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CLINICAL PROBLEM-SOLVING

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A young man with multiple joint pains and fever: A case with the importance of accurate history taking

Kento Sonoda MD[1] | Yuji Tanaka MD[1] | Yasuharu Tokuda MD, MPH[2]

[1]National Defense Medical College Hospital, Tokorozawa, Japan

[2]Japan Community Healthcare Organization Tokyo Joto Hospital, Koto-ku, Japan

Correspondence
Kento Sonoda, National Defense Medical College Hospital, Tokorozawa, Japan.
Email: kentosonoda0825@gmail.com

1 | CASE

A 38-year-old Japanese man presented to the outpatient department of orthopedics with sudden onset of back pain without radiation for 4 days followed by a 3 week history of multiple joint pains. The joint pains were involved with the major joints, including left ankle, left wrist, right knee, and right second proximal interphalangeal joint of the foot. The pains became worse with movement. Due to increased joint pains along with plantar pain, he gradually developed difficulty in walking. During this period, the patient also had intermittent fever with a range of 37-38.6°C at daily maximum temperature. He had no significant past medical history such as diabetes, hypertension, hyperlipidemia, asthma, trauma, or major surgery. He worked as a system engineer. For 17 years, he had been smoking one pack of cigarettes and drinking two cans of beer a day. He had no known drug or food allergy.

Multiple etiologies should be considered for multiple joint pains and fever. These include infectious diseases, crystal-induced arthritis, endocrine disorders, collagen vascular diseases, or seronegative spondyloarthropathies. Regarding infectious diseases, viral, bacterial, fungal, or parasitic diseases can cause multiple joint pains and fever. Crystal-induced arthritis includes gout or pseudogout, although these diagnoses at this age are not common. Endocrine disorders include hyperthyroidism, hypothyroidism, or hyperparathyroidism. For collagen vascular diseases, rheumatoid arthritis, systemic lupus erythematosus, various vasculitis, or adult Still's disease are possibilities. Seronegative spondyloarthropathies include psoriatic arthritis, ankylosing spondylitis, enteritis-associated arthritis, or Behcet disease. Among these extensive causes, infectious diseases, such as bacterial arthritis, should be considered first, as they may cause sepsis, or rapid joint destruction. Thus, taking detailed history is necessary, focusing especially on exposures to potential pathogens, including sexual history. Review of systems is mandatory for gathering additional important information.

The patient lives in Kanto area with his parents. Family history showed the absence of collagen vascular diseases or traits of hereditary diseases.

He denied any contacts with animals, people with tuberculosis, sick people, or sexual contacts in the past half year. He had no recent travel history or exposure to wildness. In review of systems, chills, night sweat, or weight loss were negative. The patient also claimed that he did not have a sore throat, rhinorrhea, a headache, chest pain, abdominal pain, cough, dyspnea, vomiting, diarrhea, dysuria, or skin rash.

Negative exposure history cannot exclude infectious diseases. Concrete sexual history should be included into social history especially for adolescent men with suspected infectious diseases. Absence of skin rash cannot eliminate collagen vascular diseases. Physical examination should differentiate between inflammatory arthropathy and noninflammatory arthropathy by inspection and palpation on the entire joints. Presence of swelling, redness, local heat, or tenderness of the points indicates inflammatory arthropathy.

He was alert and oriented, and vital signs were normal, including the blood pressure of 112/66 mm Hg, the pulse of 95/min, the respiratory rate of 18/min, and the temperature of 36.1°C. There were no skin rash, conjunctival injection, or superficial lymphadenopathies. Heart sounds were normal without murmurs, gallops, or rubs. The lungs were clear to auscultation. Abdominal examination was normal. Examination of joints showed mild swelling and tenderness of left ankle, left wrist, right knee, and right second proximal interphalangeal joints. Although there was no tenderness over the spinous processes in the cervical, thoracic, and lumbar spines, the

patient had limited range of motion in the lumbar spine because of pain and tenderness on the left ankle and plantar surface at the heel side.

Swollen and tender joints suggest inflammatory arthropathy rather than noninflammatory arthropathy. Distribution of the inflamed joints is an important clue for making a diagnosis. Asymmetric distribution of inflammatory arthropathy may indicate seronegative spondyloarthropathies such as reactive arthritis secondary to infections of gastrointestinal or genitourinary tracts or rheumatic fever as well as infective endocarditis. Among these, rheumatic fever is currently rare in Japan and there were no obvious clues of history and physical findings for infective endocarditis, although it cannot be excluded by their absence. Because of the absence of symptoms or signs suggestive of infectious diseases in gastrointestinal tract, reactive arthritis secondary to infection of this tract is less likely. Asymptomatic genitourinary infection remains a possibility, and thus, there is a need for obtaining accurate sexual history, urinalysis, and urine culture. Plantar tenderness points to the presence of enthesopathy, which is a feature of seronegative spondyloarthropathies (Table 1).

Blood laboratory tests showed the following results: total protein of 7.6 g/dL, aspartate aminotransferase of 30 IU/L, alanine aminotransferase of 42 IU/L, urea nitrogen of 12 mg/dL, creatinine of 0.74 mg/dL, sodium of 140 mEq/L, potassium of 4.5 mEq/L, chloride of 102 mEq/L, calcium of 9.3 mg/dL, C-reactive protein of 5.6 mg/dL, peripheral leukocyte of 10 300/μL, hemoglobin of 14.1 g/dL, and platelet of 44.2×10^4/μL. Differential count of peripheral leukocytes showed neutrophils of 68.2%, bands of 0%, lymphocytes of 23.0%, eosinophils of 1.2%, monocyte of 7.2%, and basophils of 0.4%.

Increased peripheral leukocytes with neutrophilia and elevated serum C-reactive protein concentration are common in the presence of inflammatory arthropathy. Blood cultures should have been ordered when we need to rule out infection in the case of acute polyarthritis. If the inflamed joints have marked swelling and severe pain, arthrocentesis along with joint fluid examination and culture is recommended.

TABLE 1 Differential diagnosis list of acute polyarthritis

Infectious diseases
Viral (Human parvovirus, Enterovirus, Epstein-Barr virus, Coxsackievirus), Bacterial (*Staphylococcus aureus*, β-hemolytic streptococci, *Neisseria gonorrhoeae*), Tuberculosis, Fungal, Parasitic
Collagen vascular diseases
Rheumatoid arthritis, Systemic lupus erythematosus, Polymyositis/Dermatomyositis, Sjogren's syndrome, Vasculitis, Adult Still's disease
Spondyloarthropathies
Reactive arthritis, Inflammatory bowel disease, Psoriatic arthritis, Behcet disease
Crystal-induced arthritis
Gout, Pseudogout
Endocrine disorders
Hyperthyroidism, Hypothyroidism, Hyperparathyroidism

The patient received nonsteroidal anti-inflammatory drugs with appointment after a week for follow-up visit waiting for collagen vascular serological test results. Blood cultures and joint fluid examination were not obtained. On the next visit, the number of painful joints increased, although the extent of joint swelling had not changed. Additional tests revealed the following results: positive antinuclear antibody (ANA) with a titer of 640 times (speckled type), elevated MMP-3 of 228.3, TSH of 0.52 μIU/mL, and free T4 of 1.22 ng/dL. Serum anti-CCP antibody level was within normal limits. The patient was referred to the department of medicine under a tentative diagnosis of rheumatologic arthritis.

In general, ANA is useful for screening of systemic lupus erythematosus (SLE) based on its high sensitivity for this disease.[1] However, many healthy persons have positive ANA, and thus, its specificity is low. Therefore, positive ANA does not directly lead to a diagnosis of SLE unless there are other characteristic symptoms, signs and laboratory test abnormality suggestive of cutaneous, mucosal or organ involvements. Additionally, reactive arthritis and other etiologies remain possibilities. Therefore, these clues should be sought at first by repeated history taking and physical examinations.

At the time of visiting the department of medicine, further sexual history was taken, after explaining the relationship between sexually transmitted diseases and arthritis. Eventually, the patient confessed his past medical history of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections. He also admitted his sexual activity including sexual contacts with commercial sex workers twice, 2 months prior to the development of illness. Urinalysis showed no organisms but some neutrophils in the sediment. Urine polymerase chain reaction test for *N. gonorrhoeae* was negative, but that for *C. trachomatis* was positive. Treatment of oral azithromycin was initiated. After 2 weeks, all the symptoms resolved. HLA typing was obtained, showing positivity in HLA-A11, HLA-A24, HLA-B62, HLA-B39, HLA-Cw9, and HLA-Cw7. Human immunodeficiency antibody was negative, but sexual counseling was provided for the prevention of future sexual transmitted diseases.

Sexual intercourses with commercial sex workers are strong risk factors for sexually transmitted diseases including *C. trachomatis* infection, especially if they were unprotected. A syndrome of reactive arthritis secondary to *C. trachomatis* infection, formerly Reiter syndrome, may not have associated conjunctivitis and urethritis. Patients with reactive arthritis lacking the HLA-B27 antigen may have a shorter duration or arthritic symptoms, affecting fewer joints, and a lower incidence of a sacroiliitis and iritis than their HLA-B27 positive counterparts.[2] An HLA-B27-positive man appears to be 10 times more likely to develop sexually acquired reactive arthritis than one who lacks the antigen.[3]

2 | DISCUSSION

Reactive arthritis is an aseptic inflammatory arthritis that occurs subsequent to an extra-articular infection, most typically of the

gastrointestinal or genitourinary tracts. In the former tract infections, the key pathogens are *Salmonella typhimurium*, *Yersinia enterocolitica*, *Shigella flexneri*, *Campylobacter jejuni*, and *Clostridium difficile*.[4] In the latter infections, these are *C. trachomatis*, *N. gonorrhoeae*, *Ureaplasma urealyticum*, and *Mycoplasma genitalium*.[4]

Chlamydia species are obligate intracellular bacterial parasites and pathogenic to their various hosts.[5] *Chlamydia trachomatis* and *Chlamydia pneumonia* are human pathogens. *Chlamydia trachomatis* is the etiologic agent for trachoma and sexually transmitted disease. Only a small proportion of all Chlamydia-infected individuals experience reactive arthritis.[6] Studies on sexually acquired reactive arthritis suggest that approximately 1%-3% of patients with chlamydia urethritis will experience arthritis.[6-8] However, about a half of patients with reactive arthritis are considered to be caused by *C. trachomatis* infection.[6,7] This organism can reach joints from the urogenital system via circulating monocytes, and these monocytes/macrophages become its hosts during long-term infection of synovial tissue.[8]

The cornerstones of treatment for reactive arthritis secondary to *C. trachomatis* infection are antibiotics effective against this organism and nonsteroidal anti-inflammatory drugs as a measure for pain control of arthritis and frequently associated enthesopathy.

Regarding the diagnosis in this case, the importance of accurate history taking should be emphasized. At the time of the first visit, the patient denied his sexual contact in the past half year, but in the next visit, he admitted the sexual contact after we explained the relationship between STDs and arthritis. Before asking a sexual history, it is crucial to provide the explanation of the reason why this private history should be obtained. It is surely important to ask appropriate questions for an accurate diagnosis, but we should not forget the importance of building rapport with patients. Taking a sexual history is very difficult even for experienced physicians, and we all should continue to train our interviewing skills. To learn more about this, I highly recommend "A Guide to Taking a Sexual History," provided by Centers for Disease Control and Prevention.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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