Case Report

Mycobacterium marinum Arthritis Mimicking Rheumatoid Arthritis

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ABSTRACT. *Mycobacterium marinum* is an atypical mycobacterium found in salt and fresh water. *M. marinum* infection occurs following skin trauma in fresh or salt water and usually presents as a localized granuloma or sporotrichotic lymphangitis. It rarely affects the musculoskeletal system. We describe a patient who presented with subcutaneous nodules and an inflammatory arthritis that was thought to be rheumatoid arthritis, and was treated as such with corticosteroids, methotrexate, and anti-tumor necrosis factor-α therapy, with worsening of his arthritis. (J Rheumatol 2006;33:817–9)

Key Indexing Terms:
MYCOBACTERIUM MARINUM INFLAMMATORY ARTHRITIS NODULE

Mycobacterium marinum is an atypical acid-fast mycobacterium. Commonly, infection occurs when contaminated water is exposed to skin that has experienced open trauma. It should be considered in patients who handle fish or swim in fresh or salt water. The skin is the most common site of infection. Disseminated disease is uncommon and typically occurs in hosts who are immunocompromised. Bones and tendons are rarely involved. We describe a patient who presented with subcutaneous nodules and an inflammatory arthritis that was thought to be rheumatoid arthritis (RA), and was treated as such with corticosteroids, methotrexate, and anti-tumor necrosis factor-α (TNF-α) therapy, with worsening of his arthritis.

CASE REPORT

A 66-year-old man with an unremarkable medical history presented with a tender nodule over the fourth digit of the right hand accompanied by joint stiffness in the affected finger. He denied any fever, rash, or other symptoms. He lives on a saltwater lagoon in New Jersey. He did not recall injuring his finger but he mentioned often being cut and scraped while handling crab traps and cleaning barnacles. Family and social history were noncontributory. Over several weeks the entire finger became swollen and tender. He received 2 courses of antibiotics (cefadroxil and dicloxacillin) for a presumed insect bite, with no response. Within 2 months his entire right hand and wrist were swollen and painful. He consulted a rheumatologist and was treated with oral prednisone for presumed RA. Laboratory investigations at that time revealed a white blood cell count of 17.8/μl, a negative rheumatoid factor, and antinuclear antibodies.

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Within 4 months all his extremities were edematous. He found it difficult to walk or use his hands. "Oozing" nodules over his right hand and fingers began to appear. These were interpreted by another rheumatologist as rheumatoid nodules. A needle aspiration of a nodule over the anterior aspect of the right wrist was performed. A routine culture was negative. Oral prednisone was continued and methotrexate (MTX) was added. Despite the treatment he had worsening extremity edema and increasing fatigue and anorexia. He was referred to an orthopedist for a second right proximal interphalangeal (PIP) and right wrist joint biopsy to rule out infection. Magnetic resonance imaging investigation of the right wrist showed tenosynovitis in the wrist and marginal erosions of the metacarpophalangeal joints and right wrist. Subsequently, a tenosynovectomy of the right wrist and a synovectomy of the second PIP were performed. A pathology report stated "severe acute and chronic non-caseating granulomas consistent with rheumatoid arthritis." Synovial tissue was sent for routine culture, which was found to be negative. Cultures for acid-fast bacilli were not performed. The patient was given 5 doses of intravenous infliximab within a 6-month period. During this time more exudative nodules appeared on his extremities, face, and penis. The ulcers seemed to coalesce and become diffuse.

Five months from the start of his complaints we saw the patient. We found him to be cushingoid and in distress secondary to pain. He was using a walker for ambulation. His hands, wrists, and legs were very edematous. He had multiple erythematous nodules, some of which were bleeding and others were exudative, on the bridge of his nose, hands, elbows, and lower extremities (Figure 1). A joint deformity was seen in the right index finger distal interphalangeal joint. The rest of his examination was unremarkable. Since we suspected him to have an infection we discontinued treatment with infliximab and MTX and started tapering his prednisone dose.

Two weeks later he presented to the emergency room with fever to 103°F and increasing pain in his right wrist. Three cubic centimeters of pus were aspirated from a right wrist nodule. An acid-fast stain of the aspirate showed abundant *M. marinum* bacilli, which later grew in the blood culture and the aspirate culture. Subsequently, he was started on an antibiotic regimen of rifampin, clarythromycin, and ethambutol.

After initiation of the antibiotic regimen and tapering of the prednisone dose he had worsening fever, edema, anorexia, weight loss, and fatigue, although the nodules seemed to be improved. After 6 months of the triple antibiotic regimen he is pain-free, his fever has resolved, and the skin lesions are healing, and he is able to walk without any assistance.

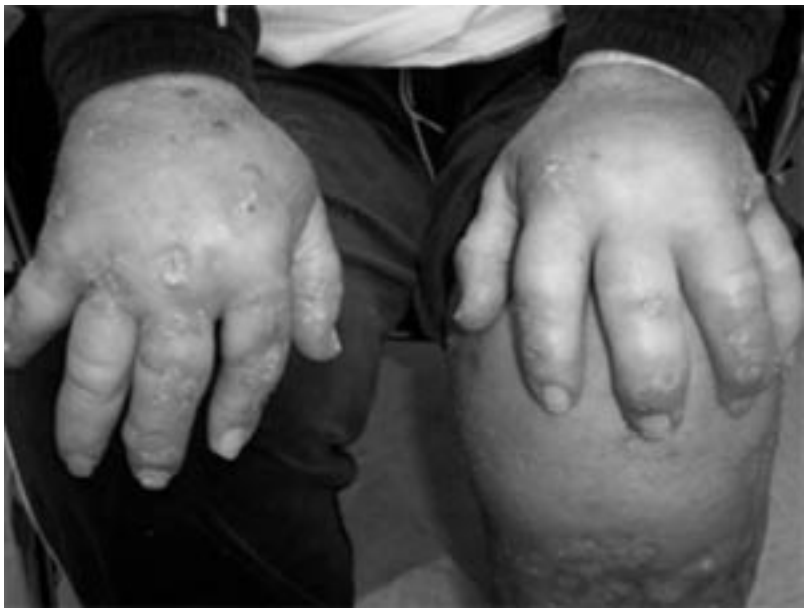

Figure 1. The patient's hands, wrists, and legs were very edematous, with multiple nodules.

DISCUSSION

M. marinum infection occurs following trauma to an extremity that is in contact with an aquarium, salt water, or marine animals. The infection usually manifests as a sporotrichoid lymphangitis 2–6 weeks after exposure. It later gives rise to a solitary red nontender papule or nodule, which may later ulcerate. These are commonly called "fish tank granulomas." They present usually on the hands or feet, since these are the areas that usually receive trauma and since the organism grows better at the lower temperature found in these areas[1]. Some lesions may self-resolve in a few months or years. Deeper infections such as tenosynovitis, septic arthritis, and osteomyelitis spread by means of lymphatics and are treated with antibiotics, debridement, and rarely amputation. Upper or lower distal extremity swelling with pitting edema due to tenosynovitis was seen in our patient, similar to that seen in patients with psoriatic arthritis[2] and in remitting seronegative synovitis with pitting edema (RS_3PE syndrome). While *M. marinum* infections usually arise from aquatic trauma in healthy hosts, delayed diagnosis and immune suppression contribute to the pathogenesis of invasive infection[3]. In a review of *M. marinum* cases immunologic impairment was a frequent component of invasive *M. marinum* infections. In that study[3], 40% of patients received a corticosteroid injection at the site of infection, 26% were taking systemic corticosteroids, as in our case, and 11% were immunocompromised secondary to acquired immune deficiency syndrome or chemotherapy treatment. Although our patient was initially a healthy host, he was prescribed not only systemic steroids, but also MTX and a TNF-α inhibitor, infliximab. Two reported cases of invasive infection due to the use of etanercept have been reported[4], but none have been reported in association with infliximab.

Delayed diagnosis is a prominent finding. The average time to diagnosis in one study was 17 months from symptom onset[3]. Acid-fast stains are positive in only 9% of tissue biopsies[5], and therefore specific cultures for *M. marinum* are strongly recommended.

Given the initial negative stains for acid-fast, arriving at the correct diagnosis in this patient was very challenging. An inflammatory arthritis such as RA was not an unreasonable diagnosis to consider. However, the asymmetrical joint involvement on initial presentation and the draining nodules made our patient's diagnosis less consistent with RA. Rheumatoid nodules do not drain spontaneously unless they are infected.

Optimal treatment of *M. marinum* infection has not been established. The infection probably resolves spontaneously in some cases, although complete resolution may take up to 2 years[6,7]. In the literature, various antibiotics have been used, including cyclines, a combination of sulfamethoxazole and trimethoprim, rifampin plus ethambutol, and, more rarely, clarithromycin, levofloxacin and amikacin[8-11]. Cure and failure have been described with all of these drugs[9,11]. The optimal duration of therapy also varied markedly in the literature reports, ranging from 6 weeks to 1 year[12]. Clarithromycin and rifampin were suggested to be the most potent[3]. Despite antibiotic treatment, surgical debridement was required in 69% of invasive infections[3].

Our patient's onset of fever and worsening of symptoms were seen after the discontinuation of infliximab and MTX and tapering of steroids. This appears to be due to an immunological reconstitution syndrome. This phenomenon has been well described in patients taking TNF-α inhibitors and patients with human immunodeficiency virus infected with other atypical mycobacteria such as *M. haemophilum*[13]. Once

the patient's immune system has recovered with the discontinuation of immunosuppressant or antiretroviral therapy, cytokines and other mediators of inflammation rise, causing worsening of fever, anorexia, and fatigue.

Inflammatory arthritis such as RA can have a presentation very similar to that seen in our patient. Delay of diagnosis is common, and invasion into deeper structures such as synovia, bursae, and bone can occur. The high frequency of delayed diagnosis in cases of invasive *M. marinum* disease emphasizes the importance of maintaining a high level of suspicion for this condition, especially in patients who have evidence of previous aquatic trauma or refractory soft tissue infections, as in our patient.

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