

CASE REPORT

A very rare case of primary meningococcal arthritis in an adult male

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Introduction

Invasive meningococcal infection is caused by the Gram-negative diplococcus, *Neisseria meningitidis*, occurring in the blood stream and spinal cord causes septicemia and meningitis, respectively. The bacterium subsequently disseminates to other parts of the body and potentially to other individuals [1–3]. Meningococcal arthritis has been seen as a complication of *N. meningitidis* infection mainly in large joints (e.g., the knee and elbow); however, it is very rare in children. Two types of meningococcal arthritis are known. The most common type is arthritis caused by local acute meningococcal infection, and the less common type is sterile arthritis caused by the immune complex or an allergic reaction. Large joints were involved in most of

Key Clinical Message

We report here a very rare case of primary meningococcal arthritis of the knee joint without clinical features associated with meningococemia, meningitis, or meningococcal complications. The patient suffered from diabetes mellitus and had experienced two episodes of joint trauma. Intravenous infusion of ampicillin/sulbactam for 18 consecutive days was successful.

Keywords

Arthritis, diabetes, joint trauma, meningococcus, *Neisseria meningitidis*.

the latter cases. While meningococcal arthritis is recognized in 2–10% of meningococcal infections, these cases are mostly the result of direct invasion to the synovium during the acute infection phase or during the course of chronic meningococcal infection [4–7]. We report here a very rare case of primary arthritis of the knee joint in an adult male caused by *N. meningitidis* without the clinical features associated with meningococemia, meningitis, or any detectable commensal meningococcus in the nasal-pharyngeal tract.

Case History/Examination

According to the patient's own recollection, 10 years ago, he was found to have high blood sugar approximately 200 mg/100 mL and positive urine sugar. However, he

did not consult a doctor regarding his condition. About 1 month before the current hospital admission, the patient visited a local ophthalmology clinic because of blurred vision and was diagnosed as having retinitis due to type II diabetes. One week later, he visited the outpatient clinic of this hospital for laser treatment for the retinitis and diabetes management. A blood test revealed the fasting blood sugar to be 179 mg/100 mL and the HbA1c was 9.9%. He had a history of joint trauma including bruising both knees at the age of 35 years and a right knee sprain at the age of 45 years. In addition, the patient had hypertension and hyperlipidemia.

Differential Diagnosis, Investigations, and Treatment

Three days before hospital admission, a 64-year-old man felt pain in his swollen right knee joint that progressed for a few more days rendering him unable to walk or even bend the knee joint. He had not eaten anything for a few days, so he was undernourished and dehydrated. He was taken to the emergency clinic of the hospital and immediately hospitalized. The patient presented with erythematous, warmth, tenderness, and severe pain upon extension and flexion of the joint, but no edema of the other limbs. Synovial fluid from the right knee was aspirated on the day of admission, and the cell count appeared 166,000 cells/mm³ dominated by polymorphonuclear cells and macrophages (P/M ratio, 76:24).

Microscopic examination of the centrifuged and Gram-stained synovial fluid revealed Gram-negative diplococci. Therefore, he was first suspected of having purulent arthritis, so we immediately administered ampicillin/sulbactam (2:1, w/w ratio) intravenously at a dose of 1.5 g × 4 times per day, for 18 consecutive days. For the diabetes, insulin detemir was administered according to the regime shown in Fig. 1. An electrolyte supplement

was given as an intravenous infusion to treat the patient's dehydration. Magnetic resonance imaging (MRI) of the right knee joint taken on the day of admission revealed effusion of the synovial fluid, thickening of the inflamed synovium, and mild degenerative bone changes (Fig. 2).

On the second day of admission, the patient's body temperature dropped to a normal level, and he was afebrile thereafter (Fig. 1). Dehydration improved, and the level of ketone bodies dropped to an undetectable level. As an analgesic, loxoprofen, a non-steroidal anti-inflammatory drug, was administered in the dosages shown in Figure 1. An insulin aspart regime was started on day 2 and continued as shown in Figure 1. For diabetes management, a calorie-limited dietary program (26 kcal/kg) was started on day 2 and was continued for 26 consecutive days. The bacteria that were found in the synovial fluid on the first day were eventually identified as being *N. meningitidis* on day 5; therefore, the patient's condition was diagnosed as meningococcal arthritis. The sputum culture on day 6 was meningococcus negative. The edematous right knee, local pain, and warmth and tenderness of the erythema phased out gradually from days 7 to 14 and the patient was able to stretch and flex both knees. Because there was no sign of headache, subconsciousness, meningeal stiffness or irritation, or of any other neurological assessments, examination of the cerebrospinal fluid was not performed. There was no sign of pain upon urination, urethritis, or inflammation of the respiratory tract. The sputum fluid culture and the synovial culture on days 6 and 12, respectively, were negative for meningococcus. Rehabilitation was given intermittently from day 19 through day 25. Because clinical symptoms abated and the synovial fluid was sterile, the patient was discharged from the hospital on day 27. The patient convalesced satisfactorily from the right knee arthritis, and there are no symptoms of recurrence to date.

Day in hospital	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27													
Clinical findings																																								
Pain				+++						++~+																														
Erythematous & warm				+++						++~+																														
Tenderness to palpation				+++						++~+																														
Treatments																																								
Antibiotic	Ampicillin/sulbactam (2:1, w/w ratio) , iv, 1.5g×4/day																																							
Insulin regime																																								
Insulin aspart (units/dose)		12	24	25	26	28	30	34	36	38					40													32	10											
Insulin detemir (units/dose)	6	8	11							13																														
Anaesthetic																																								
Loxoprofen (tablets/day)										3												2																		
Diagnostic procedures																																								
<i>N. meningitidis</i>	+	←synovial culture				-	←Sputum culture				-	←Synovial culture																												
WBC (10 ³ /μL)	14.5	12.5	10.5		8.8					10.8					8.2						7							6.3				4.4			4.7					
CRP (mg/dL)	34.1	24.7	19		10.7					6.56					4.17						1.22							0.68				0.48			0.29					
Body temperature (°C)	37.3	36.8	35.8	36.3	36.5	36.6	35.9	36.4	35.6	36.2	36.1	36.1	36.3	36.4	36.6	36.2	36.1	36.3	36.2	35.6	35.8	36.2	35.8	35.6	35.6	36.1	36													
Blood sugar (mg/dL)	403	276	236		120					140					104														116				95			118			79	
HbA1c (%)	11																																							
Rehabilitation																																								
Dietary treatment																																								

Figure 1. Clinical findings, treatments, and laboratory data during hospitalization.



Figure 2. MRI findings. (A) The coronal and (B) sagittal T2-weighted (T2-STIR) MRI images of the right knee. These images reveal effusion of synovial fluid (circles 1 and 3), thickening of the inflamed synovium (circles 1–3) and mild degenerative bone changes (circles 1–3).

Physical examination results of the patient at admission were: body weight, 61 kg; height, 163 cm; body mass index (BMI), 32.6 kg/m²; ideal body weight (IBW), 58.5 kg; body temperature, 37.3°C; blood pressure, 140/95 mmHg; pulse, 120 bpm; and respiration, 20 per minute.

A summary of laboratory examinations on admission is shown in Table 1. Blood culture on the day of admission was sterile. Data deviating from the reference ranges were as follows. The total blood count showed elevated leukocytes (14,500/mm³) dominating neutrophils and

gradually decreasing to 7,000/mm³ on day 15. Fasting blood sugar was 403 mg/100 mL on day 1 and dropped to 104 mg/100 mL on day 11. C-reactive protein (CRP) was 34.1 mg/100 mL at admission which dropped to 1.22 mg/100 mL on day 15. Hemoglobin A1c (HbA1c) and glycoalbumin were 11.0% and 28.4%, respectively. The level of sodium 147 mEq/L appeared high, perhaps due to dehydration. The level of albumin and urine protein appeared, 3.3 mg/100 mL and ++, respectively, which may be a sign of diabetic nephropathy. The synovial fluid aspirated on day 1 was centrifuged and the supernatant was subjected to Gram-stain testing microscopically revealing Gram-negative diplococci. Therefore, the specimen was subjected to a booster culture in hemin and vitamin K1 (HK) semi-solid medium (Eiken Chemical, Tokyo, Japan). The culture on a chocolate agar plate revealed homogeneous colonies of Gram-negative diplococcus, which was identified, by conventional methods, as the *N. meningitidis* serogroup Y/W135. Antimicrobial susceptibility tests revealed that the minimal inhibitory concentrations of the antibiotics in this bacterium (benzylpenicillin, ampicillin, cefotaxime, ceftazidime, aztreonam, imipenem, erythromycin, minocycline, levofloxacin, and chloramphenicol) were all within susceptible ranges.

Discussion

Infection of *N. meningitidis* worldwide had been estimated to be about 5 million cases per year, among which roughly 50,000 cases proved fatal according to a 2002 WHO report [8]. Arthritic complications of meningococ-

Table 1. Laboratory findings.

Hematology			Biochemistry			Synovial fluid	
Item	Patient	Reference value	Item	Patient	Reference value	Item	Patient
WBC ($\times 10^3/\mu\text{L}$)	14.5	4.0–9.0	T.P. (g/dL)	6.9	6.5–8.1	Color	Yellow
Neutrophile (%)	85.5	43.0–71.0	ALB (g/dL)	3.3	3.8–5.2	Opacity	Cloudy
Eosinophile (%)	0.0	2.0–6.0	AST (U/L)	16	10–35	Cell count ($/\mu\text{L}$)	166,000
Lymphocyte (%)	7.6	30.0–41.0	ALT (U/L)	17	5–40	Polymorph (%)	76.0
Monocyte (%)	6.6	3.0–6.0	BUN (mg/dL)	50.1	8.0–22.0	Monocyte (%)	24.0
Basophile (%)	0.3	0.0–2.0	Cr (mg/dL)	0.76	0.60–1.10	Others (%)	0.0
RBC ($\times 10^6/\mu\text{L}$)	5.57	4.20–5.60	UA (mg/dL)	7.5	3.8–7.0		
HGB (g/dL)	16.7	12.5–17.0	Na (mEq/L)	147	135–146		
HCT (%)	47.4	39.0–50.0	K (mEq/L)	3.9	3.4–4.8		
PLT ($\times 10^4/\mu\text{L}$)	20.1	15.0–35.0	Cl (mEq/L)	106	98–108		
			CRP (mg/dL)	34.08	≤ 0.30		
Urinalysis			Blood glucose (mg/dL)	403	70–109		
Sugar	3+	–	HbA1c (%)	11.0	4.6–6.2		
Protein	2+	–	Glycoalbumin (%)	28.4	11.0–16.0		
Ketone body	3+	–	Insulin ($\mu\text{U/mL}$)	3.21	1.15–12.15		
			Ketone body	\pm	–		

RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; PLT, platelet; T.P., total protein; ALB, albumin; AST, glutamate oxaloacetate transaminase; ALT, glutamate pyruvate transaminase; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid; CRP, C-reactive protein; HbA1c, hemoglobin A_{1c}.

cal diseases are relatively common as evidenced by 2–10% of all cases develop arthritis [4–7]. Most cases of meningococcal arthritis are the result of secondary infection from meningococcomia or meningitis [4, 9–11]. Primary meningococcal arthritis appears as a very rare form of meningococcal disease. Only 34 cases of primary meningococcal arthritis were reported in the literature from 1980 to 2002 [12] and only sporadically thereafter. For the past 5 years, we found 8 reports of primary meningococcal arthritis in the shoulder, pelvis, sacrolic joint, knee, elbow, ankle, and polyarticular joints, and 2 cases, among those, were sterile or allergic [13–20]. To our knowledge, this is the first report of primary meningococcal arthritis in Japan.

Blood culture from the patient at admission appeared sterile, therefore, meningococemia was not suspected; however, a cerebrospinal fluid culture was not done at that time. It has often been reported that meningococcus spreads among family members [21–24]. However, the patient lived alone, therefore, ruling out this possibility. Meningococcus is a normal commensal inhabitant of the human body in the nasal-pharynx cavity. Therefore, the bacterium may be transmitted through the air, after a cough or a sneeze, or by direct mouth-to-mouth contact. However, the sputum culture on day 6 was meningococcus negative. Therefore, secondary infection from normal flora meningococcus of the throat is a less likely etiology, though this possibility was not completely ruled out because chemotherapy had already been begun. Sexual transmission of meningococcus has often been reported [2, 3], however, the patient had been sexually inactive for 6 months or longer. It was reported that pre-existing joint disease is a risk factor for septic arthritis with a frequency of approximately 47% [4, 25, 26]. The patient reported here had a history of joint trauma. An association between septic arthritis and joint trauma could be suspected. The patient suffers from diabetes mellitus type II; however, a correlation to meningococcal arthritis is not clear. Whatever the route of infection, acute meningococcal septic arthritis develops very rapidly and, therefore, is a medical emergency that requires prompt treatment. The patient reported here could not walk or even move his right leg; and, therefore, he was undernourished, dehydrated, and incontinent. The patient was treated with a combination of ampicillin and sulbactam, and responded to the treatment well with improvement in the major clinical symptoms within approximately 1 week. Bacteriological examination on day 12 revealed that the synovial fluid was sterile, evidencing that the antibiotic therapy was successful. These results are consistent with an earlier report in which only 2% of clinically isolated *N. meningitidis* showed penicillin/ampicillin resistance [27]. It must be

stressed that early antibiotic treatment is important for treating meningococcal arthritis before degenerative bone damage progresses.

Incidences of primary meningococcal arthritis in Japan have not been reported to date mainly due to the fact that it is not mandatory to report cases of meningococcal infection to public health officials with the exception of cases of meningitis. However, it is important to survey and further examine meningococcal arthritis to understand the overall level of infection and stress the importance of immediate treatment.

Conflicts of Interest

None declared.

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