INTRODUCTION

*Mycobacterium kansasii* is a slow-growing, acid-fast bacillus (AFB) and belongs to the group of environmental mycobacteria, also known as atypical mycobacteria or nontuberculous mycobacteria (NTM). Local water supplies are considered as the major reservoir for *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/mL; 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.

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%) |
| Autoimmune 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%) |

Fig. 1. Papulonodular skin lesions on lower legs.
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. kansasii* infection.

### 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, stem 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, cytadine, thioquain | 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/83    | Hemodialysis | Multiple lumbar, pre-aortic, mediastinal LN, 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 granuloma, spleen abscess | Susceptible to INH, RFP, EMB, ST, KM, Ethionamide | INH, RFP, EMB | Recovered | 2006[21] |
| 18         | M/48    | MDS, Long-term steroid use | Skin, mediastinal LN, 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.

REFERENCES

1. Brown-Elliott BA, Wallace RJ. Infections Caused by Nontuberculosis Mycobacteria. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Disease. 6th ed. Philadelphia: Elsevier 2004: 2009-14.
2. Wallace RJ Jr, Cook JL, Glassroth J, Olivier KN. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. This official statement of the American Thoracic Society was approved by the Board of Directors, March 1997. Medical Section of the American Lung Association. Am J Respir Crit Care Med 1997; 156: S1-S25.
3. McGeady SJ, Murphey SA. Disseminated Mycobacterium kansasii infection. Clin Immunol Immunopathol 1981; 20: 87-98.
4. Breathnach A, Levell N, Munro C, Natarajan S, Pedler S. Cutaneous Mycobacterium kansasii infection: case report and review. Clin Infect Dis 1995; 20: 812-7.
5. Tsukamura M, Kita N, Shimoide H, Arakawa H, Kuze A. Studies on the epidemiology of nontuberculous mycobacteriosis in Japan. Am Rev Respir Dis 1988; 137: 1280-4.
6. Lillo M, Oreno S, Cernoch P, Harris RL. Pulmonary and disseminated infection due to Mycobacterium kansasii: a decade of experience. Rev Infect Dis 1990; 12: 760-7.
7. Yates MD, Pozniak A, Utley AH, Clarke R, Grange JM. Isolation of environmental mycobacteria from clinical specimens in south-east England: 1973-1993. Int J Tuberc Lung Dis 1997; 1: 75-80.
8. Yim JJ, Park YK, Lew WI, Bai GH, Han SK, Shim YS. Mycobacterium kansasii pulmonary diseases in Korea. J Korean Med Sci 2005; 20: 957-60.
9. Komeno T, Itoh T, Ohtani K, Kamoshita M, Hasegawa Y, Hori M, Kobayashi T, Nagasawa T, Abe T. Disseminated nontuberculous mycobacteriosis caused by mycobacterium kansasii in a patient with myelodysplastic syndrome. Intern Med 1996; 35: 323-6.
10. Hepper NG, Karlson AG, Leary FJ, Soule EH. Genitourinary infection due to Mycobacterium kansasii. Mayo Clin Proc 1971; 46: 837-90.
11. Stewart DJ, Bodey GP. Infections in hairy cell leukemia (leukemic reticuloendotheliosis). Cancer 1981; 47: 801-5.
12. Mead GM, Dance DA, Smith AG. Lymphadenopathy complicating hairy cell leukemia. A case of disseminated Mycobacterium kansasii infection. Acta Haematol 1983; 70: 335-6.
13. Bennett C, Vardiman J, Golomb H. Disseminated atypical mycobacterial infection in patients with hairy cell leukemia. Am J Med 1986; 80: 891-6.

14. Martin-Scapa C, Gomez-Criado C, Ortega-Nunez A, Bouza E. Disseminated infection caused by Mycobacterium kansasii presenting as fever of unknown origin. Eur J Clin Microbiol 1987; 6: 501-2.

15. Ahmed MA. Promyelocytic leukaemoid reaction: an atypical presentation of mycobacterial infection. Acta Haematol 1991; 85: 143-5.

16. Delclaux C, Laederich J, Adotti F, Kleinknecht D. Fatal disseminated Mycobacterium kansasii infection in a hemodialysis patient. Nephron 1993; 64: 155-6.

17. Flor A, Capdevila JA, Martin N, Gavalda J, Pahissa A. Nontuberculous mycobacterial meningitis: report of two cases and review. Clin Infect Dis 1996; 23: 1266-73.

18. Kotb R, Dhole R, Garcia-Ricart F, Permal S, Carlotti A, Arfi C, Christoforov B. Cutaneous and mediastinal lymphadenitis due to Mycobacterium kansasii. J Infect 2001; 42: 277-8.

19. Goldschmidt N, Nusair S, Gural A, Amir G, Izhur U, Laxer U. Disseminated Mycobacterium kansasii infection with pulmonary alveolar proteinosis in a patient with chronic myelogenous leukemia. Am J Hematol 2003; 74: 221-3.

20. Lai CC, Lee LN, Ding LW, Yu CJ, Hsueh PR, Yang PC. Emergence of disseminated infections due to nontuberculous mycobacteria in non-HIV-infected patients, including immunocompetent and immunocompromised patients in a university hospital in Taiwan. J Infect 2006; 53: 77-84.

21. Tsai CW, Wang JT, Tsai CC, Yeh KH. Disseminated Mycobacterium kansasii infection in an HIV-negative patient presenting with mimicking multiple bone metastases. Diagn Microbiol Infect Dis 2006; 54: 211-6.

22. Razavi B, Cleveland MG. Cutaneous infection due to Mycobacterium kansasii. Diagn Microbiol Infect Dis 2000; 38: 173-5.