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Polyarticular Arthritis Due to *Sporothrix schenckii*

Polyartikuläre Arthritis durch *Sporothrix schenkii*

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Summary: *Sporothrix schenckii* infection usually presents as cutaneous or lymphocutaneous disease. Rarely, this dimorphic fungus causes isolated osteoarticular infection. The patient described herein had polyarticular sporotrichosis with contiguous osteomyelitis presenting as carpal tunnel syndrome 5 years previously. He relapsed after 2 g of amphotericin B but responded to itraconazole, a new oral antifungal agent. However, he was left with severe limitation of motion in the affected joints due to the long interval from onset of symptoms to diagnosis.

Zusammenfassung: Die *Sporothrix schenckii*-Infektion ist gewöhnlich an der Haut oder im Bereich der Haut-Lymphknoten lokalisiert. Selten verursacht dieser dimorphe Pilz eine isolierte osteoartikuläre Infektion. Der hier vorgestellte Patient hatte eine polyartikuläre Sporotrichose mit benachbarter Osteomyelitis, was sich 5 Jahre zuvor als Karpaltunnel-Syndrom dargestellt hatte. Der Patient erlitt nach Verabreichung von insgesamt 2 g Amphotericin B einen Rückfall, sprach jedoch auf Itraconazol an. Es verblieben aber schwere Bewegungseinschränkungen der befallenen Gelenke wegen des langen Zeitraums vom Einsetzen der Symptome bis zur Diagnose.

Introduction

Sporothrix schenkii is a dimorphic fungus which commonly causes cutaneous or lymphocutaneous infection following direct inoculation through the skin (21). Extracutaneous disease is much less common and may include osseous and joint involvement, as well as lung, genitourinary, and central nervous system infection (25). Rarely, sporotrichosis presents as isolated joint infection without an obvious primary lesion elsewhere (2, 4, 12, 16). Given the rarity of articular sporotrichosis, the diagnosis is often not made until the disease is far advanced. We report a patient with indolent polyarticular sporotrichosis of five years duration, in whom progressive destruction of several joints occurred before the diagnosis was finally established.

Case Report

A 34 year old man presented to another hospital in 1981 with swelling of the right

wrist and numbness and tingling of the fingers. He underwent carpal tunnel release without relief of his symptoms. Over the next several years he had swelling and erythema in the right forearm and progressive limitation of range of motion and pain in the right elbow, necessitating retirement from construction work. In 1985 he developed pain, swelling, and erythema of the left wrist, left elbow, and left knee.

In January 1986 he presented to the Ann Arbor Veterans Administration Medical Center where he was found to have decreased range of motion in the right elbow, a small effusion in the left knee, and swelling of the left olecranon bursa. Past history was significant only for alcoholism and hypertension. Rheumatoid factor and anti-nuclear antibody tests were negative, the Westergren sedimentation rate was 20 mm/h, and he was found to be HLA B-27 positive. Aspirate of synovial fluid from the right elbow revealed 14 000 white blood cells/mm^3 with 74 % lymphocytes. Culture of the aspirate was negative for bacteria, fungi, and acid-fast bacilli. He was thought to have seronegative rheumatoid arthritis and was treated with high dose aspirin with only minimal improvement.

Over the next six months he continued to have swelling, pain, and limitation of movement in both elbows and the left knee. Examination in September 1986 showed effusions in both elbows and the left knee, marked swelling of the left olecranon bursa, and severe limitation of movement of the right elbow. Roentgenograms of the right elbow showed destruction of the joint and osteomyelitis of the proximal ulna and radius. Synovial fluid from the left elbow revealed 2800 white blood cells/mm^3, 75 % of which were lymphocytes. Biopsy of the right proximal ulna and radius was performed, and cultures from these specimens, as well as bursal fluid from the left olecranon bursa and joint fluid from the left knee, all yielded *S. schenckii*. Examination of the tissue revealed necrotic granulomatous inflammation, but no fungi were seen.

The patient was begun on oral fluconazole, 50 mg daily, but he was noncompliant with his medicines and began drinking heavily, necessitating hospital admission 2 weeks later. He was then treated with intravenous amphotericin B, receiving a total of 2 g. He continued to have slight swelling of the left olecranon bursa and pain in both elbows; however, the left knee no longer was swollen or painful.

He did well until September 1987 when he noted increasing pain in both elbows and marked limitation of movement in the left elbow. He felt fatigued but had no other complaints. Roentgenographic evaluation showed destruction of the left elbow joint (Fig. 1). An open biopsy of the left elbow and bursectomy were performed. Examination of the tissue revealed granulomatous inflammation and several budding yeasts. Culture of bone, as well as synovial fluid from the left elbow, again yielded *S. schenckii*. The patient was begun on 400 mg itraconazole orally daily and underwent further debridement of the joint. After 1 month *S. schenckii* was no longer recovered from the drainage, and after 3 months, the wound had healed completely. He was treated for a total of six months at which point he again began drinking and again became non-compliant with his drug regimen. Although the pain had decreased, he remained with limitation of movement in both elbows.

Discussion

Sporothrix schenckii is ubiquitous in nature, occurring in many different climates and ecosystems (21). The majority of cases involve patients with outdoor occupations or avocations, such as nursery workers, construction workers, farmers, miners, and gardeners (22). It has been suggested that the preponderance of cases in men (75 %–90 % of cases) may be re-

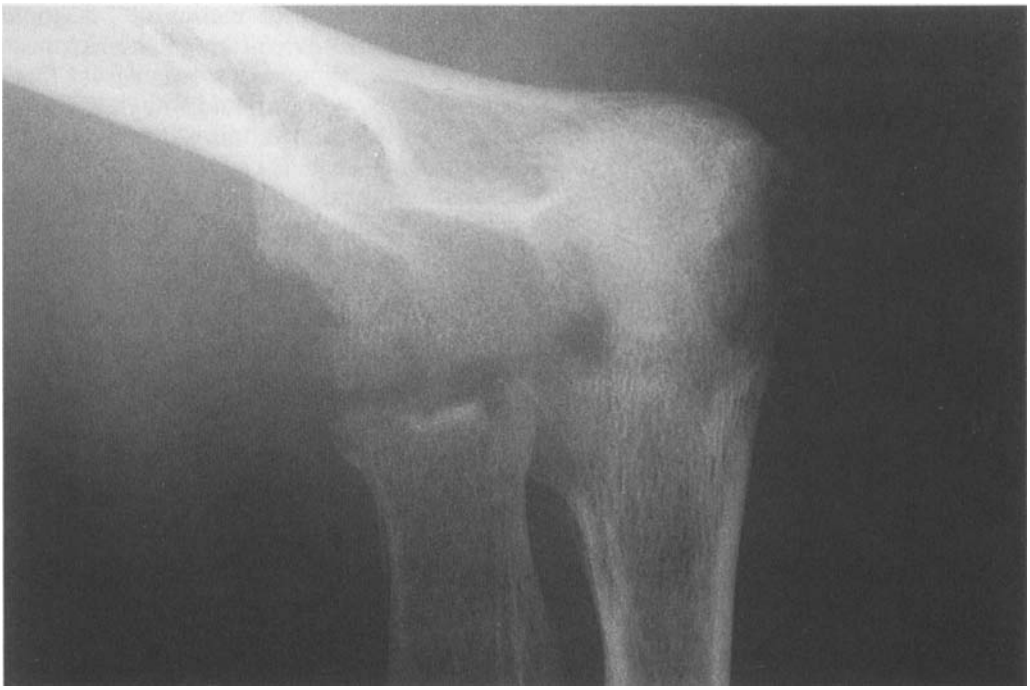

Fig. 1: Radiograph of the left elbow showing extensive demineralization and destruction of the joint due to *Sporothrix schenckii.*

lated to occupational exposure rather than any intrinsic male susceptibility.

The vast majority of cases of sporotrichosis manifest only cutaneous or lymphocutaneous involvement (21). Osseous and articular infections are uncommon and are often associated with underlying diseases, such as diabetes mellitus, hematologic malignancies, and alcoholism (2, 13, 18, 25). The association of alcoholism with serious infections with sporotrichosis is particularly strong. No explanation for this association has been found other than the increased likelihood of traumatic inoculation of the organism; however, this explanation is inadequate to explain the propensity for disseminated disease, especially in a patient without a local cutaneous lesion (2, 4, 10, 12, 16). Alcoholism appeared to play an important role in our patient's disease and also interfered with his ability to take his medications properly.

The pathogenesis of osteoarticular sporotrichosis is unclear. While some cases are clearly associated with traumatic inoculation, these are in the minority. Cutaneous disease may be associated with contiguous bone and joint involvement, but this is quite rare. It is most probable that the mode of infection is via hematogenous dissemination after initial pulmonary involvement, as occurs with other deep fungal infections.

Many cases of sporotrichal osteoarticular disease have no associated cutaneous lesions. The disease affects the knee most often, followed by involvement of the small joints of the hands and wrists, the ankles, and elbows (2). Monoarticular and polyarticular involvement occur equally frequently. Tendon sheaths and bursae

may be infected, with the popliteal and olecranon bursae involved most commonly. Isolated tenosynovitis, presenting as carpal tunnel syndrome, as noted initially in our patient, has been described (24).

Sporotrichal articular disease is manifested by joint pain, swelling, stiffness, erythema and limitation of range of motion. Low grade fever is sometimes present but there are usually no other constitutional symptoms. Frequently, as in our patient, infection is not thought of, fungi are not specifically sought, and the infection progresses slowly over years. Arthrocutaneous fistulae, parasynovial abscesses and contiguous osseous involvement may occur, usually later in the course (2).

Laboratory studies are not very helpful. The sedimentation rate may be elevated or normal, as in our patient. Leukocytosis is uncommon. In the few cases reported, synovial fluid showed from 2800 WBC/mm^3 to 60 000 WBC/mm^3 (1, 3, 7, 8, 11, 12, 13, 15, 16, 26). Neutrophils usually predominate (3, 11, 12, 15, 16) although our patient and several others had mostly lymphocytes (1, 8, 26). Generally, the synovial fluid glucose has been low when measured (3, 16). Only one case report describes *Sporothrix* seen on Gram's stain of synovial fluid (7).

Radiographic examination most commonly shows osteoporosis of the contiguous bony surfaces of affected joints, with juxtaarticular cartilage erosion and soft tissue and parasynovial swelling. Discrete punched out bony lesions may also be seen. On histopathologic examination, sporotrichal arthritis usually shows a chronic noncaseating granulomatous synovitis that is similar to that seen in rheumatoid arthritis (24). Occasionally, caseation may occur mimicking tuberculous arthritis. There are usually very few organisms noted in the synovium or bone, making it difficult to identify *S. schenckii,* even with careful serial sectioning and special stains.

The most useful method to diagnose sporotrichosis is culture of the organism from bone, synovial tissue, or joint fluid. Frequently, synovial fluid will yield *Sporothrix* on culture, in contrast to other fungal arthritides, such as coccidioidomycosis, in which synovial fluid is rarely positive.

Skin testing and serology have not been useful because of a high incidence of positive skin tests and the lack of a sensitive and specific antibody assay for *S. schenckii.* Newer serologic techniques, including a latex agglutination test and an enzyme immunoassay, appear to be useful, but will have to be studied in more patients (23).

The differential diagnosis of osteoarticular sporotrichosis includes rheumatoid arthritis, gout, sarcoidosis, pigmented villonodular synovitis, and tuberculous arthritis, as well as arthritis due to other fungi — blastomycosis, histoplasmosis and coccidioidomycosis (5, 12, 14, 16, 20). Especially with indolent polyarticular involvement, fungal infection is not considered and a diagnosis of rheumatoid arthritis is made (5, 16, 20).

The morbidity due to sporotrichal osteoarticular disease may be severe. The infection is often not diagnosed until permanent joint damage occurs, as was the case in our patient. In Bayer's review of 44 cases, the mean interval from onset of symptoms to diagnosis was 17 months (with a range from 2 months to 8 years) (2). Difficulties leading to a delay in diagnosis include low clinical suspicion in the absence of cutaneous disease, the nonspecific nature of the inflammation noted on biopsy, the paucity of organisms seen in joint fluid or histologic examination, and the failure to ask for culture for fungus.

In contrast to cutaneous and lymphocutaneous sporotrichosis, which can be cured with iodides, osseous and articular sporotrichosis are not responsive to iodides (4, 10, 17). The best results have been obtained with amphotericin B, with or without surgical debridement (17). At least 1 g of amphotericin B appears to be

necessary for cure; however, some patients, including the current case, relapsed with even greater amounts of amphotericin B (3).

Ketoconazole has been very disappointing in treating sporotrichosis (6, 9, 18). Recently, interest has centered on the use of the newer oral triazole compound, itraconazole. In vitro studies show that *S. schenckii* is inhibited by itraconazole, and preliminary evidence suggests this agent is useful in the treatment of cutaneous and lymphocutaneous sporotrichosis (19). Our patient responded well to itraconazole, showing eradication of the organism and healing of the surgical wound. However, he was left with significant loss of function of the involved joints. Given the long interval from onset of symptoms to diagnosis, this loss of function is not surprising.

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