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Letter to the Editor

Recurrent infections caused by different species of Neisseria bacteria in a patient with complement seven deficiency

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Disseminated *Neisseria gonorrhoeae* infection (DGI) is a rare systemic gonococcal infection that manifests as a combination of dermatitis, tenosynovitic and migratory polyarthralgia, purulent arthritis, endocarditis, meningitis, and osteomyelitis [1,2]. Risk factors for DGI include female sex, menstruation, pregnancy, and complement deficiency [1,4]. We report the rare case of N. meningitidis infection followed by DGI associated with seventh complement (C7) deficiency.

A 23-year-old Japanese man visited our hospital for headache, persistent pyrexia persisting, 3-week long arthralgia, and skin rash. A week before the onset of symptoms, he had had sex intercourse with his first partner. He was immediately admitted to our hospital.

The patient was previously admitted to the nephrology department of our hospital at age 19 for septic shock due to N. meningitidis infection with associated disseminated intravascular coagulation syndrome, and acute renal failure. At that time, his total complement activity (CH50) was below detectable limits, and C7 complement deficiency was subsequently confirmed [5]. After discharge, he received pneumococcal vaccination but was unable to receive meningococcal vaccination because he stopped his outpatient visits.

On physical examination for the current case, his vitals were normal, and papulae with induration were observed on his palms and soles (Fig. 1A). No signs were presented of meningeal irritation such as nuchal rigidity and jolt accentuation. Other neurological findings were also normal. Laboratory investigation showed increased aspartate aminotransferase (80 IU/L), alanine aminotransferase (80 IU/L), γ-GTP 67 (IU/L), and C-reactive protein (11.5 mg/dL). Blood tests were normal (white blood cell count 6400/μL). Complements 3 and 4 were normal, but CH50 was low at 14.0 U/mL. Cerebrospinal fluid (CSF) tests showed that CSF pressure was 190 mmH2O, cell count was 2200/μL (1840 multinuclear cells, 167 lymphocytes, and 193 other cells), protein level was 56 mg/dL, and glucose level was 35 mg/dL (blood glucose level at 105 mg/dL). Blood culture revealed gram-negative cocci, which were confirmed to be N. gonorrhoeae based on biochemical properties and 16S rRNA gene sequencing by polymerase chain reaction.

The patient was given an intravenous infusion of dexamethasone 24 mg/day for 3 days, vancomycine 3000 mg/day for 6 days, and ceftriaxone 4 g/day for 17 days. With treatment, his headache and papulae disappeared, and CSF cell count improved (Fig. 1B). He was discharged on the 19th day.

1. Discussion

This case had congenital C7 deficiency and had not received meningococcal vaccination, resulting in recurrent Neisseria infections, specifically N. meningitidis infection previously, and this time, with DGI. This is the first case in Japan of DGI associated with C7 deficiency.

C7 deficiency is the second most frequent complement deficiency in Japan after C9 deficiency, and affects about 1 in 10,000 [6]. One of the most important functions of the complement system is opsonization by C3. In addition, the membrane attack complex (MAC) formed from the C5-9 complex promotes immune protection directly by membrane disruption. Bacteria other than Neisseria are opsonized by C1-4 even without C5-9 activation, and are likewise eliminated by phagocytosis and bactericidal action by neutrophils [4]. However, Neisseria bacteria are resistant to intracellular bactericidal action even after being phagocytosed by leukocytes, and they can survive as intracellular parasites. Furthermore, late complement component deficiencies (C5-8) inhibit MAC formation and increase susceptibility to Neisseria infections. Patients with C5-9 deficiency comprise 5% to 10% of patients with initial meningococcal infection. The average age of onset of meningococcal meningitis in patients with C7 deficiency was 17 years [4]. When meningitis due to N. meningitidis or N. gonorrhoeae develops after puberty in young adults, complement protein testing should be performed with a suspicion for complement deficiency [7]. It is important to implement proper vaccination to prevent serious Neisseria infections in patients with complement deficiency.

Declaration of Competing Interest

The authors declare no financial or other conflicts of interest.

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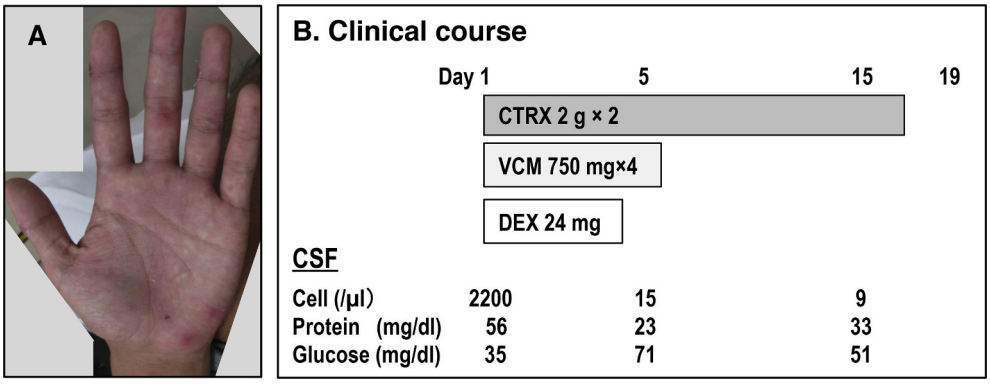

Fig. 1. A. Papulae with induration on the patient's palm and fingers. B. Clinical course. CTRX: ceftriaxone, VCM: vancomycine, DEX: dexamethasone, CSF: Cerebrospinal fluid.