First case of meningococcal meningitis due to *Neisseria meningitidis* serogroup Z' in Slovenia, December 2010

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We report here on the identification of the first meningococcal meningitis case in Slovenia caused by *Neisseria meningitidis* serogroup Z' in December 2010. The 19-year-old patient had not left the country during the incubation period. The patient was hospitalised and given the antibiotic treatment with cefotaxime very early in the course of the disease. The patient did not develop any complications during hospitalisation and was discharged on 5 January 2011.

Case report

On 27 December 2010, the epidemiologist of the Regional Institute of Public Health of Celje, Slovenia, was informed about a 19-year-old patient hospitalised in the Department of Infectious Diseases and Febrile Conditions of the General Hospital in Celje, with clinical suspicion of meningococcal meningitis.

The patient had been admitted to the Department of Infectious Diseases and Febrile Conditions of the General Hospital on 26 December 2010, with fever (39.9 °C but no chills), headache, mild sore throat and muscular pain since approximately six hours. He had no underlying chronic conditions and had been healthy previously.

When examined, the patient presented meningeal symptoms (nuchal rigidity, Kernig and Brudzinski signs). His throat was mildly reddened, but there were no other symptoms. Laboratory findings showed mild leukocytosis, but neutrophils was predominating (Table). Samples for blood cultures were taken upon admission.

Viral meningitis was suspected and the patient was hospitalised for observation. Despite his generally good condition, the physician repeated the basic laboratory tests four hours after hospitalisation and found a clinically significant increase in the white blood cell count and a small rise of C-reactive protein (Table). Approximately six hours after hospitalisation, discrete petechiae were identified on the patient's hands. Meningococcal meningitis was suspected,

lumbar puncture immediately carried out and antibiotic treatment started (2 g cefotaxime every four hours for 10 days) [1]. After 24 hours of antibiotic therapy, the patient no longer had fever or headache, but still showed petechiae and ecchymoses.

Cerebrospinal fluid (CSF) was macroscopically clear with pleocytosis (white blood cell count of 27 per mm³, predominantly neutrophils), while the protein and glucose levels were within normal range. On 27 December 2010, blood for haemoculture and CSF to test for *N. meningitidis* (Gram staining, antigen detection and culture) were sent to the Department of Medical Microbiology, Institute of Public Health Celje. Gram staining and antigen detection were negative, haemoculture was positive, and CSF remained negative. CSF for rapid molecular diagnostics (real-time polymerase chain reaction, RT-PCR) was sent to the Department of Medical Microbiology, Institute of Public Health of the Republic of Slovenia. RT-PCR was performed on the same day to detect the *ctrA* (capsular transport) gene, which is specific to *N. meningitidis* [2], and using specific primers, we have shown that the isolate did not belong to serogroups B or C.

Meningococci grew from blood cultures after two days, but not from CSF. The isolate from blood cultures was phenotypically typed using slide agglutination with monoclonal antisera (Becton Dickinson, United States of America). On 31 December 2010, we confirmed *N. meningitidis* serogroup Z' as cause of the disease.

The patient did not develop any complications during hospitalisation and was discharged on 5 January 2011. Upon discharge, his skin changes were in regression and he had no other symptoms. He was advised to undergo further tests and to check for possible immunodeficiency, and to be vaccinated against further meningococcal infection. This decision was made although the Slovenian vaccination guidelines do not recommend vaccination of the index case [3]. The patient was vaccinated with quadrivalent polysaccharide meningococcal vaccine on 16 January 2011. The

quadrivalent conjugate meningococcal vaccine is not yet available in Slovenia.

Epidemiological investigation

After microbiological confirmation of meningococcal meningitis on 27 December 2010, we started to identify close contacts for post-exposure chemoprophylaxis (PEP) in accordance with Slovenian methodology [3]. We identified seven close contacts among the family members: six adults who were given one dose (500 mg) of ciprofloxacin and an eight-month-old child who was treated with rifampicin for two days (10 mg/kg two times per day) [3,4].

We also identified 10 student friends of the patient as close contacts, as they had been in contact with him seven days before the onset of symptoms. They were also given 500 mg ciprofloxacin. Until 29 December 2010, all close contacts, from different Slovenian towns, received PEP in various Slovenian regional institutes of public health.

Discussion

N. meningitidis serogroups A, B and C cause 90% of meningococcal meningitis cases and among these, serogroup B is the most common [5]. In 1999, the incidence of meningococcal disease among participating countries in the EU-IBIS network (European Union Invasive Bacterial Infections Surveillance) varied between <1 and 14.3 per 100 000 population. In 2004 serogroup B caused invasive meningococcal diseases in different European countries in various percentage (from 40% in Italy to 95% in Ireland) [6]. Vaccine against serogroup B is still not available. As other countries in Europe, Slovenia registered a substantial increase in the number of invasive meningococcal disease cases caused by serogroup C, after 2002. Serogroup C is most common among adolescents and causes a severe clinical picture [6,7]. After 2000, in Slovenia, the frequency of serogroup W 135 isolates increased, while serogroup A was isolated for the first time in 2007 in a Tunisian tourist [8].

In 2009, 11 sporadic cases of invasive meningococcal disease caused by *N. meningitidis* were confirmed in Slovenia: nine were children under 15 years and two were adults [8]. Meningococci were isolated from blood (five cases), CSF (four cases) and from both blood and CSF (two cases). All isolates were serotyped: in seven cases, the disease was caused by *N. meningitidis* serogroup B, in three cases by serogroup C and in one case by serogroup W 135. Using RT-PCR, we confirmed four cases from CSF, three belonging to serogroup B and one to serogroup C.

According to the literature, serogroup Z' rarely causes meningococcal infections [9,10]. In epidemiological studies investigating the carriage of *N. meningitidis*, this serogroup was confirmed in a low percentage of cases of meningococcal infection (from 5.6% to 5.8%) [9]. The case described here is the first in Slovenia where the invasive meningococcal infection was caused by *N. meningitidis* serogroup Z'. The patient had not left Slovenia during the incubation period.

The Slovenian PEP methodology recommends use of rifampicin, ciprofloxacin or ceftriaxone, for all meningococcal meningitis cases, according to the age or physical condition of the contacts. For instance, ceftriaxone is recommended during pregnancy [3]. For the contacts of the case described here, 16 adults were given ciprofloxacin, while the contact who was eight-months-old was given rifampicin. None of the contacts developed the disease. In 2009, there were no *N. meningitidis* isolates in Slovenia with total or intermediate resistance to third-generation cephalosporins [8].

As there is no vaccine against serogroup Z' and the results of the complement investigation were not known, the patient was vaccinated with quadrivalent polysaccharide meningococcal vaccine.

TABLE

Results of laboratory tests for the meningococcal meningitis serogroup Z' case, Slovenia, December 2010

Variable	Reference range	On admission	Four hours after admission
White cell count (per mm ³)	4,500–10,000	11,200	17,900
Differential count (%)			
Neutrophils	40–75	86.9	NT
Band forms	<10	0	NT
Lymphocytes	20–50	6.3	NT
Monocytes	2–10	6.3	NT
Basophils	<1	0.2	NT
Eosinophils	<6	0.3	NT
Platelet count (per mm ³)	140,000–360,000	160,000	185,000
C-reactive protein (mg/L)	<5	12.8	40.5
Procalcitonin (µg/L)	<0.5	NT	23.7

NT: not tested.

Conclusion

N. meningitidis serogroup Z' rarely causes invasive meningococcal disease. Before the identification of this case, Slovenia had not registered the disease caused by this serogroup. Even though serogroup Z' infection usually does not result in serious illness, the patient described in this report had fever, headache and petechial bleeding, but his clinical condition was stable after antibiotic treatment.

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