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Original Article

Poststreptococcal reactive arthritis in Japan☆,☆☆

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ABSTRACT

Reactive arthritis after Group A streptococcal infection (poststreptococcal reactive arthritis: PSRA) that does not meet the Jones criteria for acute rheumatic fever (ARF) has been reported as a new entity for over a decade. In Japan there are few reports of PSRA. We encountered four children with arthritis accompanied with Group A streptococcal infection in our department. We investigated our cases and the recent Japanese literature. Japanese cases of PSRA are frequently accompanied with uveitis and erythema nodosum, and tonsillectomy resolved their symptoms in some cases. There were overlap cases between ARF, juvenile idiopathic arthritis, and PSRA.

1. Introduction

Acute rheumatic fever (ARF) is the most well known arthritis accompanied with Group A streptococcal (GAS; *Streptococcus pyogenes*) infection. Reactive arthritis after GAS infection (poststreptococcal reactive arthritis: PSRA) that does not meet the Jones criteria for ARF has also been reported [1–3]. As a result of improvements in the social economy, hygiene environment, and development of antimicrobial drugs, the number of these arthritis cases is decreasing. However, arthritis still occurs sporadically, particularly in developing countries, and has been estimated to affect 19 per 100,000 children worldwide [4]. We encountered four children with arthritis accompanied with GAS infection in our department. An association between HLA-DR and PSRA and/or ARF was reported from the USA [5], but was not confirmed from Italy [6]. In order to know the characteristics of Japanese PSRA and clarify issues regarding PSRA, we investigated our cases and the recent Japanese literature.

2. Materials and methods (subjected cases)

2.1. Case 1

A 2 years and 1 month old girl was referred to our hospital on July 25, 20xx because of gait disturbance. Her neonatal history (37 weeks and 5 days, 3788 g), past medical history, and family history were unremarkable. She complained of rhinorrhea and cough for 10 days. She had a fever with a body temperature of 39 °C on July 18, and became afebrile the next day. On July 25 she could not move in bed because of pain in the left lower extremity. She could stand with support but could not walk. On admission, her body temperature was 36.8 °C, her blood pressure was 113/66 mmHg, her heart rate was 100/minute, and her respiratory rate was 26/minute. Her throat was normal. Cardiovascular, respiratory, abdominal, and neurological examinations were normal. There was no lymphadenopathy or hepatosplenomegaly. No eruption was visible on her skin. The movement range of the left knee joint was limited because of pain; the joint was erythematous, but without swelling. Chest X-ray was normal. ECG showed no prolongation of PR interval. Echocardiography showed no effusion, no change in coronary flow, and no valve regurgitation. The levels of white blood

☆ The families of patients included in this manuscript agreed to this publication and their informed consents were obtained.
☆☆ All authors meet the ICMJE authorship criteria.
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Table 1
Laboratory findings of 4 cases with Arthritis accompanied with streptococcal infection.

	Case 1	Case 2	Case 3	Case 4
WBC (/μL)	11800	29000	16800	6300
Rheumatic factor (RF) (U/mL)	not done	<5	<5	<5
Anti-cyclic citrullinated peptide (CCP) antibody (U/mL)	<0.6	<0.6	<0.6	1.1
Matrix metalloproteinase 3 (MMP-3) (ng/mL)	49.7	69.5	29.7	30
ESR (mm/hr)	52	108	not done	28
CRP (mg/dl)	4.5	6.0	0.8	0.4
ANA	<40 X	<40 X	160 X	40 X
IgG (mg/dl)	1207	1743	1441	not done
IgA(mg/dl)	123	296	164	not done
IgM(mg/dl)	90	90	155	not done
Soluble IL-2 (U/mL)	1920	1920	not done	not done
ASLO (IU/mL)	2083	4460	559	346

cells, CRP, ESR, and soluble IL-2 receptor were elevated. Anti-streptolysin O (ASLO) was also high and the throat culture was positive for *Streptococcus pyogenes* (Table 1). X-ray of both knee joints showed irregularity and scuffing on the inside of epiphyses. MRI showed effusion in both hip joints, which is shown in Fig. 1.

She was given an antibiotic upon admission. Pain gradually decreased and resolved on day 3 after admission. On day 8 joint pain appeared again and aspirin was administered. Inflammation markers from blood tests and the patient's general condition improved, and she was discharged on day 17. At outpatient follow-up, neither abscess nor joint destruction was evident, and echocardiography showed no abnormality. The clinical course is shown in Fig. 2.

2.2. Case 2

This case was already reported by us [7] as acute suppurative oligoarthritis and osteomyelitis. A 4 years and 1 month old boy was referred to our hospital on May 29, 20xx because of arthralgia and fever. His neonatal history (38 weeks and 3 days, 3276 g), past medical history, and family history were not significant. In nursery, streptococcal infection was sporadic. On May 16 multiple erythematous areas approximately 2–3 mm in size appeared around the navel and ankles, accompanied with fever. On May 18 he was afebrile and the erythema disappeared. He had not been given antibiotics. Ten days later he could not move in bed because of left lower extremity pain. Since that day, his left lower extremity was extended and his knee joints were deviated due to pain. On May 28 a fever of 38.5 °C appeared again. The next day fever continued and he was admitted with a suspected diagnosis of purulent arthritis. His blood tests showed marked increase in inflammation by white blood cell count, ESR, and CRP, which were 29,000/μL, 108 mm, and 6.0 mg/dL, respectively. ASLO was high at 4460 IU/mL. His rapid strep throat test was positive, which is shown in Table 2. X-ray of left hip joint showed enlargement of the interarticular space. MRI showed effusion in the left hip joint, and a high density area from the distal edge to the proximal part of the femur, which implied extension of inflammation (Fig. 3). Combination treatment with vancomycin and panipenem/betamipron was started. However, joint symptoms and high levels of inflammatory blood markers continued. Clindamycin and NSAIDs were given additionally. On day 6 after admission CRP and pain were improved. Bacterial culture from joint synovia was negative twice. We started prednisolone because mitral regurgitation and epicardial effusion were detected by echocardiography. After start of treatments arthralgia disappeared without relapse, which is shown in Fig. 4.

2.3. Case 3

A 13-year-old boy was referred to our hospital because of left knee arthralgia. His past medical history and family history were unremarkable. He was febrile since May 10, 20xx. The antibiotic (cefcapene pivoxil) was administered for 4 days for a diagnosis of pharyngitis. Fever continued intermittently. On May 26 his throat was erythematous, and his rapid test for hemolytic streptococcus was positive. Oral penicillin prophylaxis (amoxicillin) was started. On June 4 arthralgia of the left knee joint appeared and he felt pain

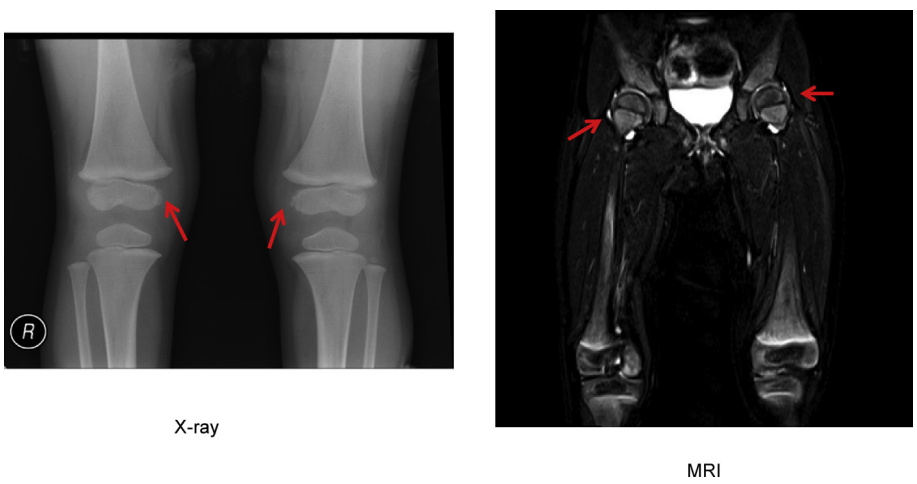

Fig. 1. X-ray and MRI (fat suppression T2-weighted image) of case 1; arrows represent irregularity and scuffing in the X-ray and effusion in the MRI.

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