The First Case of *Neisseria meningitidis* Serogrup X Meningitis in Turkey

Türkiye'de *Neisseria meningitidis* Serogrup X'e Bağlı İlk Menenjit Olgusu

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ABSTRACT *Neisseria meningitidis,* an agent of bacterial meningitis, is classified into 13 different serogroups. Serogrups A, B, C, W135 and Y are the predominant serogroups. A meningococcal vaccine containing serogroups A and C has been used to prevent recruits from this fatal disease until May 2009 in Turkey. From then on, administration of the quadrivalent vaccine consisting of "A+C+W135+Y" serogroups has been implemented because of the emergence of menigococcal meningitis cases caused by serogroup W135. We presented the first known menigococcal meningitis case caused by *N.meningitidis* serogroup X since the initiation of the quadrivalent meningococcal vaccine administration to recruits. Serogroup X has emerged as a cause of meningococcal disease in a susceptible population because of suppression of other serogroups included in the quadrivalent vaccine. The results of mass vaccination campaigns have implied that the mass vaccination programs alone cannot prevent the disease totally. The improvement of environmental conditions particularly for populations at high risk is also essential in the prevention of the disease.

Key Words: *Neisseria; Neisseria meningitidis;* meningococcal vaccines

ÖZET *Neisseria meningitidis,* 13 serogrupta sınıflandırılmış menenjit etkenlerinden biridir. Serogrup A, B, C, W135 ve Y baskın serogruplardır. Serogrup A ve C'yi kapsayan menengokok aşısı, Mayıs 2009'a kadar bu ölümcül hastalıktan askerleri korumak için Türkiye'de uygulanmaktaydı. Bu tarihten sonra, serogrup W135 nedenli menengokok menenjiti vakalarının ortaya çıkması nedeniyle, "A + C + W135 + Y" serogruplarına karşı hazırlanan dört değerlikli aşı uygulanmaya başlanmıştır. Bu makalede, askerler için dört değerlikli menengokok aşısı uygulamasına başlanmasından bu yana, *N. meningitidis*'in neden olduğu ilk menengokoksik menenjit olgusu sunulmuştur. Dört değerlikli aşının içerdiği serogrupların aşıyla baskılanması nedeniyle serogrup X, hassas nüfus içinde menengokoksik hastalık etkeni olarak öne çıkmıştır. Kitlesel aşılama kampanyalarının sonuçları, sadece kitle aşılama programları ile hastalığın tamamıyla önlenemeyeceğini vurgulamaktadır. Yüksek riskli toplumlarda, özellikle çevre koşullarının iyileştirilmesi de hastalığın önlenmesinde önemlidir.

Anahtar Kelimeler: *Neisseria; Neisseria meningitidis;* meningokok aşıları

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Neisseria meningitidis, an agent of bacterial meningitis is classified into 13 different serogroups based on the immunologic reactivity of its capsular polysaccarides. Serogrups A, B, C, W135 and Y are the predominant serogroups. *N. meningitidis* causes an estimated 1,2 million cases of bacterial meningitis and sepsis in many regions of the world each year.[1] The epidemiologic landscape is constantly changing, and currently, serogroups A and C predominate throughout Asia and Africa, whereas

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serogroups B and C are responsible for most cases in Europe and North America.[2,3] In several countries including the United States, the percentage of disease caused by serogroup Y has increased over the past decade.[4]

In Turkey, A, B, and C serogroups of *N. meningitidis* are the most common agents of menigococcal meningitis.[5-7] A meningococcal vaccine containing serogroups A and C has been used to prevent recruits from this fatal disease until May 2009. From then on, the administration of the quadrivalent vaccine consisting of "A+C+W135+Y" serogroups has been implemented because of the emergence of menigococcal meningitis cases caused by serogroup W135 among the recruits. We presented the first known menigococcal meningitis case caused by *N. meningitidis* serogroup X since the initiation of the quadrivalent meningococcal vaccine administration to the military population.

CASE REPORT

Twenty one-year old male patient presented to the primary care clinic with headache, sore throat, fever and vomiting on January 10, 2010. He was diagnosed with respiratory tract infection, and a first-generation cephalosporin combined with levofloxacin was administered. As the patient's symptoms progressed and his general condition deteriorated, he was transferred to our hospital on day15 of treatment where he was hospitalized. The medical history of the patient was unremarkable. Physical examination revealed axillary temperature 38.4 °C, pulse 92 beats/minute, respiratory rate 16/minute, and arterial blood pressure 130/80 mmHg. Despite poor orientation, the patient was fully cooperative. He had dry skin and postnasal discharge with oropharyngeal hyperemia. Blood cultures were taken.

Oral intake of the patient was limited. Biochemical findings were normal except for high blood urea nitrogen (50mg/dl) and creatinine (2.15 mg/dl). White blood cell count (WBC) was 3900/mm^3, erythrocyte sedimentation rate (ESR) was 5mm/hour; on the next day, the WBC increased to 28.000/mm^3, the ESR to 65mm/hour. His headache intensified and disseminated petechial eruptions appeared on his legs and chest (Figure1). A lumbar tap was performed and the cerebrospinal fluid (CSF) examination revealed that CSF was clear and colorless, and Pandy reaction was negative; cell count showed 80 leukocytes/mm^3 all (100%) of which were mononuclear cells.

Blood culture yielded *N. meningitidis* serotype X, resistant to penicillin G, but susceptible to ceftriaxone. The treatment was switched to ceftriaxone 2gr bid IV.

Laboratory and clinical abnormalities improved rapidly. Paranasal computed tomography revealed focal cerebral destruction. Control CSF analysis was normal. The patient was discharged after 10 days of ceftriaxone treatment.

Nasopharyngeal carriage screening of people in close contact with the patient revealed that one out of 21 was positive for *N. meningitidis* serogroup X. Repeated nasopharyngeal carriage screening test was negativ after one 750 mg dose of ciprofloxacin.

ANTIBIOTIC SUSCEPTIBILITY

Antibiotic susceptibility testing was studied by disk diffusion method according to the protocol of Clinical and Laboratory Standards Institutes (CLSI). Minimum inhibitory concentration (MIC) values for penicillin G and levofloxacin were determined with E-test® (AB Biodisk, Sweden). Disk diffusion revealed resistance to azithromycin, ciprofloxacin,

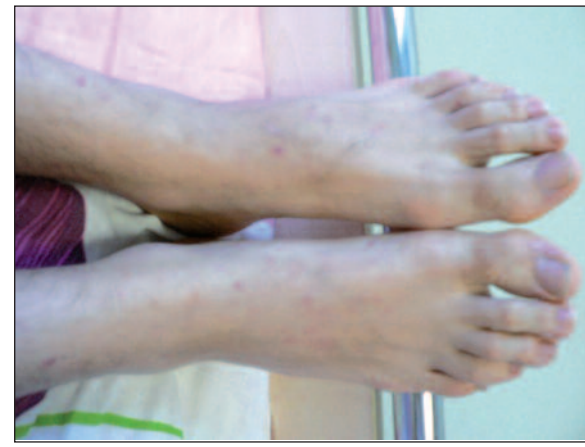

FIGURE 1: Menigococcal meningitis caused by *Neisseria meningitidis* serogrup X. The petechial eruption seen on the lower extremity including plantar ones.
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

rifampicin, and tetracycline, but susceptibility to cefotaxime and ceftriaxone. According to the E-test results the isolate was resistant to penicillin G (MIC 0.75 μg/ml), but susceptible to levofloxacin (MIC 0.004 μg/ml).

DISCUSSION

To the best of our knowledge, meningococcal disease due to *N. meningitidis* X has never been reported from Turkey. *N. meningitidis* X serotype was first identified in 1960s in northern America. This serotype X was shown to cause epidemics like serotypes A and C.[8]

The immunization records of our patient confirmed that he had received a quadrivalent (A+C+W135+Y) meningococcal vaccine two months earlier, at the beginning of his military training period. Turkish military vaccination campaigns have used the A+C+W135+Y polysaccharide vaccine successfully for six months. Since the initiation of quadrivalent meningococcal vaccination, this was the first case diagnosed with *N. meningitidis* serogroup X meningitis, with one close contact who is a carrier among 21 persons screened.

CSF examination of the patient did not reflect that of typical acute meningitis; this may be attributed to the administration of various medications including antimicrobial drugs easily penetrating the blood-brain barrier before the diagnostic lumbar puncture.

Annually, over 100,000 pilgrims from Turkey travel to Saudi Arabia. In 2000-2001, an outbreak caused by *N. meningitidis* serogroup W135 clone, (W) ET-37-a strain rarely isolated before occurred among these people.[9,10] Consequently, from 2002 to 2003, all Turkish pilgrims received a quadrivalent meningococcal polysaccharide vaccine (Mencewax ACWY, SmithKline Beecham, Genval, Belgium).

The emergence of W135 cases after mass administration of bivalent meningococcal vaccine and emergence of serogroup X after quadrivalent meningococcal vaccine can be considered an indication of selection of the serotypes not included in the vaccine. After mass administration of bivalent meningococcal vaccine in the African countries, Gagneux et al. have shown the selection of other serogroups (serogroups X and W135 not included in the vaccine) and the change in the manifestations of meningococcal disease.[11]

Serogroup X has emerged as a cause of meningococcal disease in a susceptible population due to the suppression of other serogroups included in the quadrivalent vaccine.

The results of mass vaccination campaigns have implied that the mass vaccination programs alone cannot prevent the disease totally and the improvement in environmental conditions particularly for sensitive populations is essential in the prevention of the disease.

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