**Reiter’s syndrome caused by *Streptococcus viridans* in a patient with HLA-B27 antigen**

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**CASE REPORT**

A 26-year-old male patient with mitral valve prolapse and HLA-B27 antigen received endodontic treatment for dental caries. Two weeks later fever, dysuria, diarrhea, sterile inflammatory arthritis of lower limbs, enthesitis, dactylitis, conjunctivitis, and uveitis consecutively developed. Blood culture performed at the time of active arthritis yielded *Streptococcus viridans*. He did not have any history of psoriasis, acute infectious diarrhea, chronic inflammatory bowel diseases, or sexually transmitted diseases. Laboratory studies also excluded the possibility of infections by human immunodeficiency virus, hepatitis B or C virus, chlamydia, and streptococci from the upper airway. This report indicates that *Streptococcus viridans* can be the triggering microorganisms of Reiter’s syndrome in some circumstances.

**Introduction**

Reactive arthritis is defined as a sterile inflammatory arthritis occurring in association with a primary infection at a distant site in the body (1). Reiter’s syndrome is characterized by the presence of reactive arthritis plus some extra-articular manifestations such as conjunctivitis, urethritis, heel pain, back pain, nail dystrophy, etc. (2). This syndrome is commonly associated with a primary infection by yersinia, shigella, salmonella, campylobacter or chlamydia (2). Sterile inflammatory arthritis caused by streptococci has been frequently found in patients with acute rheumatic fever or post-streptococcal reactive arthritis (PSRT) (3-5), but is occasionally reported in patients with bacterial endocarditis (6, 7).

The main triggering microorganisms of reactive arthritis in patients with acute rheumatic fever or PSRT belong to the β-hemolytic streptococci group. *Streptococcus viridans* belongs to the non-β-hemolytic group and is a normal inhabitant of human oral cavities. When people receive dental treatments that cause oral bleeding, these microorganisms may invade the blood stream and subsequently cause endocarditis (8). *Streptococcus viridans* as a triggering microorganism of Reiter’s syndrome has not been described before. We here report such a case in a male with mitral valve prolapse and HLA-B27 antigen. The relationship between Reiter’s syndrome, infection of *Streptococcus viridans*, and HLA-B27 antigen is discussed.

**Case report**

A 26-year-old previously healthy man was admitted to our hospital on June 22, 1998 because of high fever and arthritis. Six weeks prior to this admission he had received dental cleaning for caries in his molar teeth. Bleeding from his oral cavity was noted during the procedure, but he did not take any antibiotics either for prophylaxis or after this procedure. Two weeks after this operation, intermittent high fever up to 38.5°C developed. Two weeks later painful swelling of the left ankle ensued. This was soon followed by painful swelling of the right knee, dysuria, and watery diarrhea. The dysuria and diarrhea, both mild and intermittent, lasted for 3 and 7 days, respectively. Ten days prior to this admission, painful swelling of the left knee, left heel, and right big toe developed. Whenever fever or arthritis developed, the patient would take medications for 1 to 2 days as recommended by a local medical doctor or drug store. The entire clinical course is illustrated in Figure 1.

At admission, his medical history was taken and revealed that he was a heterosexual male with a constant partner. There was no history of tonsillitis, pharyngitis, acute infectious diarrhea, chronic inflammatory bowel disease or sexually transmitted diseases. Physical examination disclosed nothing particular except for high fever (39.4°C), conjunctivitis, painful swelling of both knees and the left ankle, enthesitis of the left heel, and dactylitis of the right big toe. His tonsils were not enlarged. Heart sounds were normal and there was no murmur. Liver, spleen, and lymph nodes were not palpable. There was no petchiae, splinter infarction of the nails or skin rash. Complete blood counts, urinalysis, and stool tests for occult blood and pus cells were all normal except for leukocytosis (WBC: 12,830/mm³). Blood culture performed at admission disclosed *Streptococcus viridans*, which was sensitive to cefazolin. The WBC count of the joint
fluid aspirated from right knee was 60,500/mm$^3$ (neutrophils/lymphocyte/monocyte = 90/8/2). There were no crystals, bacteria or fungi found in this joint fluid by culturing, Gram’s stain, or polarized microscope. The serum C-reactive protein (CRP) level was 21.2 mg/dl (normal < 0.5 mg/dl), HLA-B27 antigen was positive. All the following serological tests were either negative or within normal limits: antistreptolysin O titer (ASLO), rheumatoid factor, fluorescent anti-nuclear antibody, anti-chlamydia antibodies (IgG, IgA and IgM isotypes), antibodies against human immunodeficiency virus (HIV), antibodies against hepatitis B or C virus, liver and renal function tests, and serum levels of IgG, IgA, and IgM.

Echocardiographic examination disclosed mitral valve prolapse but without vegetation. X-ray examinations of the L-spine, pelvis, and affected joints were unremarkable except for mild soft tissue swelling in both knees. Technetium per-technetate ($^{99m}$Tc) whole body bone scan, performed 10 days after admission, revealed increased radioactivity over both knees, the right big toe, and the posterior end of the left calcaneus. After admission he was treated with diclofenac, cefazolin (2 gm q6h, intravenously), and joint fluid aspiration. The painful swelling of the left ankle, left heel, and right big toe improved gradually; but fever and swelling of both knees persisted. An arthroscopic examination was therefore performed in the right knee joint 5 weeks after admission. Grossly the synovial membrane appeared red, swollen, and hypertrophic, but no abscess or exudate was found. Microscopically synovial tissues were predominantly infiltrated by mononuclear cells. No bacteria was noted in these tissues. Based on all the above data, sterile inflammatory arthritis was considered to exist in our patient at this moment. Therefore we discontinued antibiotics on July 31. Instead, triamcinolone acetonide (30 mg) was injected into the right knee joint. The persistent fever subsided abruptly the next day and never returned. Because serum CRP levels remained high and the left knee remained swollen, combination therapy with methotrexate (15 mg/week) plus sulfasalazine (2,000 mg/day) was started 3 weeks after the fever had completely subsided. Two and half months after this regimen, no more swelling was noted in any of the affected joints. On October 6, 1998 red painful swelling and blurred vision developed in the patient’s right eye. Conjunctivitis plus acute anterior uveitis was diagnosed because numerous keratic precipitates were observed in the anterior chamber on slit lamp examination. The affected eye was treated with eye drops containing prednisolone acetate and became asymptomatic 6 days later.

Discussion
Our patient represents a case of possible infectious endocarditis because he fulfills 3 of the minor diagnostic criteria for this disease (8), i.e. mitral valve prolapse, fever, and bacteremia. Arthritis is not uncommon in patients with infectious endocarditis; it can be either pyogenic or inflammatory in nature (6). Pyogenic arthritis could not be absolutely excluded in our patient when he was admitted. However, the whole clinical course and the pathological findings on the synovial tissues strongly suggested that sterile inflammatory arthritis was present during the latter period of the disease course.

Five cases of sterile inflammatory arthritis have been described in patients with infectious endocarditis (6, 7). Electron-dense substances have been found in these patients’ synovial tissues (7). On the other hand, serum levels of circulating immune complexes are higher in patients with endocarditis than in normal controls or in patients with sepsis.

**CASE REPORT**

![Diagram](image-url)

**Fig. 1.** The clinical course in a patient who developed complete Reiter’s syndrome after infection with *Streptococcus viridans*. The normal CRP level is less than 0.5 mg/dl. Week 0 = date of admission; MTX = methotrexate, and SASP = sulfasalazine.
but without endocarditis (9). Chronic persistence of live bacteria or their antigens is one of the prerequisite factors for the development of reactive arthritis. In patients with infectious endocarditis the defective heart valves become a reservoir where bacteria replicate easily but are difficult to eradicate, resulting in the chronic persistence of bacteria in the body. All these findings indicate that reactive arthritis can occur in infectious endocarditis and immune complexes may play a role in this process.

Animal studies have shown that chronic inflammatory arthritis can be induced in rats when these animals are systemically injected with the cell wall extract of streptococci. The cell wall structure responsible for this chronic inflammatory reaction is peptidoglycan-polysaccharide complex (10). Clinically streptococcus group A, C and G are closely associated with the development of acute rheumatic fever or post-streptococcal reactive arthritis (3-5). These bacteria and *Streptococcus viridans* belong to the same species and may have shared similar cell wall structure including peptidoglycan-polysaccharide complex. Therefore, it would be expected that *Streptococcus viridans* can induce reactive arthritis in some circumstances.

Our patient was positive for HLA-B27 antigen and had conjunctivitis, uveitis, dysuria, diarrhea, enthesitis, dactylitis, and arthritis. All these features are compatible with the diagnosis of complete Reiter’s syndrome (2). Dysuria and watery diarrhea were considered to be a reactive rather than an infectious phenomenon because they occurred after arthritis had developed. There was no history of psoriasis, acute infectious diarrhea, chronic inflammatory bowel diseases or sexually transmitted diseases. Laboratory studies excluded the possibility of infections by HIV, hepatitis B or C virus, chlamydia, and streptococci from the upper airway. Considering this evidence and the timing between endodontic treatment, the occurrence of streptococcal infection, and the development of Reiter’s syndrome, we think that *Streptococcus viridans* was the most likely triggering microorganism of Reiter’s syndrome in our patient. The reason why our patient developed so many of the clinical manifestations of Reiter’s syndrome rather than merely simple reactive arthritis remains unclear. We speculate that the HLA-B27 antigen probably play a role. In the transgenic animal model, it has been shown that HLA-B27 transgenic rats can develop multi-system inflammatory diseases resembling human Reiter’s syndrome. These include inflammatory gastrointestinal disease, peripheral arthritis, orchitis, carditis, and a variety of skin lesions (11).

In summary, *Streptococcus viridans* can be the triggering microorganism of complete Reiter’s syndrome in some circumstances, as in our patient who was positive for HLA-B27 antigen, have a defective heart valve, and have received dental operation without antibiotics prophylaxis.

**References**