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Case Report

Septic Arthritis Complicated by Nontypeable *Haemophilus influenzae* Bacteremia in a Patient With Hypogammaglobulinemia

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Abstract

Haemophilus influenzae is part of the normal flora of the upper respiratory tract. Knowledge about the treatment of *H. influenzae* septic arthritis in patients with primary hypogammaglobulinemia is limited. Here, we present a 12-year-old boy with primary hypogammaglobulinemia and *H. influenzae* septic arthritis in his right knee. Ceftazidime and surgical debridement were not effective. After intravenous immunoglobulin infusion, his knee swelling subsided. The patient was free of symptoms at the 12-month follow-up. Serum immunoglobulin is important for the phagocytosis reaction against *H. influenzae*. In addition to antibiotics and drainage of purulent material, intravenous immunoglobulin replacement therapy is indispensible for the adjuvant treatment of *H. influenzae* septic arthritis in patients with primary hypogammaglobulinemia. (*Tzu Chi Med J* 2010;22(4):200–202)

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1. Introduction

Haemophilus influenzae, a small Gram-negative organism, was first recognized in 1892 (1). This pathogen is part of the normal flora of the upper respiratory tract and can be isolated from the nasopharynx of 60–80% of asymptomatic individuals. Normally, invasive disease caused by *H. influenzae* is unusual after the age of 6 years because of the presence of protective antibodies. *H. influenzae* septic arthritis in adults can usually be cured by antibiotics and drainage (2). However, there is limited knowledge about the treatment of *H. influenzae* septic arthritis in patients with primary hypogammaglobulinemia. Here, we present a 12-year-old patient with primary hypogammaglobulinemia and *H. influenzae* septic arthritis who was successfully treated with antibiotics, surgical debridement and intravenous immunoglobulin (IVIG).

2. Case report

A 12-year-old boy was admitted to our hospital because of painful swelling of his right knee for 2 weeks. His weight was 26 kg and height was 130 cm. This boy had been diagnosed with primary hypogammaglobulinemia at another hospital 3 years previously. He had

received IVIG injections monthly at our outpatient department but had been lost to follow-up 1 year previously. Two weeks prior to this admission, he experienced arthralgia in his right knee while riding a bicycle. No wound or skin defect was found over his knee. His right knee swelled progressively with local pain and heat. He went to a local hospital where he was admitted and received some intravenous antibiotics. The knee swelling subsided and he was discharged after a 7-day course of antibiotics. However, his right knee swelled again and fever occurred 1 day prior to this admission. He was sent to our emergency room.

On arrival, his body temperature was 38.7°C, pulse rate was 148 beats/min, respiratory rate was 20 cycles/min, and blood pressure was 117/62 mmHg. His right knee was swollen with tenderness and local heat. Pain occurred during passive movement of the right knee joint. The remainder of the physical examination was normal. His hemogram revealed a white blood cell count of 17,710/mL with 87.4% neutrophils and 9.7% lymphocytes, a hemoglobin level of 11.9 g/dL, and a platelet count of 574,000/μL. Serum C-reactive protein level was 5.56 mg/L and erythrocyte sedimentation rate was 41 mm/hr. Electrolyte levels, and liver and renal function tests were within normal limits. Radiography of the right knee showed a moderate amount of joint effusion.

He was admitted to the general ward for further treatment. Pink to red purulent synovial fluid was obtained from arthrocentesis. Intravenous oxacillin 1000 mg every 6 hours and gentamicin 50 mg every 12 hours were administered initially. Arthrotomy and debridement were performed on the 3rd day of hospitalization, and revealed turbid fluid accumulation in the joint space. Blood culture grew Gram-negative bacilli, which was identified as *H. influenzae* by the Vitek 2 system (bioMérieux, Durham, NC, USA) on the 5th day. The antibiotics were changed to intravenous ceftazidime 1000 mg every 8 hours.

Two weeks later, the knee swelling had not subsided. His serum immunoglobulin G was 23 mg/dL, immunoglobulin A was 19 mg/dL, and immunoglobulin M was 3.2 mg/dL. IVIG at a dose of 9 g was administered intravenously on the 20th day. The knee swelling subsided. Serum white blood cell count decreased to 6980/μL and erythrocyte sedimentation rate decreased gradually to 11 mm/hr. After a 4-week course of intravenous antibiotics, he was discharged with oral ceftibuten 200 mg/day and IVIG monthly. The patient was free of symptoms at the 12-month follow-up.

3. Discussion

There are six major serotypes of *H. influenzae*, designated as types "a" through "f". In addition, some strains lack a polysaccharide capsule and are referred to as nontypeable strains. Type b and nontypeable strains are the most relevant strains clinically. The pathogenesis of this infection is believed to involve nasopharyngeal colonization, invasion with bacteremia and, subsequently, localization of bacteria in the joints. The mechanisms responsible for joint localization are not fully known. However, more than 70% of patients with *H. influenzae*-induced septic arthritis have had predisposing factors, such as immune suppression/deficiency, joint disease, a prosthesis, skeletal trauma, and alcoholism [2].

Patients with primary humoral immunodeficiency are prone to arthritis. The prevalence of joint manifestations before treatment in these patients has ranged from 5% to 40% in different studies [3]. About 10–30% of arthritis cases in these patients seem aseptic [4]. *Mycoplasma*-positive cultures were obtained from 38% of arthritic joints in one study [5]. The bacteria that commonly infect the sinopulmonary tract in humoral immunodeficiency are those isolated from joints [6]. Mucosal antibodies are important in defense against invasive organisms and block the adherence of the organisms to respiratory tract mucosa [1]. In our patient, septic arthritis occurred after IVIG was discontinued. IVIG replacement therapy may be considered effective for the prevention of septic arthritis in patients with primary hypogammaglobulinemia.

Although *H. influenza* is considered an important pathogen causing septic arthritis in patients with primary hypogammaglobulinemia, only rarely have cases been reported. Twenty-one cases of septic arthritis were found in a report of 201 patients with X-linked agammaglobulinemia, but the organisms were reported in only a few patients [7]. A review of 25 cases of *H. influenzae* septic arthritis reported that humoral immunodeficiency in most patients was secondary and only one patient had primary hypogammaglobulinemia [2]. There is limited knowledge about the treatment of *H. influenzae* septic arthritis in patients with hypogammaglobulinemia. A search of the literature for contemporary reports of *H. influenzae* septic arthritis and hypogammaglobulinemia revealed only two previously reported patients with primary hypogammaglobulinemia and *H. influenza*e septic arthritis (Table 1). Two of the three patients (including the present case) had nontypeable *H. influenzae* septic arthritis [8] and the other had type b *H. influenzae* septic arthritis [2]. Two of the three patients were given IVIG and survived. Two patients infected by nontypeable *H. influenzae* had monoarticular joint involvement, but the one with type b *H. influenzae* had polyarticular joint involvement.

H. influenzae has been shown to be associated with polyarticular infection [2,9,10]. Either type b *H. influenzae* or nontypeable *H. influenzae* can cause polyarticular infection. However, in the patients with primary hypogammaglobulinemia, polyarticular infection was

Table 1 — Clinical characteristics of septic arthritis caused by *Haemophilus influenzae* in patients with primary hypogammaglobulinemia

Reference	Age (yr)/sex	Underlying disease	Type	Joint	IVIG	Major antibiotics	Surgery	Outcome
Present case	12/M	Hypogammaglobulinemia	Nontypeable	Knee	Yes	Ceftazidime	Yes	Recovery
Hawkins et al [8]	35/M	Common variable hypogammaglobulinemia	Nontypeable	Knee	Yes	Aztreonam	No	Recovery
Borenstein & Simon [2]	34/F	Common variable hypogammaglobulinemia	Type b	Knee, elbow	No	Ampicillin, chloramphenicol	Yes	Death

only found in the patients with type b *H. influenzae* infection. In addition to prevention of septic arthritis, IVIG replacement therapy has been reported to be promptly effective in many cases of immune dysregulation-related arthritis [4,11,12]. According to the results in these three patients, IVIG seems to be very important for the adjuvant treatment of *H. influenzae* septic arthritis, in addition to antibiotics and drainage of purulent material. Normal human serum is bactericidal for *H. influenzae*, which can be opsonized for phagocytosis by normal human polymorphonuclear leukocytes [13]. These reactions need the presence of antibody and complement.

In conclusion, we described a patient with primary hypogammaglobulinemia and septic arthritis caused by nontypeable *H. influenzae*. In addition to antibiotics and drainage of purulent material, IVIG replacement therapy is very important for the adjuvant treatment of *H. influenzae* septic arthritis in patients with primary hypogammaglobulinemia.

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