Reactive Arthritis Due to Asymptomatic Infection of Chlamydia trachomatis

Key words: reactive arthritis, asymptomatic infection, Chlamydia trachomatis, synovial fluid, anti-Chlamydia trachomatis antibody, polymerase chain reaction

Reactive arthritis (ReA) is clinically characterized by acute-onset polyarthralgia mainly in the lower extremities following an infection of various microorganisms, although the pathogenetic mechanism remains unclear. In Japan, ReA is extremely rare partly because of the low prevalence of human leukocyte antigen (HLA)-B27, which is closely associated with the development of this disease in the United States and Europe (1). This report concerns a Japanese patient with ReA ascribable to an asymptomatic infection of Chlamydia trachomatis in the urinary tract.

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A 45-year-old man was admitted to our hospital because of inability to walk with a one-month history of polyarthralgia in the lower extremities. The patient had no pertinent sexual history. Physical examination showed severe tenderness and swelling in the right knee, and the left ankle, and in both tarsometatarsal and left metatarsophalangeal joints, with no conjunctivitis. No tenderness suggestive of enthesitis was observed in either tendon and ligament insertions or the sacroiliac joints. In routine laboratory data there were no abnormal findings except for inflammatory reactions, including C-reactive protein (8.29 mg/dl, normal <0.50 mg/dl). Neither rheumatoid factor nor antibodies to galactose-deficient immunoglobulin G (IgG) were detected in serum, and other autoantibodies were also negative. Despite the lack of clinical symptoms suggestive of the urogenital infection, urinalysis revealed pyuria with a positive result of polymerase chain reaction (PCR) for Chlamydia trachomatis. Anti-Chlamydia trachomatis IgG and IgA antibodies were positive in both serum and the synovial fluid obtained from the right knee. The titer of IgA antibodies was higher in the synovial fluid than in serum. In PCR, Chlamydia trachomatis was not detected in the synovial fluid. The HLA phenotype was determined as being A2, B46 and B71. Soon after admission the patient was treated with a non-steroidal anti-inflammatory drug (NSAID), but polyarthralgia did not improve. Oral prednisolone was started at a dose of 30 mg/day together with an NSAID, and clinical symptoms quickly improved in parallel with a decrease in titers of anti-Chlamydia trachomatis antibodies in serum and inflammatory reactions (Fig. 1). Levofloxacin and clarithromycin were also given to the patient in order to treat the urinary tract infection, and the PCR test in urine became negative 1 month after starting these drugs. The patient was discharged from our hospital 6 weeks after admission, and has remained in good condition. Oral prednisolone was tapered, and no relapse was observed after cessation of this drug.

Based on the clinical features, including predominant involvement of the lower extremities, and the results of laboratory investigations such as PCR and antibodies, the patient was diagnosed with ReA induced by Chlamydia trachomatis. Oral prednisolone was employed for treatment in this patient because of severe pain resistant to NSAID in multiple joints (2). According to several recent reports on the diagnosis of Chlamydia trachomatis infection, the PCR test in urine is higher than 90% in both sensitivity and specificity (3), while antibodies to this agent in serum, particularly the IgA class, are often negative even in PCR-positive patients (4). Both the PCR test in urine and antibodies in serum were positive at admission in this patient, but in general, the former may be superior to the latter with respect to sensitivity and specificity for the diagnosis of Chlamydia trachomatis infection.

Regarding the pathogenetic mechanism, there are several possible hypotheses. One is molecular mimicry. Antibodies to this agent may cross-react with HLA, particularly B27, resulting in the development of arthritis. The other is a direct pathogenetic effect of Chlamydia trachomatis on the synovial tissue. Several reports have demonstrated that this agent can be detected in the synovial fluid and tissue obtained from ReA patients (5). Nevertheless, it remains unconfirmed whether Chlamydia trachomatis has arthritogenic activity or not, because this agent can be detected also in the synovial tissue in other diseases without arthritis (6). Although in this patient Chlamydia trachomatis could not be detected in the synovial fluid by PCR, IgA antibodies to this agent were higher in the synovial fluid than in serum, and correlated well with the disease activity of ReA. A recent report has also demonstrated that IgG antibodies to Chlamydia trachomatis were higher in the synovial fluid than in serum in ReA ascribed to this agent (7). These findings suggest that the local production of anti-Chlamydia trachomatis antibodies in the synovial tissue may have contributed to the pathogenesis of ReA in this patient, irrespective of the intra-articular presence of this agent (7, 8). When ReA is suspected as a possible diagnosis in patients with polyarthritis, laboratory investigations such as urinalysis, antibodies and PCR should be performed in order to confirm the implication of microorganisms, even if there are no symptoms suggestive of infection.
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