Reactive Arthritis which Occurred One Year After Acute Chlamydial Urethritis

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Abstract

A 30-year-old Japanese man developed dactylitis with sausage-like fingers in addition to balanitis and stomatitis. One year prior to these symptoms, acute chlamydial urethritis had been successfully treated by levofloxacin. On admission, *Chlamydia trachomatis* DNA was not detected in the urine sediment by PCR method, however, he was diagnosed to have reactive arthritis based on the clinical findings of asymmetric dactylitis, circinate balanitis, stomatitis and positivity for HLA B27 antigen. He was treated with methotrexate and his arthritis improved. The past chlamydial infection may have been involved in the pathogenesis of reactive arthritis in this patient.

Key words: chlamydial infection, human leukocyte antigen B27, reactive arthritis, Reiter's syndrome

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Introduction

Reiter's syndrome (RS) is characterized by non-specific arthritis, aseptic urethritis and ocular or mucosal lesions (1). The disease spectrum of RS has been broadened. Recently, the term "reactive arthritis" has been used to refer spondyloarthropathy following enteric or urogenital infections including RS (2). The etiology of reactive arthritis including RS is still not completely understood, however, two features, genetic factors and infections episodes, have a very strong correlation with the development of reactive arthritis (3). Approximately 80% of reactive arthritis patients are HLA-B27 (+) (4). In addition, infections with species from several bacteria, including *Salmonella*, *Chlamydia*, *Yersinia*, and *Shigella* have been strongly implicated as a triggering factor for the reactive arthritis (5). Infection with *Chlamydia trachomatis*, which is a common sexually transmitted bacterial disease, has emerged as a major causative agent of reactive arthritis (6, 7). Several studies have found that a large proportion of RS patients show evidence of present or prior chlamydial infection (8). However, the precise mechanism

by which chlamydial infection leads to RS, and especially to the chronicity and recurrence of some RS, is still unknown. The present report describes a Japanese patient with reactive arthritis, which developed one year after the onset of acute chlamydial urethritis.

Case Report

A 30-year-old Japanese man was admitted to our hospital in late January 2007 to undergo further examinations for dactylitis and spinal pain. In January 2006, he was diagnosed as *Chlamydia trachomatis* urethritis according to the detection of *Chlamydia trachomatis* DNA from the urine sediments. He had been successfully treated by levofloxacin and he recovered from urethritis completely. He noticed balanitis in October 2006. In December 2006, he noticed painful swelling of the second proximal interphalangeal (PIP) joint of his left hand and subsequently he developed arthralgia of the bilateral sacroiliac joints and lumbar spine. On admission, his body temperature was 36.7°C, pulse rate was regular, 78 beats/min and blood pressure was 120/78 mmHg. The patient had oral superficial stomatitis, circinate

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Figure 1. Circinate balanitis seen in the present case.

Figure 2. Dactylitis of the left second PIP joint with sausage-like appearance.

Clinical course

Figure 3. The clinical course of the present case. Clinical symptoms including dactylitis were improved by methotrexate (6 mg/week) treatment. Elevated levels of C-reactive protein (CRP) were completely normalized by this treatment.

balanitis (Fig. 1), and there was tender swelling of the second PIP joint of his left hand. The swelling of the left second PIP joint was not limited to the joint, and the presence of enthesopathy and tenosynovitis was suspected (Fig. 2). He also had arthralgia in the bilateral sacroiliac joints as well as the lumbar spine. Laboratory studies showed hemoglobin 12.9 g/dl, white blood cell count $7,800/\text{mm}^3$ (neutrophil 58.5%, lymphocyte 26.4%, monocyte 9.9%, eosinophil 4.8%, basophil 0.4%), platelet count $38.6 \times 10^4/\text{mm}^3$, erythrocyte sedimentation rate 22 mm/h, CRP 2.67 mg/dL. Liver and renal function tests showed no abnormality. Rheumatoid factor and anti-nuclear antibody were negative. Urinalysis also revealed no abnormal finding with negative results for bacterial cultures, and *Chlamydia trachomatis* DNA was not detected by the polymerase chain reaction (PCR) method. Serum immunoglobulin (Ig) A antibody for *Chlamydia trachomatis* was negative (0.06 U/ml, normal <0.9) by enzyme-linked immunosorbent assay [ELISA]. Serotyping of HLA

class I was positive for B27. In the roentgenograms of the fingers, the sacroiliac joint showed no particular findings including bone erosions. In bone scintigraphy, the uptake in the sacroiliac joints was slightly elevated. In radiography of the sacroiliac joint, neither erosive change nor eburnation was noted. Based on the presence of the typical manifestations, including dactylitis, stomatitis and circinate balanitis, he was diagnosed as reactive arthritis (Reiter's syndrome) and treatment with azithromycin 1,000 mg/day for 1 day and methotrexate (6 mg/week) was started. After this treatment, he recovered from these manifestations and the elevated levels of CRP and ESR were normalized (Fig. 3).

Discussion

Reiter's syndrome (RS) is a clinical triad of non-septic arthritis, urethritis and conjunctivitis (1). A number of other clinical features were also observed to be associated with

RS. According to the American Rheumatism Association criteria, reactive arthritis patients generally have asymmetric polyarthritis that lasts at least 1 month, as well as one or more of the following features, urethritis, inflammatory eye disease, mouth ulcers, circinate balanitis or radiographic evidence of sarcoiliitis, periostitis, or heel spurs (9). The present patient developed manifestations that are characteristic of reactive arthritis, including asymmetric dactylitis with a sausage-like finger, sarcoiliitis, stomatitis and balanitis. In addition, reactive arthritis is closely associated with HLA-B27 and the present patient had HLA-B27. Although reactive arthritis is rare in Japan, based on these typical manifestations, a diagnosis of reactive arthritis was made in the present case. The etiology of reactive arthritis is still not completely understood, however, it has been reported that the development of reactive arthritis is closely associated with infections of certain bacteria, including *Salmonella*, *Shigella*, *Yersinia*, and *Chlamydia* (5-7). It should be noted that the patient had a past history of *Chlamydia trachomatis* infection one year prior to the onset of reactive arthritis. His acute chlamydial urethritis was successfully treated by levofloxacin. Indeed, *Chlamydia trachomatis* DNA was not demonstrated in urine sediments by PCR method and the elevation of IgA anti-*Chlamydia* antibodies were not detected in the sera on the admission to the hospital. Several studies have found that a large proportion of reactive arthritis patients show clear evidence of present or prior chlamydial infection (8). To our knowledge, no case of reactive arthritis, occurring 1 year after prior chlamydial infection has been reported. The majority of RS patients have recurrent episodes of active arthritis (10), however, these recurrences are generally not related to overt genitourinary infections (11). It was also reported that about 43% of RS patients with recurrent attacks showed no discriminate urethritis infection (12). Either a persistent or unrecognized chlamydial infection could thus have been one of the factors that con-

tributed to the delayed onset of reactive arthritis from the infectious episode in the present case. Recently, increasing data show that in *Chlamydia*-induced arthritis, non-replicative but live bacteria exist in the joints or elsewhere in the body (13). The nature of such persistent chlamydial infection was studied by several groups (14, 15). Gerard et al demonstrated that viable, metabolically active *Chlamydia* reside in the synovial tissue of patients with *Chlamydia*-associated reactive arthritis (16). Direct evidence of persistent chlamydial infection in the role of pathogenesis of reactive arthritis has not been demonstrated, therefore, the concept of persistent infections in the trigger of chronic arthritis of reactive arthritis is only one of the possible explanations. Alternatively, the immunological factors, such as HLA-B27, may be attributed to the persistent chlamydial infection. A possible interaction between HLA-B27 and chlamydial antigen may alter the T cell response or expansion in response to some auto-antigens, as demonstrated in reactive arthritis (17). Since we could not completely rule out the persistent chlamydial infection, we administered azithromycin, which is recommended for *Chlamydia trachomatis* urethritis (18). Although studied in a mainly uncontrolled trial, methotrexate has been shown to be effective in the treatment of peripheral arthritis in patients with spondyloarthritis (19). Therefore, we started methotrexate treatment against dactylitis and sarcoiliitis observed in our patient.

Although the concept of persistent chlamydial infection in reactive arthritis and the factors that lead to its persistence in the synovium have not yet been established, the present case suggests that reactive arthritis could occur in the Japanese population even after the long-term duration of a chlamydial infection. There is still a need to further assess the relationship between the occurrence of reactive arthritis and the chlamydial infectious state using a large number of patients with reactive arthritis.

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