Case Report

A case of Chlamydia-associated arthritis

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(Received November 6, 2009)

summary

We report a case of Chlamydia-associated arthritis in a 40-year-old man. The patient experienced four episodes of Chlamydia trachomatis urethritis within a few years. During the present episode, polyarthritis developed a few days after Chlamydia trachomatis urethritis was noted. The patient was diagnosed as having Chlamydia-associated arthritis. Loxoprofen sodium and azithromycin were started. Antibiotics induced clinical improvement of urethritis, although arthritis persisted for 3 months. HLA-B27 was negative, but both HLA-B35 and B40 were positive. Thus, we speculate that positivity for both HLA-B35 and HLA-B40 contributed to the persistence of arthritis in this case. During the course, the levels of Th1, Th17 and regulatory T cells in the peripheral blood were increased on flowcytometry. Thus, we speculate that Th17 may play, at least in part, an important role of the pathogenesis in this case.

Key words — reactive arthritis; seronegative; Chlamydia; spondyloarthropathy; HLA

Introduction

Reactive arthritis is an inflammatory joint disorder that may occurs following genito-urinary infection with Chlamidia trachomatis or enteral infection with Yersinia, Salmonella, Shigella or Campylobacter1-2). Reactive arthritis is usually self-limited and can be either monoarticular or oligoarticular, although some cases progress to chronic arthritis. The disease is strongly associated with HLA-B27 in Caucasian, but not in Japanese population, and it is likely that cytokines play a critical role in the pathogenesis of arthritis, although the exact pathogenesis remains unknown3).

Here, we describe a case of Chlamydia-associated arthritis. The patient had experienced four episodes of Chlamydia trachomatis urethritis within the few years. During the present episode, polyarthritis developed a few days after Chlamydia trachomatis urethritis was noted. Antibiotics induced clinical improvement of urethritis although arthritis persisted for 3 months. HLA-B27 was negative, but both HLA-B35 and B40 were positive. During the course, we also detected elevated levels of Th1, Th17 and regulatory T cells (Treg cells) in his peripheral blood on flowcytometry. Our patient is the first case in which Th17 and Treg cells were measured in the peripheral blood.

Case

A 40-year-old man was referred to our outpatient clinic because of right plantalgia in March 2008. A few days earlier, the patient had been diagnosed as having Chlamydia trachomatis urethritis at the urology unit. He had a history of Chlamydia trachomatis urethritis three times during the last few years. During the present episode, right plantalgia developed. During previous episodes of Chlamydia trachomatis urethritis, there had not been any sign of arthritis, uveitis nor conjunctivitis. On examination, blood pressure was 120/80 mmHg. The patient had right plantalgia and pain in the left ankle. Urethritis and balanitis were noted. Laboratory data were as follows: ESR 16 mm/h, WBC 9900/μL (neutrophils 68%, lymphocytes 20%, monocytes 6%), Hb 13.5 g/dl, PLT 32.3×104/μL, Uric acid 4.9 mg/dl and C-reactive protein (CRP) 0.88 mg/dl. Urinalysis demonstrated (+) protein on dipstick. White blood cell count was 30-40/field. Renal and liver functions were normal. Immunological tests demonstrated immunoglobulin (Ig) G, IgA and IgM were 1851, 271 and 79 mg/dl, respectively. Antinuclear antibody and RAPA were negative. CH 50 49.0 U/ml, C3 126 mg/dl and C4 34 mg/dl. MMP-3 81.0 ng/ml and anti CCP antibody <0.6 U/ml. HLA-A2, 31, B35 and B40 were positive. Levels of serum IgA and IgG antibodies for Chlamydia trachomatis were 4.01 and 3.70 on enzyme linked immunosorbent assay (ELISA), respectively. On urology examination, Chlamydia trachomatis DNA was detected by the polymerase chain reaction (PCR) method. Finally, he was diagnosed as having Chlamydia-associated arthritis and treated with loxoprofen sodium and azithromycin. Subsequently, he
noticed painful swelling of the left ankle (Fig 1a), right foot (Fig 1b), second proximal interphalangeal (PIP) joint of the right hand (Fig 1c), left jaw, left hip and right elbow (Fig 2). Radiography showed that these joints were intact. Three weeks later, urethritis was completely resolved. However, polyarthritis persisted. Both ophthalmology exam and cardiac echocardiogram were intact. At that time, we were able to detect Th1, Th17 and Treg cells among CD4 positive cells in the peripheral blood by flowcytometry. The ratios of Th1 and Th17 in CD4 positive T cells in peripheral blood were 1.06% and 0.88%, respectively. The ratio of Treg in CD4 positive T cells was 5.68% (Fig 3a, b). After three months, polyarthritis finally resolved and the elevated level of serum CRP was normalized.

Discussion

Here, we present a case of Chlamydia-associated arthritis. The patient experienced four episodes of Chlamydia trachomatis urethritis within the past few years. During the present episode, polyarthritis developed a few days after Chlamydia trachomatis urethritis was noted. In this case, polyarthritis developed in both ankles, PIP joint of the right hand, left

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Figure 2. Clinical course of the patient.
* shows the day when Th17 and Treg cells were measured.
that sixty-seven percent of Chlamydial arthritis patients were positive for HLA-B27 in Turkey. They speculated that this fact was related to cross-react or to have homology with B27, B22, B37 and B39. Since HLA-B22, B37 and B39 have been reported to be associated with the disease. Wagener et al reported that in HLA-B27 negative reactive arthritis patients, synovial fluid concentration of IFN-γ was significantly lower in HLA-B27-positive patients than in HLA-B27-negative patients. We previously demonstrated that IFN-γ and IL-10 are relatively abundant in synovial tissue of early Chlamydia-associated arthritis patients. Thiel et al detected antigen-specific IL-10 secretion in Chlamydia-associated arthritis, which might mediate the inhibition of effective bacterial clearance. In our patient, the ratio of Th1 and Th17 in CD4 positive T cells in peripheral blood was 1.06% and 0.88%, respectively. The ratio of Th17 among CD4 positive T cells was elevated. Thus, we speculate that Th17 may play, at least in part, an important role of the pathogenesis of reactive arthritis. We need to examine more cases to elucidate the role of Th17 in the pathogenesis of Chlamydia-associated arthritis.

Data on cytokine concentrations from patients with reactive arthritis are contradictory, based on studies with small sample sizes. Singh et al measured cytokine levels in synovial fluid and sera from 51 patients with reactive arthritis and 40 patients with rheumatoid arthritis. They showed significantly higher synovial fluid IL-17, TGF-β, IL-6 and IFN-γ levels in reactive arthritis compared to those in rheumatoid arthritis. IL-17, IL-6, IFN-γ and IL-10 were significantly higher in synovial fluid than in serum in patient with reactive arthritis. The synovial fluid IFN-γ/IL-10 ratios were higher in reactive arthritis than in rheumatoid arthritis. Thus, they speculated that Th1 and Th17 in T cells could be the major agents of inflammation in reactive arthritis. However, Jendo et al reported that the level of TNF-α, IL-6 and IL-1 in serum and synovial fluid did not differ between Chlamydia trachomatis-induced arthritis and rheumatoid arthritis. Further investigation is needed to clarify the pathogenesis of reactive arthritis.

Treg cells are responsible for active suppression of autoimmunity, playing an important role in pathogenesis in autoimmune disorders. The average percentage of Treg cells in CD4 positive T cells in
healthy controls was 1.5%, while in this patient, the percentage of Treg cells among CD4 positive T cells was 5.68%. Thus, Treg cells may have played an important role in the pathogenesis in our patient; we speculate that the ratio of Treg cells was elevated to suppress the activated Th17.

In summary, we described herein a case of Chlamydia-associated arthritis. Reactive arthritis is usually self-limited. This case developed arthritis, and positivity for HLA-B35 and HLA-B40 may have contributed persistence of arthritis in this case. In addition, we detected elevated levels of Th17 and Treg cells by flowcytometry during the course. Th17 and Treg cells may play a pivotal role in the pathogenesis of Chlamydia-associated arthritis.

References


