CASE REPORT

ECTHYMA GANGRENOSUM-LIKE LESIONS ASSOCIATED WITH DISSEMINATED NONTUBERCULOUS MYCOBACTERIAL INFECTION IN AN HIV-INFECTED PATIENT

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Abstract. Ecthyma gangrenosum typically occurs in patients who are immunocompromised. It is most often associated with a *Pseudomonas aeruginosa* bacteremia but other pathogens can be found. We report an HIV-infected patient with disseminated nontuberculous mycobacterial infection who presented with fever, mucous bloody diarrhea and cutaneous lesions on both legs. The cutaneous lesions had ecthyma gangrenosum feature and the histopathology was compatible with erythema induratum. Hemoculture was positive for nonchromogen slowly growing mycobacteria.

Keywords: ecthyma gangrenosum, disseminated, nontuberculous mycobacteria, mycobacterium, erythema induratum

INTRODUCTION

Ecthyma gangrenosum is a cutaneous necrotizing vasculitic lesion considered as a pathognomonic feature of bacteremia, especially from *Pseudomonas aeruginosa* (Greene *et al*, 1984; Reich *et al*, 2004). It typically occurs in patients who are immunocompromised, including patients with acquired immunodeficiency syndromes (AIDS), immunosuppressive therapy, hematologic malignancies, and diabetes mellitus. Immune failure leads to increased susceptibility to invasion of vessel walls by bacteria spread either hematogenously or by direct inoculation (Greene *et al*, 1984). This invassion produces vasculitides in the dermis and subcutaneous tissues; interruption of blood supply from extravasation and edema around the vessel progresses to ischemic necrosis (Downey *et al*, 2007). Ecthyma gangrenosum-like lesions have also been described with other organisms, including

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other *Pseudomonas* species (Aygencel *et al*, 2008), *Morganella morganii* (Del Pozo *et al*, 1998), *Escherichia coli*, *Staphylococcus aureus* (Sen *et al*, 2009), *Candida albicans* (Leslie *et al*, 2005), *Mucor, Aspergillus fumigatus* and herpes simplex virus (Kimyai-Asadi *et al*, 1999). The characteristic skin lesions of ecthyma gangrenosum include vesicles or hemorrhagic pustules, followed by gangrenous areas with a black eschar surrounded by an erythematous halo (Weber *et al*, 2005).

We present an HIV-infected patient who developed ecthyma gangrenosum-like lesions due to disseminated infection caused by nontuberculous mycobacteria (NTM).

CASE REPORT

A 61-year-old Thai man with a five month history of acquired immunodeficiency syndrome (AIDS) came to the hospital because of fever for one week. He had multiple painless ulcers on both legs for five days, abdominal discomfort and bloody diarrhea with mucus for two days. Five months previously he was diagnosed as having disseminated penicillosis of the lung and bone marrow and had a CD4 count of 8 cells/ l (1%). He was successfully treated with amphotericin B for four weeks and was continued on itraconazole 400 mg/day without antiretroviral treatment. Physical examination revealed a body temperature of 38.5ºC, mild pale conjunctivae, and mild tenderness of the left lower quadrant of the abdomen. He had multiple necrotic vesicles on both his legs and feet, a 1.5x2 cm round necrotic lesion on his left lower leg and 2.8x3.3 and 3x3.2 cm necrotic ulcers with black eschars on his right leg (Figs 1 and 2). Investigations showed a hemoglobin of 9.2 g/l, a white blood cell count of 8,800/mm^3

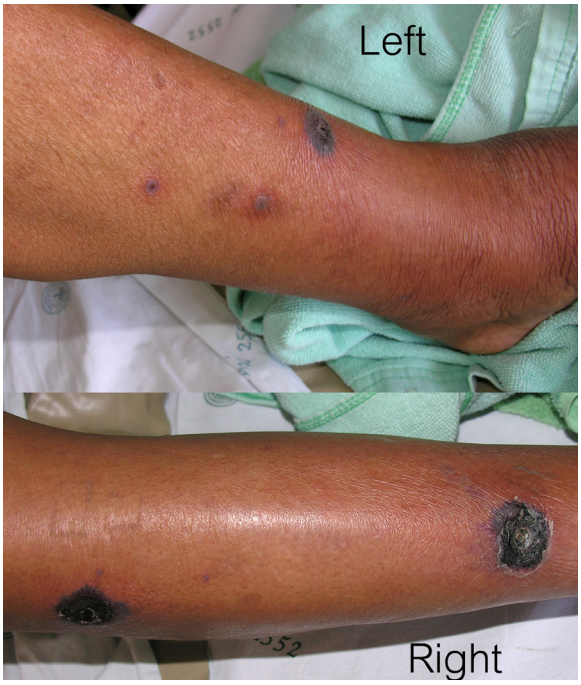

Fig 1–Multiple necrotic vesicles and multiple necrotic ulcers with black eschars of both legs.

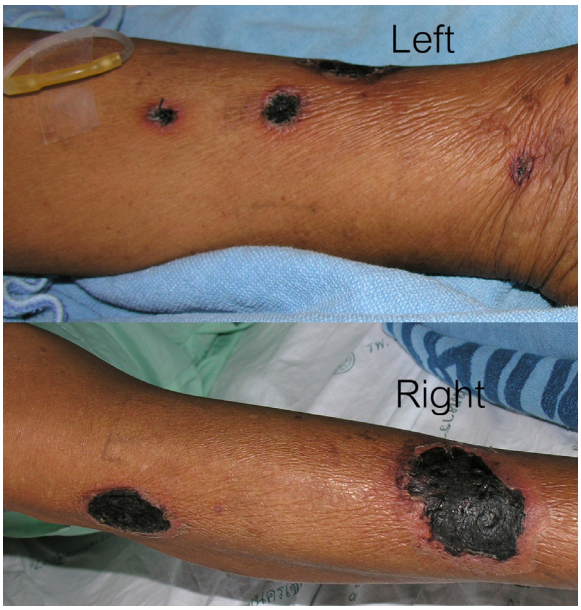

Fig 2–Necrotic vesicles progress into necrotic areas and necrotic ulcers with eschar formation, ten days after admission.

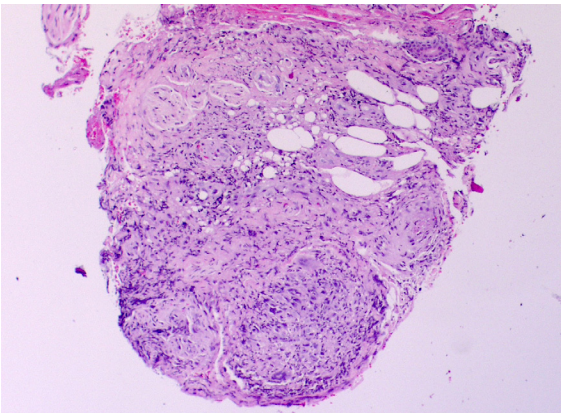

Fig 3–Histopathology showed lobular granulomatous panniculitis.

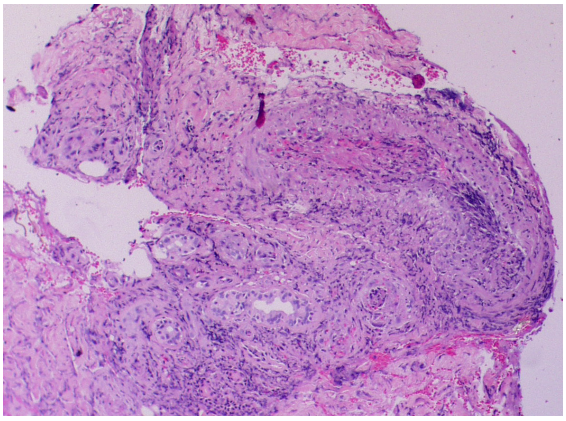

Fig 4–Thrombosis and fibrinoid deposits in the lumen and wall of small and medium-sized blood vessels which were infiltrated by inflammation.

(85% neutrophils, 7% lymphocytes, 1% eosinophils, 1% basophils, 6% monocytes) and a platelet count of 417,000/mm^3. Stool examination showed a white blood cell count of 10-20 cells/HPF, a red blood cell count of 5-10 cells/HPF. A stool exam for acid-fast bacilli was positive. A stool culture was negative for bacteria. Liver function tests showed an albumin of 1.9 g/dl, a globulin of 5.0 g/dl, an alkaline phosphatase of 283 U/l (normal range = 21-128), a cholesterol of 100 mg/dl (normal range < 200), a SGOT of 58 U/l (normal range = 3-37), an SGPT 33 U/l (normal range 7-42), a total bilirubin of 0.62 mg/dl (normal range = 0.2-1.1) and a direct bilirubin of 0.17 mg/dl (normal range = 0-0.3). Chest x-ray showed a minimal infiltration of the right upper lobe that had improved compared to a previous study five months earlier. Sputum for acid-fast bacilli was negative.

The hemoculture grew NTM which produced no pigment by the 2nd week with the BACTEC™ 9050 system. The mycobacterium was identified by polymerase chain reaction (PCR)-based genotype mycobacterium method (INNO-LiPA MYCOBACTERIA v2: Innogenetics, Ghent, Belgium). It was positive for mycobacterium but was negative for *M. tuberculosis*, *M. tuberculosis* complex, *M. bovis*, *M. microti*, *M. africanum*, *M. kansasii*, *M. gastri*, *M. xenopi*, *M. gordonae*, *M. genavense*, *M. simiae*, *M. marinum*, *M. ulcerans*, *M. celatum*, *M. avium* complex, *M. haemophilum*. *M. chelonae* and *chelonae* complex, *M. fortuitum*. *M. peregrinum* complex, and *M. smegmatis*. The diagnosis of disseminated infection caused by nonchromogen, slowly growing, nontuberculous mycobacteria was made.

Histopathology of a skin biopsy of the left leg lesion showed an absence of the epidermis and a hemorrhage in the dermis. In the deep dermis and subcutaneous tissue, there were diffuse noncaseating granulomatous inflammation, thrombosis and fibrinoid deposition in the lumen and wall of the small and medium-sized blood vessels, which were infiltrated by the inflammation (Figs 3 and 4). An acid-fast bacilli stain and a stain for fungal organisms (PAS and GMS) were negative. The pathological findings were compatible with erythema induratum.

Initial treatment included ceftriaxone 2 g/day and ciprofloxacin 1,000 mg/day for the acute infectious diarrhea and ecthyma gangrenosum, acyclovir for the necrotic vesicles and azithromycin 1,000 mg/week for prophylaxis of *Mycobacterium avium* complex. Because of elevated transaminases due to long term itraconazole use the treatment was changed to ethambutol 1,000 mg/day, ofloxacin 600 mg/day, streptomycin 1 g/day IM and clarithromycin 1,000 mg/day. Streptomycin was replaced by amikacin 750 mg/day intravenously because the patient could not tolerate the streptomycin intramuscular injection. Isoniazid 300 mg/day, pyrazinamide 1,500 mg/day and itraconazole 200 mg/day were added during the third and fourth weeks of treatment, respectively, without deterioration in the liver function test results. After four weeks of treatment, the patient was treated with isoniazid 300 mg/day, ethambutol 1,000 mg/day, ofloxacin 600 mg/day, pyrazinamide 1,500 mg/day and clarithromycin 1,000 mg/day for two months. The plan is to continue isoniazid, ethambutol, ofloxacin and clarithromycin for ten months. The skin lesions improved within one week of starting treatment and slowly healed.

DISCUSSION

NTM is distributed in the environment. NTM has a broad range of pathogenicities and is non-transmissible from human to human, which distinguishes it from *M. tuberculosis* (Tortoli, 2009). Classification of NTM using the Runyon system uses rate of growth and the ability to produce visible colonies on culture media (Runyon, 1959). Recent culture techniques using the radiometric assay BACTEC™ system can shorten the time to detection (Kirihara *et al*, 1985). Probe hybridization or DNA sequencing PCR techniques are useful tools for determining mycobacterial species (El Amin *et al*, 2000). The blood culture of our patient grew mycobacteria which produced no pigment by the 2nd week in the BACTEC™ 9050 system. Mycobacterial genus was identified but the species of mycobacteria could not be identified by techniques available at our hospital. This NTM was slow growing and nonchromogenic: Runyon group III. Some species of NTM (*eg*, *Mycobacterium tarrae* complex and *Mycobacterium malmoense*) can not be identified by this method.

The incidence of NTM infections has increased over the past few decades, particularly in immunocompromised hosts. Nontuberculous mycobacterial infections have several clinical presentations. The most common of these are: pulmonary disease, lymphadenitis, skin or soft tissue infections and disseminated disease (American Thoracic Society, 1997). Disseminated NTM infections usually occur in patients with advanced HIV disease or a CD4 count <100 cells/ l (Al-Abdely *et al*, 2000). A major source of infection is the respiratory tract. More than 90% of NTM disseminated infections in HIV-infected patients are due to *M. avium* (Griffith *et al*, 2007). The clinical presentation includes fever, night sweats, abdominal pain and diarrhea (Daley and Heifets, 2009). Cutaneous NTM infections have rarely been reported (Bartralot *et al*, 2005). The lesions may be multiple crusted ulcers or abscesses, multiple subcutaneous nodules or grouped erythematous papules or pustules (Lillo *et al*, 1990; Palenque, 2000; Smith *et al*, 2001; Bartralot *et al*, 2005). To our knowledge, NTM cutaneous lesions have never been reported as ecthyma gangrenosum-like lesions.

The most characteristic histopathological features of cutaneous NTM infec-

tion are suppurative granulomas in which infiltrations tend to extend into the subcutaneous tissue and are more diffuse with abscess formation in immunosuppressed patients (Bartralot *et al*, 2000). Histopathological findings in this patient included lobular granulomatous panniculitis with vasculitis, compatible with erythema induratum (Segura *et al*, 2008; Gilchrist and Patterson, 2010). The panniculitis with erythema induratum results from hypersensitivity and is strongly associated with *M. tuberculosis* (Baselga *et al*, 1997). It has also been reported to be associated with hepatitis C infection (Cardinali *et al*, 2000; Segura *et al*, 2008; Fernandes *et al*, 2009), but has not been reported in NTM infections. Vasculitis in our patient may have been caused by an altered immune response due to HIV infection and/or the effect of septic vasculitis in a severe NTM infection.

In conclusion, to the best of our knowledge, this is the first report of ecthyma gangrenosum-like lesions associated with disseminated NTM infection. The histopathological findings included erythema induratum/nodular vasculitis in this NTM infected AIDS patient.

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