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Disseminated *Mycobacterium kansasii* Infection Associated with Skin Lesions: A Case Report and Comprehensive Review of the Literature

Mycobacteruim kansasii occasionally causes disseminated infection with poor outcome in immunocompromised patients. We report the first case of disseminated *M. kansasii* infection associated with multiple skin lesions in a 48-yr-old male with myelodysplastic syndrome. The patient continuously had taken glucocorticoid during 21 months and had multiple skin lesions developed before 9 months without complete resolution until admission. Skin and mediastinoscopic paratracheal lymph node (LN) biopsies showed necrotizing granuloma with many acid-fast bacilli. *M. kansasii* was cultured from skin, sputum, and paratracheal LNs. The patient had been treated successfully with isoniazid, rifampin, ethmabutol, and clarithromycin, but died due to small bowel obstruction. Our case emphasizes that chronic skin lesions can lead to severe, disseminated *M. kansasii* infection in an immunocompromised patient. All available cases of disseminated *M. kansasii* infection in non HIV-infected patients reported since 1953 are comprehensively reviewed.

Key Words : Mycobacterium kansasii; *Myelodysplastic Syndromes; Skin; Disseminated Infection*

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INTRODUCTION

Mycobacterium kansasii is a slow-growing acid-fast bacillius (AFB) and belongs to the group of environmental mycobacteria, also known as atypical mycobacteria or nontuberculosis mycobacteria (NTM). Local water supplies are considered as the major reservoir for the *M. kansasii*, and evidence of person-to-person transmission has not been reported. The most common presentation of *M. kansasii* infection is a chronic bronchopulmonary disease, which manifests typically in adult patients with chronic obstructive pulmonary disease or cystic fibrosis. In addition, *M. kansasii* can cause skeletal infections, skin and soft tissue infection, cervical or other lymphadenitis, and disseminated infection (1).

Disseminated infection by *M. kansasii* occurs almost exclusively in immunocompromised patients, such as solid organ transplant recipients, HIV-infected individuals, patients with hematologic malignancy, or patients receiving long-term steroid regimens (2). In the case of disseminated *M. kansasii* infection, involvement of multiple organs including the lungs, liver, spleen, bone marrow, lymph node (LN), bowels, central nervous system, pericardium, pleura or kidneys, has been reported (3) but disseminated *M. kansasii* infection associated with skin involvement is not frequent (4).

Recently, we encountered a rare case of disseminated *M. kansasii* infection involving multiple skin areas together with lung and multiple LNs. To our knowledge, this is the first case of disseminated *M. kansasii* infection that has involved the skin in Korea. Therefore, we report this unusual case with a comprehensive review of previously reported disseminated *M. kansasii* infections in non HIV-infected patients.

CASE REPORT

A 48-yr-old man was admitted with a 1-month history of fever and a 2-week history of dyspnea on exertion at Severance Hospital in Seoul, Korea. He had a history of myelodysplastic syndrome (MDS) diagnosed 21 months ago prior to admission and had been treated with oral glucocorticoid (prednisolone, 10 mg daily) with regular follow-up. A year after MDS was diagnosed, multiple erythematous tender nodules developed on both lower legs, and a skin biopsy of the calf revealed Sweet's syndrome. He continuously had these skin lesions without complete resolution until admission. On admission, several papulonodular skin lesions on his arms, chest, back, abdomen, buttocks, and legs were noted (Fig. 1). Multiple LNs were palpated on the medial side of the right thigh

and left cervical area. Initial laboratory tests showed leukopenia with a white blood cell count of 1,950/μL; severe anemia with a Hb level of 6.8 g/dL; mild thrombocytopenia with a platelet count of 113,000/μL; an elevated ESR (73 mm/hr) and C-reactive protein level (10.8 mg/dL). Chest computer tomography (CT) confirmed multiple LNs enlargement at the mediastium, paratracheal area, subcarina and right perihilar bronchovascular interstitial and interlobular septal thickening. Initially, sputum AFB smears revealed a negative finding. Meanwhile, both excisional LN biopsies, which were performed at the palpable LNs of the thigh and neck, and skin and mediastinoscopic paratracheal LN biopsies revealed necrotizing granuloma with many AFB. Also, an AFB smear of a pus-like discharge obtained from the paratracheal LN revealed a positive finding.

With a presumptive diagnosis of disseminated tuberculosis, anti-tuberculosis therapy was started with HERZ (isoniazid [INH], rifampin [RFP], ethambutol [EMB], and pyrazinamide [PZA]) regimens on hospital day (HD) 16. However, as the skin lesions progressed rapidly and high spiking fever persisted despite HERZ treatment, we assumed he had a rapidly growing NTM such as *M. Abscessus* or *M. fortuitum*, and started him on amikacin, clarithromycin, levofloxacin and cefoxitin instead of EMB and PZA. However, improvement of the skin lesions was not evident.

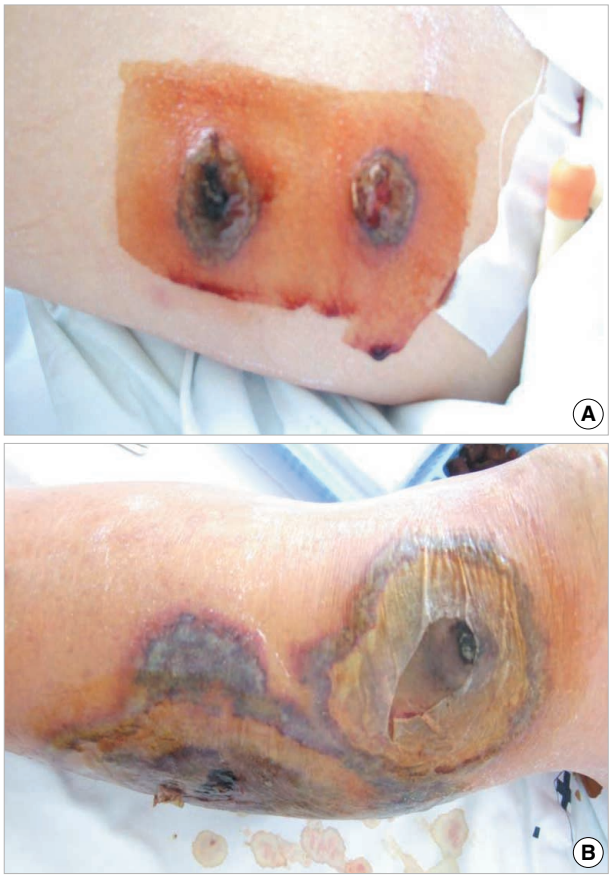

Fig. 1. Papulonodular skin lesions on lower legs.

Three weeks after anti-tuberculosis therapy was started, a mycobacterium culture of skin and pus-like discharge obtained from the paratracheal LN revealed NTM, and repeated sputum mycobacterium culture also revealed NTM. At HD 43, all NTMs cultured in sputum, paratracheal LNs, and skin were identified as *M. kansasii* by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) of the polymorphic region of the *rpoB* gene. In vitro drug

Table 1. Clinical characteristics of disseminated *M. kansasii* infection in non-HIV infected patients

Age (N=58), mean±SD	45.0±22.3 yr
Sex (N=59), M:F	47 (79.7%):12 (20.3%)
Underlying diseases/associated conditions (N=63)	
No (previously healthy)	15 patients (23.8%)
Yes (multiple, N=83)	48 patients (76.2%)
Hematologic malignancy	30 (36.1%)
Steroid use	19 (22.9%)
Immunosuppressive agents use	8 (9.6%)
Post-splenectomy	7 (8.4%)
Diabetes	4 (4.8%)
Primary immunodeficiency	3 (3.6%)
Solid cancer	3 (3.6%)
Autoimmiune disease	2 (2.4%)
Solid organ transplantation	2 (2.4%)
Pregnancy	2 (2.4%)
Hemodialysis	1 (1.2%)
Neutropenia	1 (1.2%)
Renal failure	1 (1.2%)
Infection site (multiple, N=208)	
Lung	37 (17.8%)
Lymph nodes	32 (15.4 %)
Spleen	27 (13.0%)
Liver	25 (12.0%)
Bone marrow	20 (9.6%)
Skin	12 (5.8%)
Bone and joint	9 (4.3%)
G-I tract	8 (3.8%)
Urinary tract	7 (3.4%)
Cerebrospinal fluid	6 (2.9%)
Male reproductive organ	6 (2.9%)
Pleural fluid	5 (2.4%)
Peritoneal fluid	4 (1.9%)
Abscess	2 (1.0%)
Blood, cellulitis, blood vessels, nose, tongue, pericardium, adrenal gland, thymus	1 (Respectively, 0.5%)
Reported year (N=63)	
1950-1959	4 (6.3%)
1960-1969	9 (14.3%)
1970-1979	17 (27.0%)
1980-1989	15 (23.8%)
1990-1999	11 (17.5%)
2000-2007	7 (11.1%)
Outcome (N=63)	
Recovered	19 (30.2%)
Not recovered	38 (60.3%)
Unknown	6 (9.5%)

susceptibility testing of *M. kansasii* showed that the isolate was susceptible to RFP, EMB, PZA, streptomycin, moxifloxacin, and cycloserine but resistant to INH and para-aminosalicylic acid. At HD 43, we altered the anti-mycobacterial treatment regimens to INH, RFP, EMB, and clarithromycin.

Gradual improvement of the general condition and symptoms with regression of skin lesions was noted. Sputum AFB, which was examined at HD 51, was converted into negative and mycobacterial culture of sputum did not identify any mycobacteria. However, during treatment for *M. kansasii*, the patient developed small bowel obstruction and ischemic colitis. Although he underwent a small bowel resection and intensive conservative management, the patient died on HD 121.

DISCUSSION

M. kansasii is the second most frequently recognized NTM pathogen and second most frequent cause of disseminated NTM disease, after *M. avium* complex (MAC), in the Unites States and Japan (2, 5, 6). Furthermore, in southeast England, *M. kansasii* is more common than MAC (7). In South Korea, *M. kansasii* is the fourth most commonly isolated NTM pathogen, after MAC, *M. abscessus-chelonae* complex, and *M. fortuitum*, but its incidence has increased, especially in highly industrialized areas (8).

In agreement with previously established risk factors (2), our patient's risk factors for disseminated *M. kansasii* infection included a history of hematological malignancy and long-term steroid use. The patient had a disseminated *M.*

Table 2. Clinical characteristics of 18 patients with disseminated *M. kansasii* infection reported since 1990 yr

Patient No.	Sex/ age	Underlying disease/ associated conditions	Infection or isolated sites/ clinical disease	*In vitro* drug susceptibility test	Anti-NTM Tx regimens	Outcome	Reported year [Reference]
1	F/30	Renal transplantation, post-splenectomy, steroid use, cyclophosphamide	Joint	NA	NA*	Unknown	1990[9]
2	M/47	Metastatic clear cell carcinoma, silicosis, DM, steroid use	Lung, LN	NA	NA*	Unknown	1990[9]
3	M/48	Lymphoma, neutropenia	BM	NA	NA*	Died	1990[9]
4	M/54	Hairy cell leukemia, cyclophosphamide, vincristine, steroid use	Lung, pleura, LN	NA	NA*	Recovered	1990[9]
5	M/40	AML, cytarabine, thioguanine	BM	NA	NA*	Unknown	1990[9]
6	M/64	CML, DM, steroid	Lung, skin, bone	NA	NA*	Died	1990[9]
7	F/72	Breast cancer	Spleen	NA	NA*	Unknown	1990[9]
8	M/65	Vasculitis, renal failure, steroid use	BM, spleen, skin	NA	NA*	Died	1990[9]
9	F/25	Pregnancy	BM, urine	NA	INH, RFP, STM	Recovered	1991[15]
10	M/63	Hemodialysis	Multiple lumbar, pre-aortic, mediastinal LNs, liver granuloma, gastric juice, skin	NA	INH, RFP, EMB	Died	1993[16]
11	M/38	MDS	Mediastinal LN, gastric lavage, stool, BM granuloma, liver	Susceptible to INH, RFP, EMB, ethionamide, cycloserine	INH, RFP, EMB	Recovered	1995[5]
12	F/79	None	Disseminated skin lesion, mediastinal LN	NA	INH, RFP, EMB	Recovered	2001[18]
13	F/64	CML, PAP	Lung/liver granuloma	NA	NA*	Recovered	2003[19]
14	F/80	None	Blood	NA	NA*	Died	2006[20]
15	M/47	Malignancy of unknown origin	BM	NA	No treatment	Died	2006[20]
16	M/71	None	Pleural effusion, abscess	NA	No treatment	Died	2006[20]
17	F/26	None	Vertebral osteomyelitis, sacroiliitis, psoas abscess, BM/liver graunloma, spleen abscess	Susceptible to INH, RFP, EMB, STM, KM, Ethionamide	INH, RFP, EMB	Recovered	2006[21]
18	M/48	MDS, Long-term steroid use	Skin, mediastinal LNs, lung	All susceptible except INH, PAS	INH, RFP, EMB, Clarithromycin	Died	2007[Present case]

*NA, The anti-mycobacterial treatment was performed, but their regimens were not available.
NA, not available; BM, bone marrow; LN, lymph node; PAP, pulmonary alveolar proteinosis; INH, isoniazid; RFP, rifampin; EMB, ethambutol; STM, streptomycin; KM, kanamycin; PAS, para-aminosalicylic acid.

kansasii infection with multiple skin lesions, as well as lung and multiple LNs. In addition, because an abdominal CT scan revealed a splenic abscess, we speculated that splenic infection with *M. kansasii* was also probable. An autopsy, however, was not performed.

We comprehensively reviewed the literature written in English and available in abstract or full text form that reported disseminated *M. kansasii* infection in non HIV-infected patients (3, 4, 6, 9-21). Among a total of 67 cases including the present case, 4 cases were excluded from analysis because of insufficient information. Table 1 shows the characteristics of the 63 remaining cases of disseminated *M. kansasii* infection in non-HIV infected patients. The mean age was 45 yr old and 79.7% of all patients were male. The most common underlying disease was a hematological malignancy. However, the frequency of previously healthy persons with no underlying diseases was relatively high as 23.8%. Also, the table shows that *M. kansasii* caused infection in diverse visceral organs; commonly involved sites included the lungs, LNs, spleen, liver, and bone marrow. The prognosis of disseminated *M. kansasii* infection was poor as the percentage of patients that died was 60.3%. As previously known that the presence of underlying disease and/or immunosuppression seemed to be the best predictor of outcome of disseminated *M. kansasii* infection (4), the mortality of patients with underlying disease was higher than those without underlying disease (75% and 53.3% respectively). We summarized the clinical characteristics of 18 patients with disseminated *M. kansasii* infection in non HIV-infected patients reported since 1990 yr at Table 2.

The *M. kansasii* isolates cultured from our patient were resistant to an INH *in vitro* susceptibility test. The concentrations of INH used in susceptibility testing are those chosen for their usefulness with *M. tuberculosis*. Some *M. kansasii* isolates may be reported resistant to INH at 0.2 or 1.0 μg/mL. However, these isolates of *M. kansasii* are susceptible to slightly higher INH concentrations, and are still susceptible to achievable blood levels. Thus, INH should be used regardless of the in vitro susceptibility test results (8). We also used anti-mycobacterial regimens containing INH and noted a gradual improvement of skin lesions and negative sputum mycobacterial culture after this treatment.

Cutaneous NTM disease is most often caused by rapidly growing mycobacteria such as *M. abscessus-chelonae* complex and *M. fortuitum* rather than *M. kansasii*. It is known that *M. kansasii* can rarely cause a primary cutaneous infection, which usually results from penetrating injuries or disseminated disease (22). The patient described in this case had skin lesions for a long time before disseminated infection at the multiple LNs and lung developed. We surmised that minor local trauma by initial skin lesions of Sweet's syndrome resulted in the inoculation of *M. kansasii* and caused disseminated infection in the immunocompromised condition brought about by long-term steroid use. The natural course of untreated, non-disseminated skin infection by *M. kansasii* is one of non-serious, indolent progression. However, as seen in this case, skin infection associated with systemic dissemination in a patient with underlying disease in immunosuppressive conditions is associated with poor outcome (22).

In conclusion, our case emphasizes that chronic skin lesions can lead to severe, disseminated *M. kansasii* infection in an immunocompromised patient. Particular attention to the aggressive diagnostic work-up, such as biopsy, should be given in immunocompromised patients with chronic skin lesions to diagnose infection by an unusual pathogen, such as NTM, before the infection disseminates.

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