Tuberculous Cellulitis in a Patient with Chronic Kidney Disease and Polymyalgia Rheumatica

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Abstract

An 89-year-old man with advanced renal failure, polymyalgia rheumatica and a past history of tuberculosis was admitted with a high fever. Erythema and swelling appeared in the femoral region. Since the cellulitis failed to respond to antibiotic therapy, a skin biopsy was performed. The specimen showed the presence of epithelioid cell granuloma and panniculitis. Acid-fast organisms were found on Ziehl-Neelsen staining. A polymerase chain reaction test of tuberculosis was positive. Although a diagnosis of miliary tuberculosis was suggested, examinations of a bone marrow biopsy and fundoscopy revealed normal results. The patient’s symptoms improved following treatment with isoniazid, rifampicin and ethambutol. This case represents an unusual presentation of tuberculous cellulitis in an immunocompromised patient.

Key words: cutaneous tuberculosis, cellulitis, chronic kidney disease, polymyalgia rheumatica


Introduction

Tuberculosis is a common life-threatening disease worldwide and two million people die from the disease annually (1). Although the number of patients with tuberculosis has gradually decreased in Japan, approximately 25,000 patients with tuberculosis are newly registered each year. Among these patients, 20% exhibit onset of extrapulmonary tuberculosis (2). Extrapulmonary tuberculosis often affects the lymph nodes, pleura, urinary tract, bone and joints and occurs primarily in elderly people, patients with chronic diseases or those taking immunosuppressive agents. Although Mycobacterium tuberculosis may reactivate at any site, the occurrence of cutaneous tuberculosis is rare (3, 4).

Cutaneous tuberculosis is divided into two types: true cutaneous tuberculosis and tuberculid. True cutaneous tuberculosis occurs via exogenous direct infection in the skin, proliferation in the lymph nodes or hematogenous dissemination from the lungs (4). Tuberculosis cutis verrucosa, scrofuloderma and lupus vulgaris are included in this type. Tuberculid involves an allergic reaction in the skin against M. tuberculosis. Although acid-fast bacilli are not usually found in these skin lesions, antituberculosis agents are effective against the disease. Erythema induratum, papulonecrotic tuberculid and lichen scrofulosorum are included in this type. Cellulitis caused by tuberculosis has rarely been reported (5, 6); however, many of cases have been shown to occur as skin manifestations of miliary tuberculosis (7-9).

We herein report the case of a patient with chronic kidney disease and polymyalgia rheumatica complicated by tuberculous cellulitis.

Case Report

An 89-year-old man was treated in our hospital for chronic kidney disease (serum creatinine level 3.0-3.5 mg/dL, stage 4) caused by hypertensive nephrosclerosis and polymyalgia rheumatica (PMR). He had a past history of typhoid fever occurring at 17 years of age and pulmonary tuberculosis and caries of the left rib occurring at 19 years of age that were not systemically treated. He had undergone distal pancreatectomy and splenectomy for pancreatic cancer at 76 years of age and endoscopic submucosal dissection for early gastric cancer at 88 years of age. He had been treated with antihypertensive agents and 5 mg/day of prednisolone.
was clear, his body temperature was 38.0°C, his blood pressure was 140/70 mmHg and his pulse rate was 99/min. He had no symptoms of cough or sputum. The physical findings of the chest and abdomen were normal. The white blood cell (WBC) count was 7,600/μL, with 87.9% neutrophils. Normocytic anemia with a hemoglobin level of 8.3 g/dL was observed. The C-reactive protein level was 6.1 mg/dL. The blood urea nitrogen level was 61.9 mg/dL, the creatinine level was 4.04 mg/dL, the total protein level was 5.3 g/dL and the albumin level was 2.7 g/dL. The urinary WBC count was 0-4/high-power field. A purified protein derivative (PPD) test was negative (6×7 mm). A QuantiFERON test was negative (5×7 mm). A chest X-ray was performed on day 17 (Fig. 5). Although the patient's symptoms improved. Approximately six months later, the skin lesion relapsed in spite of the patient's good systemic condition. The administration of antituberculosis agents was continued; however, the patient died due to a worsening renal function. Since the cellulitis did not improve following treatment with meropenem, magnetic resonance imaging (MRI) of the patient's legs was completed to rule out fasciitis. Inflammation was limited to the subcutaneous adipose tissue of the left femoral region (Fig. 3). A skin biopsy was performed on day 18. The pathological study of the specimen revealed epithelioid cell granuloma and panniculitis (Fig. 4A). Acid-fast organisms were found to be present in the same lesions on Ziehl-Neelsen staining (Fig. 4B). A polymerase chain reaction test for the *M. tuberculosis* complex in the specimen was also positive. The *M. tuberculosis* detected on culture showed susceptibility to all antituberculosis agents. The number of small nodules in the lungs was increased on chest CT performed on day 17 (Fig. 5). Although a diagnosis of miliary tuberculosis was suspected, neither granuloma nor mycobacterium were found on a bone marrow biopsy or fundoscopy. After the initiation of antituberculosis agents, including 200 mg/day of isoniazid, 300 mg/day of rifampicin and 500 mg/alternate day of ethambutol, the patient's symptoms improved. Approximately six months later, the skin lesion relapsed in spite of the patient’s good systemic condition. The administration of antituberculosis agents was continued; however, the patient died due to a worsening renal function after nine months of therapy.

**Discussion**

The incidence of cutaneous tuberculosis has been reported to range from 0.15% to 0.26% (3). Although approximately 100 patients with cutaneous tuberculosis are registered annually in Japan, many of them are diagnosed with tuberculid in which *M. tuberculosis* is not found (2). The infectious route of true cutaneous tuberculosis consists of exogenous direct infection, proliferation via contiguous lymph nodes or hematogenous dissemination (4). In addition to other extrapulmonary manifestation of tuberculosis, cutaneous tuberculosis may appear in elderly people, patients with chronic diseases and those taking immunosuppressive agents. Our patient was an elderly immunocompromised patient with advanced renal failure and a past history of splenectomy who was taking prednisolone. Hemodialysis patients are six to 25
times more likely to develop tuberculosis than the general population, and the rate of extrapulmonary tuberculosis in these patients is reported to be high (1, 10). Since impaired cellular immunity occurs in patients with long-term renal failure, advanced renal failure that is not treated with dialysis may be also risk factor for extrapulmonary tuberculosis.

In cases of cellulitis resistant to antibiotic agents, a diagnosis of fasciitis must be excluded. In patients with fasciitis, debridement is often required in addition to treatment with antibiotic therapy. In this case, MRI examinations were performed; however, the inflammation was limited to the subcutaneous adipose tissue. Because tuberculosis, as well as nontuberculous mycobacterial infection, metastasis of malignancy, T-cell lymphoma and Weber-Christian disease, were considered in the differential diagnosis, a skin biopsy was ultimately performed. The specimen revealed epithelioid cell granuloma and panniculitis with acid-fast bacilli, which is typical of tuberculosis. We diagnosed the skin lesion as tuberculous cellulitis, not tuberculid, because tuberculid bacilli were found in the lesion, a phenomenon that does not usually occur in tuberculid. Cellulitis caused by tuberculosis has rarely been reported, and many of the reported cases were showed to be skin lesions in patients with miliary tuberculosis (7-9). The infectious route in our patient was thought to be hematogenous dissemination from the lungs based on the clinical findings and the patient’s past history. The number of small nodules in the lungs on chest CT performed on day 17 was increased compared with that observed on day 4. Miliary tuberculosis usually involves diffuse minute nodules in the bilateral lungs. Although the findings in our case were not typical for miliary tuberculosis, examinations of a bone marrow biopsy and fundoscopy were performed. Neither granulomas nor acid-fast organisms were found. To our knowledge, only a few cases with tuberculous cellulitis without other extrapulmonary tuberculosis manifestations have been reported (5, 6). A common feature of these cases is treatment with immunosuppressive agents. One case included steroid therapy for arthralgia (5) and another case involved treatment with steroids and cyclophosphamide for systemic lupus erythematosus (6). The long-term administration of prednisolone for PMR was used in this case. On the other hand, there are some reports concerning the occurrence of cutaneous miliary tuberculosis in subjects with HIV infection (11, 12). The degree of immunosuppression might be related to the clinical features of extrapulmonary tuberculosis. Polymyalgia rheumatica is a syndrome characterized by a low grade fever, fatigue and pain or stiffness primarily in the proximal portions of the extremities. Prednisolone is very effective for treating PMR. However, these symptoms may be also found in patients with tuberculosis. Diagnosing PMR and treating patients with a past history of tuberculosis with steroids must be completed carefully.

Because our patient was elderly and had advanced renal failure, reduced doses of three antituberculosis agents, isoniazid, rifampicin and ethambutol, were administered. With this treatment, the patient’s fever rapidly resolved. When other lesions suggestive of tuberculosis are not found, diagnosing cutaneous tuberculosis is considered difficult even for dermatologists. In cases of refractory cellulitis resistant to antibiotics, a diagnosis of tuberculosis must be ruled out, especially in elderly patients with chronic diseases or those receiving immunosuppressive therapy.

The authors state that they have no Conflict of Interest (COI).
Figure 5. Computed tomography of the chest performed on days 4 and 17. Growing minute nodules were seen (circles).

References


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