

Sporotrichal Tenosynovitis Diagnosed Helpfully by Musculoskeletal Ultrasonography

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Abstract

A 72-year-old man presented with persistent oligoarthritis and positive results for rheumatoid factor and was suspected of having rheumatoid arthritis (RA). However, the musculoskeletal ultrasonography (MSUS) findings were not consistent with those of typical RA. He had undergone surgery for carpal tunnel syndrome, which allowed both histopathological and microbiological examinations to be performed. A synovial tissue culture was positive for *Sporothrix schenckii*, and he was diagnosed with sporotrichal tenosynovitis. He received anti-fungal therapy, and the sporotrichal tenosynovitis resolved. This case suggests that MSUS is a useful modality, and sporotrichal tenosynovitis, though rare, should be considered in the differential diagnosis of RA.

Key words: sporotrichosis, tenosynovitis, fungal infection, rheumatoid arthritis, musculoskeletal ultrasonography

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Introduction

Sporotrichosis is a chronic fungal infection caused by *Sporothrix schenckii*. The fungus enters the body usually through injured skin in contact with contaminated soil, plants and organic matter (1). Although rare, it can cause articular manifestations, especially in immunocompromised hosts, such as patients treated with corticosteroids or immunosuppressants (2). In cases of polyarthritis without skin lesions, sporotrichosis resembles rheumatoid arthritis (RA). We report a case of sporotrichal tenosynovitis that initially presented with articular manifestations, specifically oligoarthritis, and no skin lesions. Musculoskeletal ultrasonography (MSUS) proved very useful for the differential diagnosis of sporotrichal tenosynovitis.

Case Report

A 72-year-old Japanese man visited our hospital with bilateral wrist pain and swelling. The symptoms began about one month prior to his visit. Two weeks before presentation, he had consulted a local orthopedist. At the orthopedic clinic, he had bilateral wrist swelling and showed positive findings for rheumatoid factor (RF). The doctor suspected that he had RA and referred him to our hospital for further examinations.

The patient was a farmer who smoked 30 cigarettes/day for 40 years and drank alcohol occasionally. He had ulcerative colitis and had been treated with mesalazine (3.6 g/day) and prednisolone (5 mg/day); the disease was relatively well controlled. At the first visit, the patient's physical examination showed a blood pressure of 104/64 mmHg, a pulse rate

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Figure 1. The left wrist is markedly swollen.

of 101 beats/min, and a body temperature of 36.6°C. A musculoskeletal examination revealed marked swelling on both the dorsal and palmar surfaces of the left wrist (Fig. 1) and tenderness in both wrists. Sensation was attenuated in the palm of the left hand. Tinel's sign and Phalen's test were both positive in the left hand, indicating carpal tunnel syndrome. No skin trauma or lesions were noted. No particular findings were noted in any other systems.

Laboratory tests revealed the following: white blood cells, 9,040/mm³ (normal range, 3,500-9,000/mm³); C-reactive protein, 4.78 mg/dL (normal range, 0-0.3 mg/dL); matrix metalloproteinase-3, 199.2 ng/mL (normal range, 36.9-121 ng/mL); positive RF, 63 IU/mL (normal range, 0-15 IU/mL); negative anti-citrullinated protein antibody, 0.7 U/mL (normal range, 0-4.4 U/mL); and β-D glucan, 9.1 pg/mL (normal range, 0-20 pg/mL). Serum urea, electrolytes, creatinine, and glucose levels were within the normal range. Wrist radiographs showed swelling of the soft tissue around the left wrist, but no bone erosions. The gray-scale image obtained from MSUS showed marked thickening of the flexor and extensor tendon sheaths in the left wrist. In addition, marked power Doppler signals were detected in the margin of the tendon sheath (Fig. 2a). The tenosynovium was filled with rice bodies (Fig. 2b). A small amount of straw-colored, cloudy synovial fluid was drained by joint-puncture from the left wrist. Neither crystals nor microorganisms were detected. *Mycobacterium tuberculosis* DNA was not detected by a polymerase chain reaction analysis of the synovial fluid.

Given the above clinical history and findings, he did not have typical RA and was instead suspected of having other diseases, including chronic infection. To identify the cause of the swelling in the left wrist and to relieve the carpal tunnel symptoms, we performed surgical synovectomy of the dorsal and palmar surfaces of the left wrist. Macroscopically, the extensor and flexor tendon sheaths were markedly thickened (Fig. 3a). The inside of the tendon sheaths showed marked hyperplastic synovium filled with abundant rice bodies that compressed the median nerve. In contrast, the synovia of the radiocarpal and midcarpal joints were almost intact. A histopathological examination of the resected teno-

synovium revealed granulomatous tissue accompanied by plasma cell and lymphocyte infiltrations (Fig. 3b). No bacteria were found through Gram staining or Ziehl-Neelsen staining. However, Grocott's methenamine silver (GMS) stain detected a small number of oval-shaped yeasts (Fig. 4). The resected synovial tissue culture was positive for *Sporothrix schenckii*, and sporotrichal tenosynovitis was diagnosed.

Initially, saturated solution potassium iodide, the standard therapy for sporotrichosis, was administered (3). However, shortly after starting the treatment, the patient developed hypothyroidism. The treatment was promptly changed to itraconazole, an anti-fungal drug, which he continued for a total of six months without any adverse effects. Two years following completion of treatment, the patient has shown no sign of recurrence or a change in the wrist radiography findings.

Discussion

Thus far, only six cases of sporotrichosis with articular manifestations resembling RA have been reported (Table). All of these previous cases were mistakenly treated for RA. In addition, it took quite a long time to achieve the correct diagnosis, resulting in a poor joint prognosis.

In cases of sporotrichosis with no skin lesions, the disease is usually chronic and indolent. *Sporothrix schenckii*, a dimorphic fungus, is thought to be a causative microorganism. The disease sometimes accompanies some articular manifestations such as arthritis and tenosynovitis (4). The knees are the most common affected joints, followed by the wrists, hands, elbows, and ankles. Often, multiple joints are affected simultaneously (2). It also frequently accompanies osteoporosis and juxta-articular erosions (10). No specific characteristics of synovial fluid have been reported (11). Histopathology of the synovium demonstrates chronic granulomatous inflammation (1). Thus, these clinical features resemble those of RA. However, since sporotrichosis is relatively rare, as described above, it is hardly ever considered in the differential diagnosis of RA. Furthermore, even if a patient is suspected of having sporotrichosis, it is also difficult to make a correct diagnosis because of the low sensitivity in the detection of the organism. Like other infectious diseases, detection of the organism in a specimen is the gold standard for making a correct diagnosis. Typically, with special staining methods such as GMS stain, an oval-to-cigar-shaped yeast is observed (12). Unfortunately, there are many false negative cases because of the small number of organisms (11). Thus, sporotrichosis mimics the clinical features of RA, and its diagnosis is often challenging.

Recently, the role of MSUS in the management of RA has been established (13). This modality visualizes the joint structures, such as bone, cartilage, and tendons, and demonstrates tissue inflammation by detecting microvascular blood flow (14). In our case, MSUS helped diagnose sporotrichosis. It clearly revealed the tendon sheath filled with rice bod-

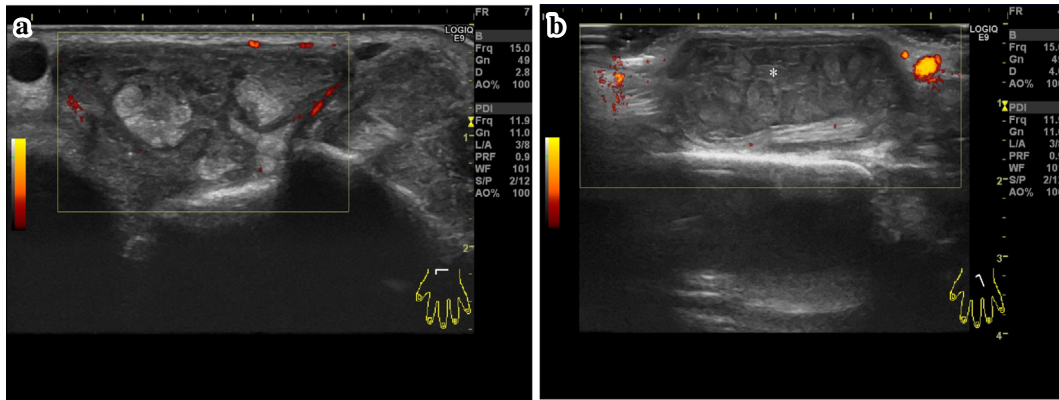


Figure 2. (a) Transverse musculoskeletal ultrasonography of the third and fourth compartments of the left wrist. The grayscale image shows a markedly thickened extensor tendon sheath, and power Doppler signals are detected in the margin of the tendon sheath. (b) The longitudinal view of the extensor tendon sheath. Multiple isoechoic rice bodies surround the tendon (white asterisk).

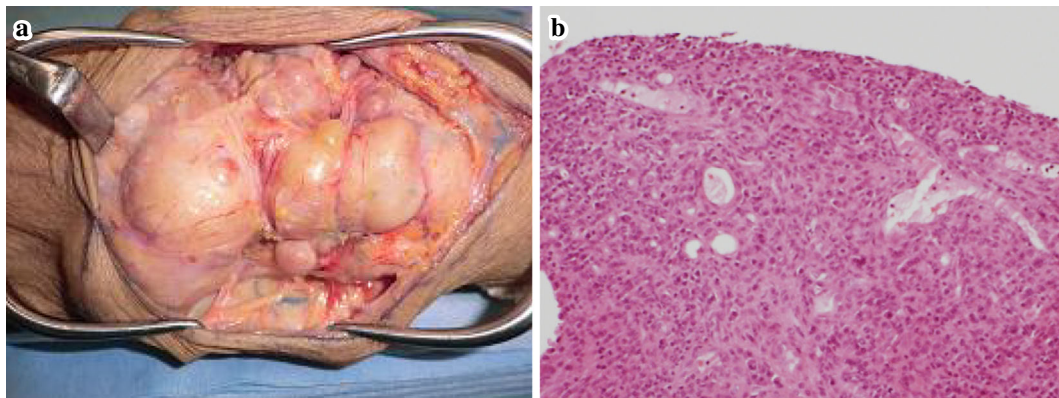


Figure 3. (a) The operative findings show a markedly thickened extensor tendon sheath. (b) Hematoxylin and Eosin staining of the tenosynovium shows chronic inflammatory tissue with plasma cell and lymphocyte infiltration. Original magnification $\times 20$.

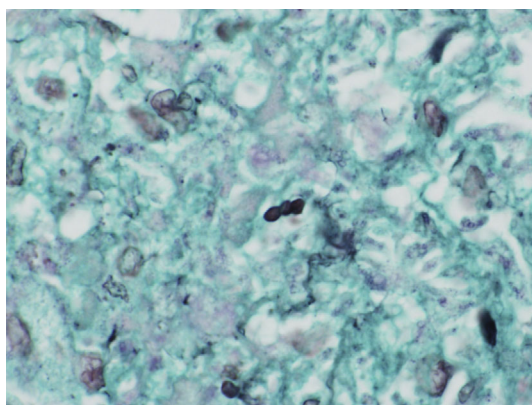


Figure 4. Grocott's methenamine silver staining shows oval-shaped yeasts. Original magnification $\times 1,000$.

ies that caused swelling of the wrist. In patients with RA, intra-articular rice bodies are often detected, regardless of disease duration (15). However, a tendon sheath filled with rice bodies is a typical finding for tuberculosis tenosynovitis (16) but is rarely seen in non-tuberculosis tenosynovitis,

including RA (17). In the present case, the findings of MSUS were not consistent with RA, and this prompted further histopathological and microbiological testing. Thus, MSUS aided our search for the cause of the atypical joint swelling. Furthermore, the presence of rice bodies around a tendon is an important finding that suggests chronic infection.

However, patients with RA are often in an immunocompromised state because they are usually treated with immunosuppressive drugs, such as corticosteroids and/or DMARDs, including biologics (18). Thus, the differentiation between infective and non-infective articular manifestations in patients with RA is quite difficult. In particular, chronic and indolent septic arthritis are difficult to distinguish from an RA flare (19). When RA patients receiving immunosuppressive therapy experience worsening of their joint symptoms, whether the exacerbation is actually caused by RA or by some other organism should be carefully considered. There are some reports that MSUS is helpful for the diagnosis of musculoskeletal infective diseases. The accumulation of MSUS images has revealed some characteristic

Table. Previous Case Reports of Sporotrichosis Mimicking Rheumatoid Arthritis.

Reference	Age/sex	RF	Skin lesions	Involved joints	Time to diagnosis	Treatment	Outcome
4	41/M	N/A	-	fingers and wrist	14 months	SSKI, AMPH-B, Synovectomy	restricted range of motion
5	34/M	N/A	-	finger, wrist, ankle, and knee	8 months	AMPH-B, Synovectomy	cane required for walking
6	34/M	-	-	fingers, wrists, elbows, and knee	5 years	FLCZ, AMPH-B, ITCZ	restricted range of motion
7	49/M	-	-	wrist, elbow, knee, and ankle	16 months	AMPH-B, Synovectomy	joint erosion
8	49/M	+	hand and arm ulcer	wrists and knee	4 months	ITCZ, AMPH-B	not described
9	78/M	-	arm, leg, and scrotum	wrist, knees, and ankle	3 years	AMPH-B	death
Present	72/M	+	-	wrists	7 months	SSKI, ITCZ, Synovectomy	contracture of finger

AMPH-B: amphotericin B, FLCZ: fluconazole, ITCZ: itraconazole, SSKI: saturated solution potassium iodide, RF: rheumatoid factor, N/A: not available, M: male

sonographic features suggestive of infective conditions, such as musculoskeletal abscesses (20, 21). Thus, MSUS may help us differentiate between infections and non-infective inflammatory conditions, not only at the time of the initial diagnosis, but also during the follow-up period.

In conclusion, we herein described a patient with sporotrichal tenosynovitis and no skin lesions. Sporotrichosis, though rare, should be considered in the differential diagnosis of RA. MSUS is a useful imaging modality for investigating the cause of joint swelling. This case also reminds us of the importance of exercising caution in the management of patients with atypical joint symptoms.

The authors state that they have no Conflict of Interest (COI).

References

- Barros MB, de Almeida Paes R, Schubach AO. *Sporothrix schenckii* and Sporotrichosis. *Clin Microbiol Rev* **24**: 633-654, 2011.
- Bayer AS, Scott VJ, Guze LB. Fungal arthritis. III. Sporotrichal arthritis. *Semin Arthritis Rheum* **9**: 66-74, 1979.
- Kauffman CA, Bustamante B, Chapman SW, Pappas PG. Clinical practice guidelines for the management of sporotrichosis: 2007 update by the Infectious Diseases Society of America. *Clin Infect Dis* **45**: 1255-1265, 2007.
- Dehaven KE, Wilde AH, O'Duffy JD. Sporotrichosis arthritis and tenosynovitis. Report of a case cured by synovectomy and amphotericin B. *J Bone Joint Surg Am* **54**: 874-877, 1972.
- Molstad B, Strom R. Multiarticular sporotrichosis. *JAMA* **240**: 556-557, 1978.
- Lesperance M, Baumgartner D, Kauffman CA. Polyarticular arthritis due to *Sporothrix schenckii*. *Mycoses* **31**: 599-603, 1988.
- Chowdhary G, Weinstein A, Klein R, Mascarenhas BR. Sporotrichal arthritis. *Ann Rheum Dis* **50**: 112-114, 1991.
- Gottlieb GS, Lesser CF, Holmes KK, Wald A. Disseminated sporotrichosis associated with treatment with immunosuppressants and tumor necrosis factor-alpha antagonists. *Clin Infect Dis* **37**: 838-840, 2003.
- Yamaguchi T, Ito S, Takano Y, et al. A Case of disseminated sporotrichosis treated with prednisolone, immunosuppressants, and tocilizumab under the diagnosis of rheumatoid arthritis. *Intern Med* **51**: 2035-2039, 2012.
- Comstock C, Wolson AH. Roentgenology of sporotrichosis. *Am J Roentgenol* **125**: 651-655, 1975.
- Kauffman CA. Sporotrichosis. *Clin Infect Dis* **29**: 231-236, 1999.
- Crout JE, Brewer NS, Tompkins RB. Sporotrichosis arthritis: clinical features in seven patients. *Ann Intern Med* **86**: 294-297, 1977.
- Backhaus M, Burmester GR, Gerber T, et al. Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis* **60**: 641-649, 2001.
- Kane D, Balint PV, Sturrock R, Grassi W. Musculoskeletal ultrasound--a state of the art review in rheumatology. Part 1: Clinical indications for musculoskeletal ultrasound in rheumatology. *Rheumatology (Oxford)* **43**: 829-838, 2004.
- Popert AJ, Scott DL, Wainwright AC, Walton KW, Williamson N, Chapman JH. Frequency of occurrence, mode of development, and significance of rice bodies in rheumatoid joints. *Ann Rheum Dis* **41**: 109-117, 1982.
- Pimm LH, Waugh W. Tuberculous tenosynovitis. *J Bone Joint Surg Br* **39**: 91-101, 1957.
- Iyengar K, Manickavasagar T, Nadkarni J, Mansour P, Loh W. Bilateral recurrent wrist flexor tenosynovitis and rice body formation in a patient with sero-negative rheumatoid arthritis: A case report and review of literature. *Int J Surg Case Rep* **2**: 208-211, 2011.
- Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. *Arthritis Rheum* **46**: 2287-2293, 2002.
- Goldenberg DL. Infectious arthritis complicating rheumatoid arthritis and other chronic rheumatic disorders. *Arthritis Rheum* **32**: 496-502, 1989.
- Bureau NJ, Chhem RK, Cardinal E. Musculoskeletal infections: US manifestations. *Radiographics* **19**: 1585-1592, 1999.
- Chau CL, Griffith JF. Musculoskeletal infections: ultrasound appearances. *Clin Radiol* **60**: 149-159, 2005.

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