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Recurrent Meningococcal Meningitis in an Iranian Conscript: a Brief Report

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Introduction

Infections with *Neisseria meningitidis,* an etiologic agent of meningitis and sepsis, are a feared public health emergency (1). Meningococcal meningitis is endemic throughout most of the world; its annual incidence rate varies between 1 and 12 per 100,000 population. The rates of disease have been on the increase because of epidemics in non-industrialized regions (2,3). Immunogenicity and safety trials of meningococcal polysaccharide vaccines have been reported by the United States, Africa, and some developing countries (7,8). Although infants are at highest risk (4) for serious meningococcal meningitis, epidemics have also been reported among military personnel (5,6). In the Islamic Republic of Iran, mass immunization of conscripts with divalent meningococcal vaccine has the potential to actively protect soldiers before they are dispatched to army training centers (7,8). However, a recently vaccinated conscript was hospitalized because of typical meningococcal meningitis. Thus, we describe results of our investigation into this unusual case.

Case Report

The patient was a 20-year-old male conscript dispatched to an army basic military training camp in the north of Tehran after having received divalent meningococcal polysaccharide vaccine on 9 December 2003. Thirty-five days later, he had a precipitous onset of fever and headache, and within hours he felt neck pain when moving his head. The following day, his blood pressure fell to 100/70 mmHg, and as a result, he was rushed to the hospital where he exhibited signs of confusion. Lumbar puncture was performed, and the cerebrospinal fluid (CSF) was divided into two culture bottles. A direct Gram stained smear of the CSF was prepared. The bacterial culture was performed as follows: 100 µl (each) of CSF was inoculated onto a chocolate agar plate and a Trypticase soy agar plate supplemented with goat serum and into thioglycolate medium. The culture media were incubated in 3% CO_2 at 37°C for 24 h (9). The identification of *Neisseria meningitidis* was accomplished by biochemical tests and polyclonal antibody capsular polysaccharide serotyping. Before the laboratory reports were reviewed, empiric antibiotic therapy was started. After 2 weeks of receiving 2 g intravenous ceftriaxone and 2 g chloramphenicol daily, the patient almost completely recovered and left the hospital. On 29 February 2004, he was readmitted to the hospital with the same symptoms. As on the previous occasion, before empirical antibiotic therapy was begun, lumbar puncture was performed and 100 µl of CSF was inoculated onto chocolate agar medium. A Gram-stained smear of the CSF revealed small gram-negative diplococci and numerous leukocytes. Biochemical and cell counts were also performed. Serum samples for measuring IgG and C_3, C_4, and CH_{50} complement components were taken, and serotyping of the isolate was carried out.

Antimicrobial Susceptibility Pattern

Empiric therapy during the patient's first hospitalization consisted of 2 g ceftriaxone and choloramphenicol/day for 12 consecutive days. However, on the second occasion, treatment was determined by the results of the antibiotic susceptibility test. The isolate was susceptible only to extended-spectrum ceftriaxone, which was administered for 10 days. The patient's signs and symptoms resolved, and he was discharged from the hospital.

Results of Laboratory Studies

The patient's extremities, especially the extensor surfaces of the forearms and anterior surfaces of the legs, showed a maculopapular rash. The lesions had a diameter of about 0.5 cm. Laboratory results revealed that the erythrocyte sedimentation rate was 65 mm in the first hour and that leukocytes were 16.8×10^9/l with 78% neutrophils. CSF analysis showed a protein of 4.6 g/dl and glucose of 7 mg/dl. The direct Gram-stained smear of the CSF revealed small, gram-negative, intracellular diplococci and numerous leukocytes. After 24-h incubation at 37°C in 3% CO_2, the culture grew gram-negative diplococci, which were identified as *Neisseria meningitidis.* Serotyping revealed that a serotype C strain of *Neisseria meningitidis* had been isolated from the patient's CSF sample. Furthermore, laboratory investigations showed that the level of IgG was higher than the normal range, but levels of C_3, C_4, and CH_{50} components were lower than the normal range, and thus, the patient was most likely complement component deficient.

Discussion

After several clusters of meningococcal meningitis occured among recruits to the armed forces of the Islamic Republic of Iran, vaccination against seroptype A and C *Neisseria meningitidis* was introduced in 1983. Since then, no further clusters of meningococcal meningitis have been reported; nonetheless, there have been sporadic cases of meningococcal meningitis among conscripts for no identifiable reason. The case of meningitis reported in this study is that of a male conscript who had been immunized 35 days before arrival at the barracks. He fell ill during basic military training and developed typical signs of meningo-

coccal meningitis, which resulted in his hospitalization. Following clinical diagnosis of his disease and rapid antibiotic administration, he made a complete recovery and left the hospital. Forty days later, however, he became ill with the same symptoms of meningitis and was readmitted to the hospital. Questions arose as to why the conscript's illness had recurred and which serotype of *N. meningitidis* was responsible. Serotyping investigations revealed that the *N. meningitidis* strain isolated from the CSF was serotype C. We were not able to show the biovar similarity of this agent of recurrent meningitis because of a lack of laboratory molecular technology.

Of note, IgG levels were higher than the normal range, indicating that the vaccine was immunogenic in this patient.

Several reports indicate an association between a deficiency of mannose-binding lectin, complement component deficiency, and meningococcal disease (10,11). Others have described the influence of human genes on susceptibility to bacterial pathogensis (12). In our patient, the amounts of C_3, C_4, and CH_{50} were less than normal, and he was probably complement component deficient.

There are several reports of the failure of antibiotic treatment and recurrence of *Neisseria meningitidis* meningitis (13,14), but the relationship between antibiotic-therapy failure and terminal complement component deficiency is unknown.

Conclusion

The eradication of meningococci and many other pathogens is critically dependent upon complement components, which are activated either by specific antibody or protein constituents of the innate immune response. The importance of complement in protection against meningococcal disease is highlighted by the observation that individuals deficient in their terminal components are susceptible to recurrent episodes of meninigococcal disease, even in the presence of a specific antibody.

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