Meningococcemia without Meningitis in Japan

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Abstract

We report a case of meningococcemia without meningitis, which is a rare infectious disease in Japan. A 32-year-old woman was referred to our hospital with fever and joint pain. Her clinical presentation and the results of laboratory examination on admission suggested viral infection. However, her condition rapidly progressed to septic shock with fulminant purpura. Blood culture grew *Neisseria meningitidis*. She received antimicrobial therapy and underwent localized therapy for skin lesions. Meningococcal infection should be considered in patients who have fever along with skin rash or petechiae even when there are no signs of meningitis. In this report, we also review case reports of meningococcemia without meningitis in Japan.

Key words: *Neisseria meningitidis*, meningococcemia, fulminant purpura

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Introduction

Meningococcemia is a serious illness with a high fatality rate of up to 40% (1). Half of all nonsurviving patients with shock die within the first 12 hours of hospital admission (2). Furthermore, 11-19% of survivors require amputation or plastic surgery for skin and limb necrosis (3). Therefore, early diagnosis and administration of adequate antibiotics are essential. In this case report, we present a case of fulminant purpura due to meningococcemia without meningitis.

Case Report

A 32-year-old woman was admitted to our hospital because of high fever with polyarticular pain, especially bilateral ankle joint pain. Fourteen hours before admission, she came to the outpatient clinic because of sudden chills and shivering along with polyarticular pain. Because her physical examination was not abnormal, she received nonsteroidal anti-inflammatory drugs (NSAIDs) under suspicion of viral infection, such as incipient influenza virus infection. NSAIDs temporarily alleviated her fever and polyarticular pain, but after 6 hours, she again developed high fever with polyarticular pain. She came to the emergency department and was admitted to the hospital.

On examination at admission, she appeared ill and could not walk because of her polyarticular pain, especially bilateral ankle joint pain. Her temperature was 40.3°C, pulse 96 beats/min, and blood pressure 106/56 mmHg. She was lucid and had no positive meningeal signs. The heart and lungs were normal on auscultation. She had epigastric tenderness without hepatosplenomegaly. There was skin erythema in the extremities, especially the lower legs and forearms. We did not find petechiae on the hard palate, palpebra, or conjunctiva. The remainder of the physical examination was unremarkable. As shown in Table 1, laboratory data revealed thrombocytopenia and elevated C-reactive protein, but not leukocytosis. Liver and renal function tests showed values within normal ranges. She had a history of atopic dermatitis and bronchial asthma that was controlled without medical therapy. She had never visited a foreign country.

Because we considered that she had a viral infection, such as parvovirus B19, we treated her symptoms but did not give antibiotics. Six hours after admission, however, her blood pressure decreased to 60/52 mmHg and we found purpura.

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puric lesions in the limbs, which were not present at the time of admission, but no skin eruptions (Fig. 1). Septic shock with fulminant purpura was diagnosed and treatment with meropenem (0.5 g IV every 6 hours) and vasopressor was initiated. Culture of a blood sample taken on admission yielded *Neisseria meningitidis*, and analysis of serogroup typing and multilocus sequence typing showed that *N. meningitidis* in this case was classified as serogroup B and sequence type 32 (electrophoretic type 5). Antibiotic treatment was changed from meropenem to penicillin G (400 mU every 4 hours) based on results of an antimicrobial susceptibility test. Although the hemodynamic status stabilized and blood culture became negative after adequate antibiotic administration, the spike fever persisted and purpura progressed to skin necrosis with edema (Fig. 2). As shown in Table 2, laboratory findings showed neither autoimmune disorder nor abnormality of protein C or protein S. The pathologic feature of skin ulcer showed vasculitis with fibrin thrombi, suggesting sepsis-induced skin necrosis (Fig. 3). Therefore, betamethasone (1.5 mg/day) was administered as the anti-inflammatory agent for skin ulcer from day 7. In addition, she was administered morphine intravenously to relieve pain from the skin ulcers. We continued administration of antibiotics for 14 days and gave localized treatment for the skin ulcers. Her general status, including fever spike and ulcers, gradually improved and she was discharged on foot 11 weeks later (Fig. 4). Pharyngeal cultures from her household (husband, mother,
and father) did not yield *N. meningitidis*, suggesting that they were not carriers of *N. meningitidis*. Because close contacts with invasive meningococcal disease are at a high risk of meningococcal infection, they were administered ciprofloxacin as secondary prophylaxis against *N. meningitidis* infection.

**Discussion**

Although *N. meningitidis* is divided into 13 serogroups based on capsular polysaccharide structure, only six serogroups (A, B, C, W-135, X, and Y) cause life-threatening diseases. Analysis of serogroup typing and multilocus sequence typing showed that *N. meningitidis* in the present case was classified as serogroup B, which is dominant in Japan (4), and sequence type 32 (electrophoretic type 5). The patient has not visited any foreign countries and had had no direct contact with patients with meningococcal infection. Consequently, we thought that she was infected with *N. meningitidis* from carriers in Japan.

We searched PubMed and Japana Centra Revuo Medicina (Igaku-Chuo-Zasshi), which is a database of Japanese medical journals, to identify case reports of meningococcal meningitis in Japan. Including this case, 72 cases have been reported in Japan from 1983 to 2007. Of these, 19 patients had meningococcemia without meningitis, 45 had meningi-
Figure 3. Skin biopsy specimen of the right lower leg, showing fibrin thrombi in the vessels of the dermis (arrows). Hematoxylin and Eosin staining; original magnification ×40.

Figure 4. Clinical course of the patient. BT: body temperature, MEPM, meropenem, PCG: penicillin G, WBC: white blood cells.
coccus pneumoniae (12) but also other bacteria. At present, the number of cases of meningococcal meningitis is fewer than 30 per year in Japan. In addition, Tanaka et al, in a study of 5,886 healthy persons in Japan, demonstrated that only 25 strains (0.4%) of N. meningitidis were isolated (13). Thus, the incidence of meningococcal infection and the number of carriers in Japan are low compared with other countries (2). Serogroup B, belonging to sequence type 32 (electrophoretic type 5), however, circulates slowly through the population with low transmissibility but a high degree of virulence (3). Therefore, meningococcal infection should be considered as a differential diagnosis of fever, especially in the presence of skin rash or petechiae, even when there are no signs of meningitis.

References