Short Communication

A Case of Sepsis and Meningitis Caused by Probable Travel-Related Neisseria meningitidis Serogroup B Infection: the First Report of N. meningitidis ST-4893 in Japan

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SUMMARY: Herein we present a case of Neisseria meningitidis-related sepsis and meningitis in a 60-year-old woman. The N. meningitidis strain was identified as serogroup B and sequence type (ST)-4893 by multilocus sequence typing (MLST). The patient in this case had visited France prior to development of symptoms. No meningococcal isolate belonging to ST-4893 has been identified in Japan previously, whereas an ST-4893 strain from France has been reported in the MLST database. These results strongly suggest that this case is likely to have been imported from France.

Neisseria meningitidis is a leading cause of both life-threatening acute meningitis and meningococcal bacteremia, which can lead to thrombocytopenia, disseminated intravascular coagulation, and shock. The largest recorded outbreak of meningococcal disease in history occurred in Africa in 1996, when over 20,000 deaths were reported to the World Health Organization (WHO) (1). In the 2009 epidemic season, 14 African countries reported a total of 78,416 suspected cases and 4,053 deaths (2). Despite the availability of vaccines, meningococcal disease remains a serious illness with a case-fatality rate of up to 40% (3). Over 4,000 cases of meningococcal infection were reported annually in Japan before World War II (4). However, even without the introduction of meningococcal vaccine, the number of cases has fallen to approximately 10 cases of meningococcal meningitis per year (4). Herein we describe a probable case of travel-related meningococcosis.

A 60-year-old woman was admitted to our hospital because of high fever, general feeling of malaise, vomiting, and faintness in June 2009. Two weeks before her hospitalization, the patient had traveled to France for one month. Upon examination at admission, her body temperature was 38.0°C, with a heart rate of 103 beats/min and a blood pressure of 81/63 mm Hg. The patient presented with a mild headache without nuchal rigidity. Petechiae were present on the trunk and lower extremities. Laboratory analyses showed a leukocyte count of 20,700/μl and C-reactive protein of 7.6 mg/dl. Based on clinical suspicion of sepsis, antimicrobial therapy with 9 g/day of sulbactam/ampicillin (SBT/ABPC) was started. Blood cultures taken on admission were positive on the next day, with growth of Gram-negative diplococcus demonstrating a distinct halo around the cells consistent with the presence of capsule. As the organism was subsequently identified as Neisseria meningitidis group B/Escherichia coli K1 by antibody-sensitized latex agglutination using the Pastorex™ Meningitis kit (Bio-Rad Japan, Tokyo, Japan), antimicrobial therapy was changed from SBT/ABPC to cefotaxime (8 g/day). Following blood culture subculture, growth after 24 h of incubation on sheep blood and chocolate agars revealed the presence of smooth, glistening, moist, and grayish colonies. Identification was based on a positive oxidase reaction, cell morphology, acidification of glucose and maltose, serogrouping, and the ID-a positive oxidase reaction, cell morphology, acidification of glucose and maltose, serogrouping, and the IDTest-HN-20 Rapid (Nissui Pharmaceutical Co., Tokyo, Japan). The N. meningitidis isolate was definitively identified as serogroup B, sequence type (ST)-4893, which belongs in the ST-41/44 complex lineage, on the basis of serotyping and multilocus sequencing typing (MLST). Antimicrobial susceptibility testing was performed using the CLSI micro-broth dilution method with Mueller-Hinton medium plus 5% horse blood and incubation in 5% CO2 at 35°C (5). The isolate was susceptible to all antimicrobial agents tested, including penicillin, ampicillin, cefotaxime, minocycline, and levofloxacin.

On the third day after admission, a lumbar puncture was performed because of posterior cervical tenderness. The cerebrospinal fluid (CSF) was clear and colorless, with protein of 77 mg/dl, glucose of 30 mg/dl (blood glucose of 100 mg/dl), and a cell count of 3,232/μl with 80% neutrophils and 20% monocytes. Bacterial culture of the CSF sample was negative; however, PCR targeting of the ctrA (capsule transport operon) gene (6) and the siaD (sialyltransferase) (B) gene (6) were positive. Although the ctrA gene is unique to N. meningitidis, with parts of the gene being highly conserved and com-
mon to all meningococcal serogroups, the siaD (B) gene is associated with sialic acid synthesis in serogroup B (6). The patient recovered fully after 3 weeks and was discharged from hospital.

*N. meningitidis* is classified into 13 serogroups based on the capsular polysaccharide structure, of which groups A, B, C, W-135, X, and Y are responsible for life-threatening diseases. Serogroups A, B, and C in particular account for most cases of meningococcal disease throughout the world, with serogroups B and C being responsible for the majority of cases in Europe and the Americas and serogroups A and C predominating throughout Asia and Africa (3). Characterization of *N. meningitidis* isolates recovered from clinical specimens in Japan over a 30-year period by Takahashi et al. showed that serogroups B and Y were dominant together with the presence of well-documented ST complexes such as ST-23, which are distributed globally (4).

With respect to the patient’s *N. meningitidis* serogroup B isolate, MLST identified the isolate as ST-4893, which was previously described in an isolate from France in 2005 (*Neisseria* Sequence Typing Home Page. Online at http://pubmlst.org/neisseria). In addition, serogroup B accounts for 50% of all isolates in France, with 25% belonging to the ST41/44 complex (7). As the patient had visited France prior to the onset of symptoms and ST-4893 has not previously been reported in Japan, we hypothesize that the patient is likely to have been infected in France.

MLST is widely used for molecular epidemiological analysis for two major reasons. Firstly, the cost of MLST analysis is relatively low, thus making it suitable for handling either a few isolates or much larger number. Furthermore, MLST data can easily be shared among laboratories via the internet since the results are digitalized sequences of seven housekeeping genes (8).

The definitive diagnosis of meningococcal infection has relied on the isolation of *N. meningitidis* from sterile body fluid. However, the sensitivity of routine diagnostic bacteriology methods, such as the Gram stain and culture, are limited once empirical antimicrobial therapy has been initiated. In a study from Norway, the Gram stain smear and culture from blood and/or CSF were both negative. Furthermore, the sensitivity of routine diagnostic bacteriology methods, such as the Gram stain and culture, are limited once empirical antimicrobial therapy has been initiated. In a study from Norway, the Gram stain smear and culture from blood and/or CSF were both negative.

**Conflict of interest** None to declare.

**REFERENCES**