Mycobacterium kansasii belongs to Runyon group I and is a photochromogen [1], antigenically related to Mycobacterium tuberculosis. Thirty-two cases of cutaneous M. kansasii infections have been reported since Mayberry et al reported the first in 1965 [2]; however, only one case was found to be associated with systemic lupus erythematosus (SLE) [3]. SLE patients are immunosuppressed due to the underlying pathogenesis of their disease and the use of immunosuppressants, so they are prone to opportunistic infections. Here, we report the case of a female SLE patient with M. kansasii infection presenting with cellulitis that was treated successfully with combined antimycobacterial agents.

Case Report

This 38-year-old woman had a 26-year history of SLE. Her disease had relapsed several times and she was maintained on immunosuppressive therapy. Before this episode, she had been taking prednisolone (20 mg daily), meloxicam (7.5 mg on alternate days), hydroxychloroquine (200 mg twice a day), azathioprine (50 mg twice a day), and indapamide (2.5 mg daily).

Two months before admission, a small wound over the right pretibial area was noticed. After she went swimming at the beach on May 15, 2000, the wound was contaminated by seawater, and erythematous swelling with local heat over the right lower leg was noted the next day. She went to our outpatient clinic and oral antibiotics (cefixime, dicloxacillin, ampicillin) were given for 10 days, followed by cefuroxime for 7 days. Though the erythema gradually faded, local tenderness persisted. Because osteomyelitis could not be ruled out, she was admitted on May 31, 2000. No lymphadenopathy, fever or chills were noted.

Laboratory data showed hemoglobin 2.7 mmol/L, a white blood cell count of 12.86 x 10⁹/L, with 79% neutrophils and no band cells, and a platelet count of 228 x 10⁹/L. Antinuclear antibody was positive (1:80), with a speckled pattern. Anti-double-stranded DNA antibody was present (9.2 IU/mL), as were C3 (633 mg/L), C4 (138 mg/L),
and C-reactive protein (5.4 x 10^3 µg/L). Chest roentgenograms showed no evidence of pulmonary infection. Whole-body bone scan revealed no evidence of osteomyelitis. After replacement of oxacillin with intravenous amoxicillin-clavulanate, erythematous induration over the right leg improved, but new-onset cellulitis over the left leg was noted with erythematous swelling and local heat (Fig. 1). Antibiotic therapy was shifted to intravenous vancomycin, ceftazidime and amphotericin B, but the symptoms persisted. Pathologic examination of a biopsy specimen from the cutaneous lesion revealed perivascular mononuclear cell infiltration without granuloma formation. Gram-stain and Gomori-methenamine-silver (GMS) stain for fungus were negative. A few acid-fast bacilli were seen on Ziehl-Neelsen staining (Fig. 2); however, polymerase chain reaction for M. tuberculosis complex using Cobas Amplicor MTB test (Roche Diagnostic System, Somerville, NJ, USA) was negative. Finally, culture of the biopsied skin specimen yielded M. kansasii. Drug sensitivity testing using the modified proportional agar dilution test revealed that this isolate was susceptible to rifampin, ethambutol and streptomycin, and resistant to isoniazid. Antimycobacterial agents including isoniazid (300 mg daily) rifampin (600 mg daily), and clarithromycin (250 mg twice a day) were prescribed. Her skin lesion improved gradually and she was discharged 1 month after admission.

Flare-up of the erythematous swelling over her left lower leg was noted at the outpatient department at follow-up, and she was admitted again 4 months after the initial infection. Bone scan revealed no evidence of osteomyelitis. The antimycobacterial regimen was adjusted to ethambutol (1,200 g daily), clarithromycin (500 mg twice a day), rifampin (600 mg daily), and isoniazid (300 mg daily) with satisfactory clinical improvement. She continued therapy for 1 year with complete clearing of the cutaneous lesion.

Discussion

M. kansasii was first described in 1953 by Buhler and Polack [4], who isolated a slow-growing mycobacterium that produced yellow pigment on exposure to light, and, so, called the organism a Runyon group I photochromogen [1, 4]. The most common presentation of M. kansasii infection is a cavitary pulmonary lesion resembling tuberculosis, typically in older men with pulmonary diseases such as chronic bronchitis, emphysema, and chronic obstructive pulmonary disease [5]. Other sites of infection include the bone, joints, spleen, liver, lymph nodes, peritoneum and skin [6, 7]. Cutaneous infection by M. kansasii is rare. In a large series of patients with M. kansasii infection, between 2.5 and 4.5% of isolates caused cutaneous infection [7].

Many reports suggest the presence of M. kansasii in water samples, such as drinking water and swimming pools [8]. M. kansasii is capable of surviving in water for 12 months, but incapable of long-term survival in soil [9]. Thus, water is a possible source of infection. Infections due to M. kansasii are sporadic with no evidence of person-to-person spread [7]. Our patient had recent exposure to seawater that might have been contaminated by the pathogen.

In a review of the literature, Czelusta and Moore found that cutaneous M. kansasii infections had been reported in both immunosuppressed and immunocompetent patients [3]. The mean age of these patients was 43 years; most patients were male (66%) and had evidence of altered immunity (75%, 24/33 patients), either from an iatrogenic condition due to the use of corticosteroids or other immunosuppressants, or from some underlying disease or medical condition. Underlying conditions included HIV infection, hematologic malignancy leiomyosarcoma, autoimmune disease, alcoholism and renal transplantation [3, 10]. Four cases were
associated with autoimmune disease including one dermatomyositis, one vasculitis and two SLE patients (including our patient) [3]. Our patient had a 26-year history of SLE. Because the disease activity fluctuated, she had been repeatedly treated with immunosuppressive therapy prior to this episode.

Cutaneous lesions associated with M. kansasii infections vary greatly, from verrucous papules, crusted ulceration, necrotic papulopustules, spirotrichoid eruption and cellulitis to granuloma plaques, and are nonspecific in nature [11]. Immune competent patients usually present with raised lesions or ulcers, whereas immunodeficient patients, who represent 75% of cases, may have a more atypical presentation, including cellulitis and seromas [7]. Histopathologic characteristics depend on the duration of the lesion and range from subacute lymphocytic vasculitis to granulomatous vasculitis with focal infarction and coagulative necrosis [12]. Because of its nonspecific clinical and histologic features, it is difficult to diagnose cutaneous infection by M. kansasii. Acid-fast organisms and granulomas were not found in all cases. Culture of biopsied tissue is the most reliable diagnostic method. M. kansasii grows best on Löwenstein-Jensen culture medium at 37°C for at least 2 weeks. It characteristically produces yellow pigment within 24 hours of exposure to bright light [9]. Isolates produce both catalase and nitrate reductase, and hydrolyze Tween 80. Niacin reduction is negative [13]. These characteristics form the basis for the identification of M. kansasii. Both positive acid-fast stain and tissue culture together with the clinical manifestations provided strong evidence for the diagnosis in this case. The patient had no evidence of disseminated infection such as pulmonary disease or bone involvement.

Treatment of mycobacterial infection depends on the results of drug susceptibility testing of the isolated organism. Effective therapy includes monotherapy with erythromycin, clarithromycin, monocyte, doxycycline, ciprofloxacin or ofloxacin, and combination therapy with more traditional antituberculous agents [7]. Erythromycin, a macrolide antibiotic with excellent tissue-penetrating characteristics, shows marked activity against M. kansasii. The macrolides and quinolones seem promising inasmuch as they are simpler and less toxic, and may be used for immunocompetent patients with uncomplicated infections [14]. Treatment with rifampin combined with two or more agents such as ethambutol, isoniazid, streptomycin and macrolides is more suitable for immunocompromised patients because most immunodeficient patients respond poorly to monotherapy. Some isolates of M. kansasii are resistant to low concentrations of streptomycin or isoniazid [9]. In addition, up to 4% of M. kansasii isolates are rifampin-resistant [15]. Many reported cases have been successfully treated with combined antituberculous therapy, although the organism may be resistant to one or more of these agents in vitro. Wolinsky suggested treatment for 12 to 24 months [13].

Immunosuppression or immunodeficiency, abnormal skin or skin injury, and exposure to potentially contaminated water are commonly associated with M. kansasii infection. Because of nonspecific clinical, histologic and distribution patterns, infection with nontuberculous mycobacteria should always be kept in mind when evaluating unusual skin infections, especially in immunocompromised patients. Acid-fast staining and culture for acid-fast organisms should be performed. To avoid drug resistance, a combination of agents is preferred in immunocompromised patients. Prognosis is also strongly associated with the underlying condition.

References