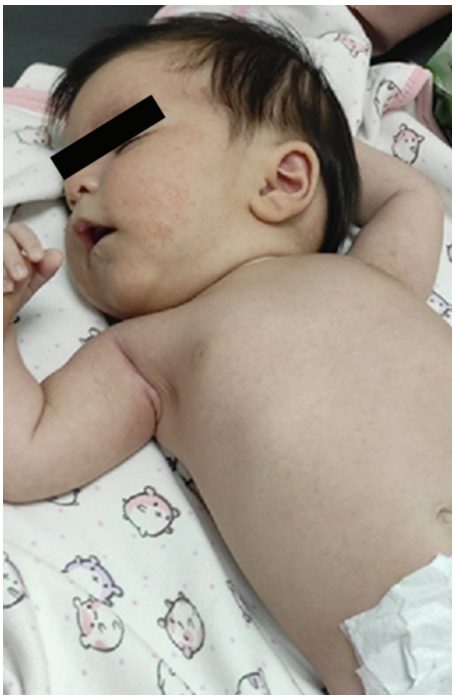

Fig. 1 Nonspecific macular rashes on the trunk.

Case Presentation

A previously healthy 1-month 23-day-old female infant was brought to the emergency department for fever and groaning from the day before. She was born at $38^{4/7}$ weeks by cesarean section and with uneventful postnatal history. On physical examination, the following was measured: body temperature, 37.8°C; pulse, 130/min; respiratory rate, 55/min; blood pressure, 90/50 mm Hg; capillary refill time <2 seconds. Neck stiffness and fontanelle bulging were not observed. There were several macular, pink-colored rashes on the trunk (►**Fig. 1**). The patient appeared inclined to sleep during the examination with impaired oral intake. The following blood tests were obtained: white blood cell count, 6,180/mm^3; platelet count, 282,000/mm^3; C-reactive protein, 152 mg/L; complete urinalysis, normal. A lumbar puncture was performed, and the cerebrospinal fluid (CSF) showed the following: leukocytes, 1,220/mm^3; proteins, 135 mg/dL; and glucose, 20 mg/dL (simultaneous blood glucose, 114 mg/dL). Bacterial meningitis was considered, and dexamethasone, cefotaxime, ampicillin, and vancomycin were started. The patient, whose general conditions were unstable, was admitted to the pediatric intensive care unit with the diagnosis of meningitis and sepsis. Gram-negative diplococci were detected in Gram staining of the CSF. *N. meningitidis* polymerase chain reaction was positive. Dexamethasone, ampicillin, cefotaxime, and vancomycin were discontinued, and the antibiotic therapy continued with ceftriaxone.

On the second day after hospitalization, she had no rash on follow-up and was transferred to the pediatric infectious diseases service. *N. meningitidis* growth was observed in CSF and blood culture. Antibiotic susceptibility tests were performed for penicillin, ceftriaxone, and ciprofloxacin. The strain was susceptible to all the tested antibiotics, including penicillin, with a minimum inhibition concentration (MIC) of 0.0016 µg/mL. The strain was typed as *N. meningitidis* serogroup Z by the Public Health Agency of Turkey. Ciprofloxacin prophylaxis was administered to the patient's contacts (mother and father). On the fourth day, she was evaluated for complications due to subfebrile temperature values. Echocardiography and transfontanelle and abdominal ultrasound were normal, and follow-up was uneventful. Antibiotic treatment was given for 7 days and then discontinued. A hearing test was performed on the patient, and it was found to be normal. After discharge, the patient developed mild neutropenia (total neutrophil count: 600/mm^3). However, no immunodeficiency has been diagnosed in this patient, who was followed up in the pediatric immunology department.

Discussion

The geographic distribution and epidemic potential of *N. meningitides* strains are variable.[6] A limited number of cases of meningococcal disease (1%) attributable to serogroups 29E, X, and Z have been reported worldwide. Epidemiologic studies have reported a range of 0.6 to 6.6% of nasopharyngeal carriage rates for serogroup Z, but these are considered low frequencies.[7] The first pediatric case of meningococcal disease caused by serogroup Z was reported in the United States in 1980.[8] In the literature, the incidence of serogroup Z–induced invasive meningococcal infections is rare.[9] In a multicenter study on nasopharyngeal carriages in Turkey, serogroup Z was not found.[10] In contrast, a study on meningococcal meningitis showed that *N. meningitidis* serogroup W was the most prevalent in Turkey during 2005–2012,[11] while serogroup B was prominent between 2015 and 2018.[12] In Turkey, serogroup Z has not been reported in the meningitis surveillance started since 2005.[11,12]

The incidence and prevalence of the invasive meningococcal disease vary geographically and temporally. Surveillance systems differ across the world. Invasive meningococcal disease may occur sporadically, in small clusters, localized, or as large outbreaks.[1,6] Serogroup-specific vaccines are used to prevent and respond to outbreaks.[1] Identification of the dominant *N. meningitidis* serogroups in a given country is essential for developing local vaccination strategies.

In Turkey, prevention and control strategies against invasive meningococcal disease include vaccination and antimicrobial prophylaxis. Close contact with invasive meningococcal cases is closely monitored and/or chemoprophylaxis is given. Vaccination recommendations vary according to age group, country, and serogroup incidence.[6] Although not routinely included in the National Immunization Program of Turkey, there are licensed quadrivalent vaccines containing serotypes A, C, W-135, and Y, as well as a MenB-4C vaccine developed against the meningococcal B serotype. These vaccines may be administered to high-risk patients or as private vaccines without reimbursement.[13] It has been reported that protection can be achieved by vaccination against the serogroups that account for the majority

of invasive meningococcal disease, with a decrease in the incidence of invasive meningococcal disease in countries where routine vaccination has been adopted.[13] However, it does not cover all serogroups of invasive meningococcal disease.[6] Meningococcal vaccines are given no earlier than 2 months of age.[13] In the Turkish National Immunization Program, Bacillus Calmette–Guérin, diphtheria, tetanus, acellular-component pertussis, inactivated poliovirus, *Haemophilus influenzae* type b, and 13-valent pneumococcal conjugate vaccines are included in the second month.[14] We have observed that the private sector physicians, who make the most meningococcal vaccines in practice, generally postpone the meningococcal vaccines to the third month in practice thinking that the second month of the Turkish National Immunization Program is overcrowded.

This is the first case in Turkey in which invasive meningococcal infection was originated from *N. meningitidis* serogroup Z. *N. meningitidis* serogroup Z rarely causes invasive meningococcal disease.[9] Although it does not usually lead to serious illness, our patient had meningitis and sepsis, a nonspecific macular rash was observed, and her clinical condition improved rapidly after antibiotic treatment. Vaccination as early as possible and covering as many serogroups as possible is the most important step in preventing this disease, and our patient was diagnosed at a very early age with the nonvaccine meningococcal serogroup.

The increase in the incidence of invasive meningococcal disease originating from nonvaccine serogroups should be monitored. If necessary, efforts should be made to develop new vaccines with a broader serogroup coverage and establish an effective prevention and control strategy.

Conflict of Interest
None declared.

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