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Ultrasonographic evaluation of knee joint synovitis in two patients with palindromic rheumatism

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Abstract The aim was to evaluate synovial proliferation ultrasonographically in order to identify the period of conversion from palindromic rheumatism to the early-stage of rheumatoid arthritis. Two patients, a 35-year-old man and a 44-year-old man, had been suffering from episodic attacks and remission of oligoarthralgia for 15 years and 6 years, respectively. Both patients were negative for rheumatoid factors, and exhibited slightly elevated levels of C-reactive protein and erythrocyte sedimentation rate at the times of the attacks. Radiograms of the affected joints showed no erosion of the bones in either patient. Ultrasonographic examination revealed both synovial effusion and synovial proliferation in the 35-year-old patient, suggesting conversion from palindromic rheumatism to rheumatoid arthritis, whereas only synovial effusion was found in the 44-year-old patient, suggesting the persistence of palindromic rheumatism. Ultrasonographic evaluations of synovial proliferation in the knee joints provide data that can be used to identify the period of conversion from palindromic rheumatism to the early-stage of rheumatoid arthritis.

Key words Knee joint · Palindromic rheumatism (PR) · Rheumatoid arthritis (RA) · Synovial proliferation · Ultrasonography

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Introduction

Palindromic rheumatism (PR) is a disease in which the patient experiences recurrent episodes of oligoarthritis that occur suddenly and disappear in a few days. This disease typically persists for a long period.[1] PR generally occurs in middle-aged people, and one-third of patients later have chronic arthritis, especially rheumatoid arthritis (RA).[2–4] The conversion period from chronic PR to early-stage RA is fairly difficult to detect.

The appearance of rheumatoid factor (RF) and the erosion of bones have been proposed as indicators of conversion from PR to RA.[3–7] No other laboratory tests or imaging methods have clearly been shown to aid in the detection of the conversion period from PR to RA. Some studies have shown that ultrasonography with a high-frequency transducer is an effective method for imaging synovial effusion and synovial proliferation in RA patients.[8–10]

Here we present reports on two patients who had been suffering from recurrent episodes of oligoarthritis for a long period. Their knee joints were examined by ultrasonography in order to obtain articular findings that could be used to detect the period of conversion from PR to RA.

Case reports

Case 1

The patient was a 35-year-old man (patient 1) who had been suffering from episodic arthralgia since 1985. The arthralgia occurred unilaterally in the right or left knee, and persisted for a few days until it ceased spontaneously. In 1987, the patient suffered from severe pain and swelling in the left knee, and underwent an arthroscopic examination and biopsy performed by an orthopedic surgeon. The pathohistology of synovial tissue obtained by the biopsy indicated a nonspecific chronic inflammation. During the following 10 years, the episodic attacks of arthralgia

occurred once every 1–3 months, with each episode followed by complete remission until the next attack. When the pain was severe, the patient was given nonsteroidal anti-inflammatory drugs (NSAIDs) prescribed by the family doctor. In May 1998, arthralgia occurred in both knees and the right ankle, and swelling of the knee joints persisted even after the pain had disappeared. The patient visited the Division of Orthopedic Surgery of the Ohta Nishinouchi Hospital, where he was treated with NSAIDs. He never complained of extraarticular symptoms such as aphtha, eye symptoms, or urogenital distress. Laboratory data obtained on September 14, 2000 (in remission), were as follows: white blood cells (WBC), 6400/mm^3; hemoglobin (Hb), 14.2 g/dl; platelets (PLT), 35.2×10^4/mm^3; uric acid (UA), 4.5 mg/dl (normal level, 3.5–6.8 mg/dl); erythrocyte sedimentation rate (ESR), 13 mm/h; C-reactive protein (CRP), 1.2 mg/dl (normal level, less than 0.2 mg/dl); antistreptolysin O antibody, 215 U/ml (normal value, less than 160 U/ml); negative for RF (5.0 U/ml, normal level less than 5 U/ml) and RA-hemagglutination (RAHA) (<40 x, normal level <40 x); negative for antinuclear antibody (ANA); elevated levels of serum IgG (2140 mg/dl) and IgA (455 mg/dl); normal level of serum IgM (73 mg/dl). Radiograms of the knee and ankle joints showed no erosion or destruction of the bones, but did show a deposit of calcification at the medial upper site of the patella in the anteroposterior aspect (Fig. 1a) of the right knee.

Ultrasonography performed on September 8, 2000 (in remission), using a 7.5-MHz annular array transducer attached to the ultrasonograph (SSA-250-A, Toshiba, Tokyo, Japan), revealed mild synovial effusion and mild synovial proliferation with a villonodular pattern (Fig. 2a,b). In October 2000, the patient complained of pain and swelling in both knees and the right ankle to a greater degree than that experienced in previous attacks, and he was referred to the Division of Rheumatology of Ohta Nishinouchi Hospital. Laboratory data obtained on October 6, 2000, was as follows: WBC, 7100/mm^3; Hb, 14.7 g/dl; PLT, 35.9×10^4/mm^3; ESR, 42 mm/h; CRP, 3.75 mg/dl; elevated level of serum CH50, 54.3 U/ml (normal level, 30–45 U/ml); negative for RF, myeloperoxidase–antineutrophil cytoplasmic antibody (MPO–ANCA), and proteinase (PR) 3-ANCA.

Ultrasonography of the knees performed on October 8, 2000 (during an attack), showed severe synovial proliferation in both knees, with a villonodular pattern and a large amount of synovial effusion (Fig. 2c,d). Administration of salazosulfapyridine at 1000 mg/day was started on November 8, 2000, and the frequency of the arthritic attacks subsequently decreased.

Case 2

The patient was a 44-year-old man (patient 2) who had been suffering from episodic attacks of arthralgia since 1994. The arthralgia occured in the right or left elbow or the right or left knee, and ceased in a few days. The patient had never suffered from mucocutaneous lesions, urogenital or intestinal complaints, or febrile infection, all of which would suggest diseases other than PR. In May 2000, he suffered from pain and swelling in the right elbow and the right knee. He visited the Soeda Clinic of Orthopedic Surgery, where 30 ml of synovial effusion was drained from the right knee. The administration of a NSAID relieved the arthralgia.

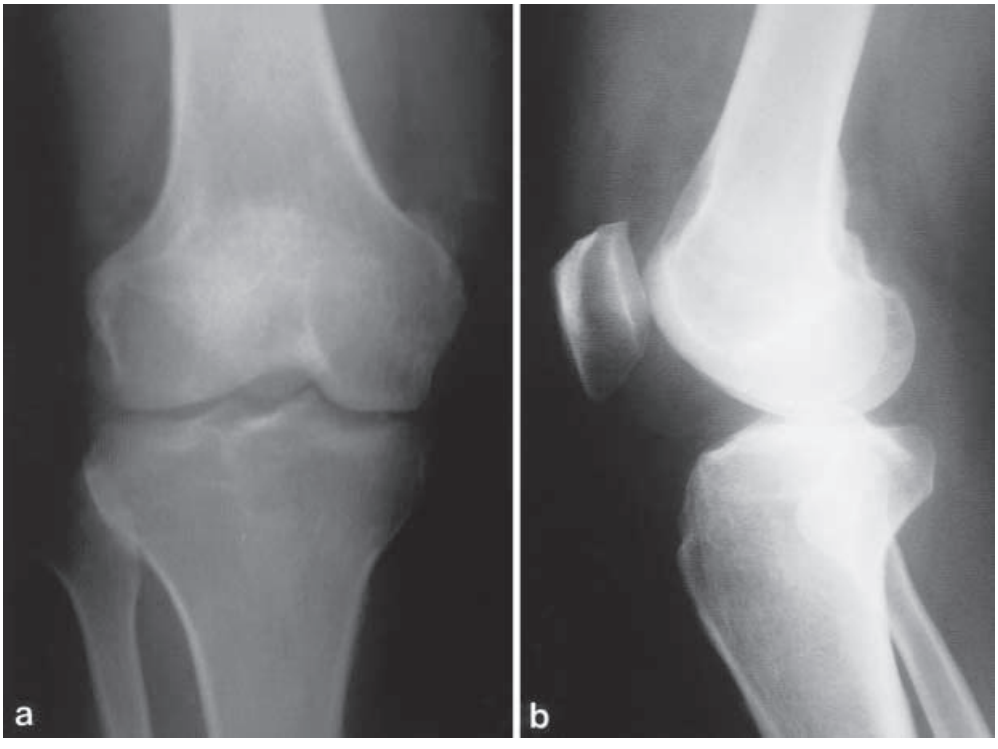

Fig. 1. Radiograms of **a** the anteroposterior and **b** the lateral aspect of the right knee of patient 1, taken on September 8, 2000. Neither narrowing of the joint space nor erosion of bone can be seen. A calcified deposit can be seen at the medial upper site of the patella (**a**). The image is blurred in areas where swelling of the soft tissue has occurred

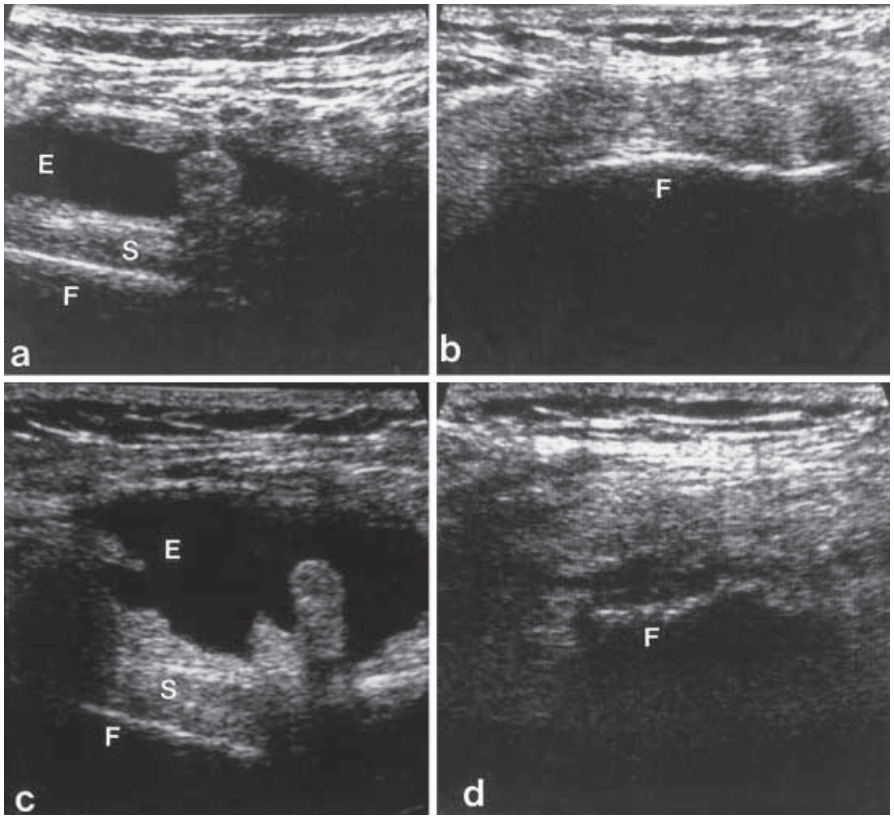

Fig 2. **a**,**b** Ultrasonograms of the right knee of patient 1, taken on September 8, 2000 (in remission). A slight accumulation of synovial effusion and low-grade synovial proliferation with a villonodular pattern can be seen in the longitudinal scans of the lateral (**a**) and medial (**b**) aspects of the patella. **c**,**d** Ultrasonograms of the right knee of patient 1, taken on October 8, 2000 (during an attack). A severe accumulation of synovial effusion and high-grade synovial proliferation with a villonodular pattern can be seen in the longitudinal scans of the lateral (**c**) and medial (**d**) aspects of the patella. *E*, effusion; *F*, femur; *S*, synovial proliferation

On September 8, 2000, pain and swelling occurred in both knees. The patient was referred to the Division of Rheumatology, Ohta Nishinouchi Hospital. The laboratory data obtained on September 8, 2000, were as follows: WBC, 4500/mm^3; Hb, 14.5 g/dl; PLT, 24×10^4/mm^3; ESR, 57 mm/h; CRP, 6.7 mg/dl; UA, 5.2 mg/dl; negative for RF (2.1 U/ml), RAHA (40 x), and IgG-RF; negative for MPO–ANCA; negative for anti-*Chlamydia* IgM and IgG antibodies and anti-*Yersinia* antibodies; elevated serum levels of ferritin, 341.6 mg/dl (normal value, 10–250), and CH50 (51.1 U/ml). Serum immunoglobulin levels were normal. Radiograms of both knees and both elbows showed that there had been no changes due to the erosion or destruction of bones, no narrowing of the joint space, and no calcification either inside or outside the joints (Fig. 3).

On September 10, 2000 (during an attack), both knees were still painful and swollen. Ultrasonography was performed on that day, and the ultrasonograms revealed large amounts of synovial effusion with slight synovial proliferation (Fig. 4a,b). Soon after the ultrasonograms were obtained, intraarticular puncture was performed, and synovial effusion was drained from the knees (65 ml from the right and 50 ml from the left).

A second round of ultrasonographic scans was performed on November 27, 2000 (in remission). Synovial effusion with a moderately echogenic fibrous material was found in the joint space of both knees (Fig. 4c,d), but in smaller amounts than had previously been observed.

Fig. 3. Radiogram of the left knee of patient 2, taken on September 10, 2000. Neither narrowing of the joint space nor erosion of bone can be seen

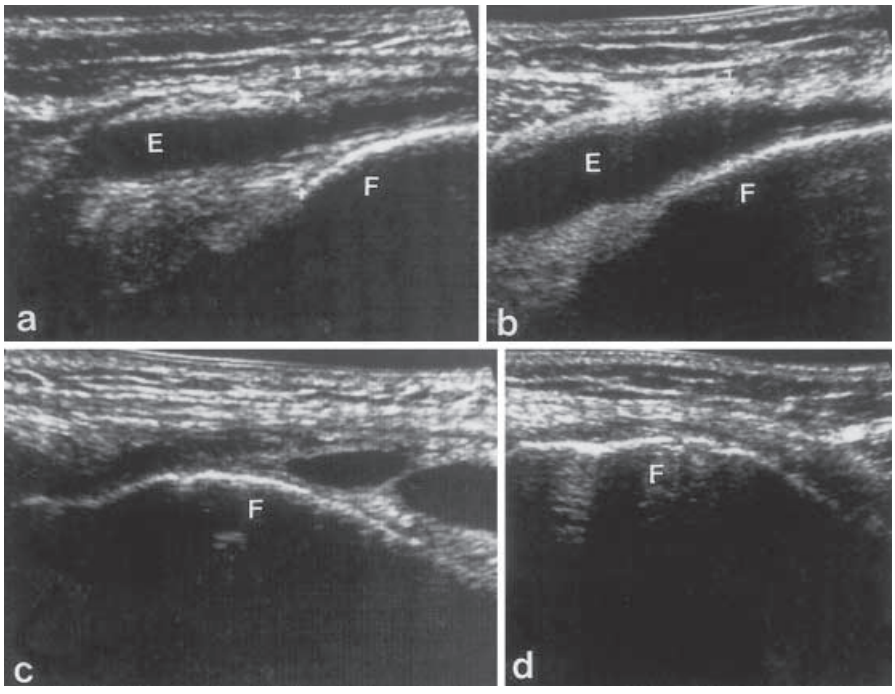

Fig. 4. **a**,**b** Ultrasonograms of the left knee of patient 2, taken on September 10, 2000 (during an attack). A large amount of synovial effusion can be seen in the longitudinal scan at the lateral aspect of the patella (**a**), and in the transverse scan at the superior aspect of the patella (**b**) **c**,**d** Ultrasonograms of the left knee of patient 2, taken on November 17, 2000 (in remission). A small amount of synovial effusion with fibrous material can be seen in the longitudinal scan of the lateral aspect of the patella (**c**), and in the transverse scan of the superior aspect of the patella (**d**). *E*, effusion; *F*, femur

Discussion

During the early stages of palindromic rheumatism, it is not easily distinguished from other arthritides. In addition, detection of the conversion period from PR to RA is difficult. We believe that the two cases presented here are examples of palindromic rheumatism. Both cases satisfy the five diagnostic criteria for PR proposed by Guerne and Weismann:[11] (1) a 6-month history of brief, sudden onset, and recurrent episodes of monoarthritis or (rarely) polyarthritis; (2) direct observation of one attack by a physician; (3) the involvement, during different attacks, of three or more joints; (4) the absence of radiographic evidence of erosion; (5) the exclusion of other arthritides. In patient 1, however, synovial osteochondromatosis (SOC) was a possibility because of the calcification noticed in the upper part of the right knee joint. Nevertheless, we considered that SOC could be excluded from criterion 5 in patient 1 since the patient has solitary calcinosis, and has been suffering from oligoarthritis in three joints with elevated levels of CRP and ESR, which does not occur with multiple calcification, or with the monoarticular and non-inflammatory arthropathy of SOC. We therefore considered that the calcification could have been produced by the repeated synovitis for a period as long as 15 years. In earlier studies, normal values were obtained for the laboratory data of PR patients,[1,12] but later studies showed that elevated values for acute-phase proteins (such as CRP) or ESR are not inconsistent with a diagnosis of PR.[6,11] Both patients in the present study had slightly elevated values of CRP and ESR during an attack.

In the present study, RF test results remained negative for both patients throughout the disease duration. In previous studies, PR patients have been found to have elevated levels of serum IgA[5] and complement component C3.[4,5] We observed elevated serum levels of IgA (455 mg/dl) and IgG (2140 mg/dl) in patient 1, and elevated levels of serum CH50 in both patients (patient 1, 54.3 U/ml; patient 2, 51.1 U/ml). With both patients, tests for ANA and MPO–ANCA were negative, and no elevation of serum uric acid was found in either patient. Patient 1 was negative for anti-*Chlamydia* antibody and anti-*Yersinia* antibody. These clinicolaboratory findings strongly indicate a diagnosis of palindromic rheumatism for both patients.

There have been reports of an accumulation of synovial effusion in PR patients.[1,4,13] Hench and Rosenberg[1] reported synovial effusion and periarticular edema in PR patients. Schumacher[13] observed an accumulation of polymorphonuclear leukocytes in the synovial fluids of PR patients that was similar to accumulations that have been observed in RA patients. In the present study, rather large amounts of synovial effusion were observed in the knee joints of both patients (imaging by ultrasonography). In fact, 50 and 65 ml of synovial fluid were drained from the left and right knee joints, respectively, of patient 2 during an attack. The synovial proliferation in PR patients reported by Schumacher[13] consisted of a slight proliferation of synovial lining cells at the stage immediately before conversion to RA. Hench and Rosenberg[1] reported a thickening of synovial villi, but not pannus formation, in the arthritic joints of PR patients. In contrast, in the present study, prominent synovial proliferation with a villonodular pattern[8–10] was detected ultrasonographically in the knee joint of patient 1. Synovial proliferation is a characteristic feature of RA synovitis, and it occurs in the early stages of the disease prior to bone erosion. The knee joint synovitis found in patient 1 may therefore indicate an early stage of seronegative RA, after conversion from PR. These findings suggest that the degree

of synovial proliferation in the joints of PR patients can be used to detect the period of conversion to RA. Synovial effusion and synovial proliferation can probably be demonstrated more clearly by magnetic resonance imaging (MRI). However, as far as we know, there have been no reports of MRI examinations of PR patients. Ultrasonography can be performed more quickly than MRI at the time of episodic arthritis attacks in PR patients. Thus, ultrasonography may detect positive indicators of arthritis that MRI might miss.

In conclusion, ultrasonographic examinations of knee joint synovitis in two PR patients revealed synovial effusion and synovial proliferation in patient 1 (disease duration 15 years), suggesting conversion from PR to RA, and synovial effusion only in patient 2 (disease duration 6 years), suggesting the persistence of PR. It appears that synovial proliferation in the knee joints of PR patients indicates conversion of the disease from PR to RA.

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