YY Leung 梁盈盈
KW Choi 蔡健榮
KM Ho 何景文
EWL Kun 靳惠蓮

Disseminated cutaneous infection with *Mycobacterium chelonae* mimicking panniculitis in a patient with dermatomyositis

彌散性皮下感染龜分支桿菌擬似脂膜炎的病例

We report a case of disseminated cutaneous *Mycobacterium chelonae* infection. A patient with dermatomyositis associated with malignancy presented with features of panniculitis. This was later confirmed to be cutaneous *Mycobacterium chelonae* infection. Disseminated cutaneous *Mycobacterium chelonae* infection and panniculitis are reviewed.

本文報告一個彌散性皮下感染龜分支桿菌的病例。病者患有皮肌炎及大腸惡性腫瘤，表徵有深層性皮下脂肪炎，最後證實為龜分支桿菌感染。本文載有龜分支桿菌感染及脂肪炎的回顧及評論。

Key words:
Dermatomyositis;
Mycobacterium chelonae;
Mycobacterium infections, atypical;
Panniculitis;
Skin diseases, bacterial

關鍵詞：
皮肌炎；
龜分支桿菌；
分枝杆菌感染，非典型；
脂膜炎；
皮膚病，細菌性

Hong Kong Med J 2005;11:515-9

Department of Medicine and Geriatrics, Tai Po Hospital, 9 Chuen On Road, Hong Kong
YY Leung, MB, ChB, MRCP
EWL Kun, FRCP, FHKAM (Medicine)
Department of Medicine, Alice Ho Mui Ling Nethersole Hospital, 11 Chuen On Road, Hong Kong
KW Choi, MB, ChB, FHKAM (Medicine)
Fanling Integrated Treatment Centre (Social Hygiene Service), Centre for Health Protection, Department of Health, 2 Pik Fung Road, Fanling, Hong Kong
KM Ho, FRCP, FHKAM (Medicine)

Correspondence to: Dr YY Leung (e-mail: katyccc@hotmail.com)

Introduction

Mycobacterium chelonae is a rapidly growing atypical mycobacterium. It is a free-living saprophyte commonly found in water, soil, and dust. It typically causes localised skin lesions, often following trauma or injections. Disseminated infection usually occurs in immunocompromised patients. We report a case of disseminated *M chelonae* infection previously misdiagnosed as lupus profundus in an immunocompromised patient receiving corticosteroid and immunosuppressant therapy for dermatomyositis.

Case report

In October 2003, a 52-year-old woman with dermatomyositis was referred to the rheumatology clinic of Alice Ho Miu Ling Nethersole Hospital. She had been seen initially in the dermatology clinic for indurated tender red lesions on the medial side of both thighs. A skin biopsy was compatible with lupus profundus, revealing lobular panniculitis with lymphocytes and plasma cell infiltration and increased stromal mucin in the dermis. She then developed a rash typical of dermatomyositis marked by heliotrope rash, gottron papules, and poikiloderma, and associated with proximal muscle weakness and elevated muscle enzymes. An electromyogram revealed a myopathic picture. Dermatomyositis was diagnosed and the patient was prescribed prednisolone 1 mg/kg per day. Carcinoma of the rectum was also diagnosed for which colectomy was performed. The skin rash, proximal muscle weakness, and muscle enzyme levels improved after surgery, but tender red nodules that were slow to heal later appeared around the laparotomy wound. Similar nodules developed around the buttocks and thighs, but the upper body and upper limbs were spared. Some lesions were suppurative although aspirations were initially sterile. A provisional diagnosis of panniculitis relative to the underlying

autoimmune disease was made. The patient was maintained on low-dose prednisolone and methotrexate.

Skin problems persisted and progressed to ulcers and draining abscesses (Fig). On one occasion, aspirate grew mycobacterium within 2 weeks of incubation. The organism was later identified as *M chelonae* and was subsequently confirmed from multiple aspirations from different sites on multiple occasions. The organism was multidrug-resistant: the minimal inhibitory concentration by broth dilution method to amikacin, cefoxitin, clarithromycin, doxycycline, and levofloxacin were 32, 32, 2, >32, and 8 μg/mL, respectively (Table 1). Susceptibility to clarithromycin was intermediate. An infectious disease specialist suggested clarithromycin as the treatment of choice because it could achieve high tissue and intracellular concentrations. Despite the mean minimal inhibitory concentration required, it was thought that amikacin and imipenem would act synergistically with clarithromycin during the early phase of therapy. Intravenous imipenem and amikacin were prescribed with concomitant oral clarithromycin and linezolid for at least 6 months. Daily wound debridement was carried out in the initial phase of treatment. Methotrexate and prednisolone were discontinued, then hydroxychloroquine was prescribed until the lesions began to heal.

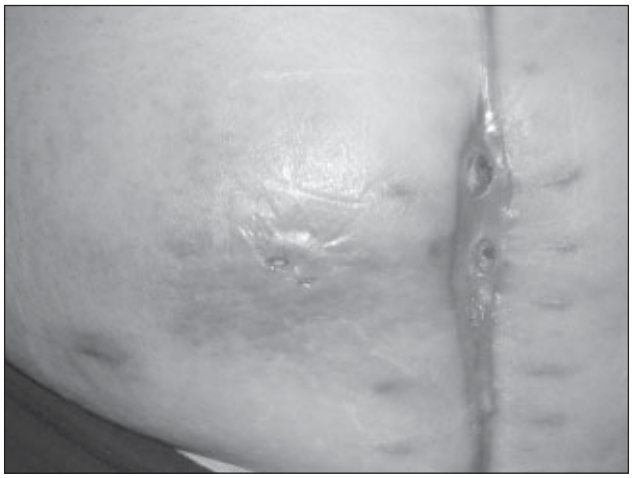

Fig. Skin lesions around the laparotomy scar

Discussion

Atypical or non-tuberculous mycobacteria are commensals and commonly found in water, soil, and dust. The Runyon classification, based on growth rate and pigment production, has traditionally been used to group the atypical mycobacteria. Newer classification according to clinical diseases has been proposed.[1] The slow-growing organisms, *Mycobacterium marinum, Mycobacterium kansasii* (Group 1), and *Mycobacterium ulcerans* (Group 3) have caused the majority of cutaneous disease in immunocompetent hosts. Cutaneous infections with the rapid growers (Group 4) are more common in immunocompromised hosts. *Mycobacterium fortuitum, M chelonae*, and *Mycobacterium abscessus* are the major distinct species of rapidly growing mycobacteria.

Transmission of *M chelonae* is by direct inoculation. There is no evidence of human-to-human spread. Cutaneous *M chelonae* infection may occur by accidental penetrating trauma, injections, surgical procedures, or acupuncture.[2,3] Outbreaks of *M chelonae* or *M abscessus* infections associated with surgical procedures and injections have been reported.[4,5] The lesions are often nodules or pustules. It can also present as draining abscesses, ulcers, cellulites, and regional lymphadenopathy. Sporotrichoid spread has been reported but is rare.[6] Cutaneous lesions sometimes mimic lesions of vasculitis,[7] panniculitis, and erythema nodosum. Extracutaneous infections include catheter infections, arteriovenous graft infections, osteomyelitis, dermatitis, and pulmonary disease.[2]

Mycobacterium chelonae generally causes localised abscesses or cellulitis. Disseminated cutaneous disease (defined as >5 nodular subcutaneous lesions) is more often seen in immunocompromised hosts. Wallace et al[2] identified 53 patients with disseminated cutaneous *M chelonae* infection, 49 of them received corticosteroids, with or without other immunosuppressants. The most common underlying disorders were organ transplantation, rheumatoid arthritis, and other connective tissue diseases.[2]

Mycobacterium chelonae infection can be diagnosed histologically or following recovery of the organism from tissue culture. The histological features

Table 1. Results of sensitivity test of *Mycobacterium chelonae* using broth dilution method

Anti-microbial tested	Minimal inhibitory concentration (μg/mL)	Interpretation
Amikacin	32	Resistant
Cefoxitin	32	Resistant
Clarithromycin	2	Intermediate
Doxycycline	>32	Resistant
Levofloxacin	8	Resistant

of atypical mycobacterial infection include large numbers of neutrophilic infiltrates, abscess formation, suppurative granulomatous inflammation, and the presence of acid-fast bacilli. It can also be non-specific. The inflammation may involve the dermis and underlying fat, and necrosis may be present. Immunosuppression may affect the type of inflammatory response. A comparative histopathological study showed that deeper inflammatory infiltrate, suppurative granulomas, epidermal acanthosis, and lack of epidermal response were more common in immunosuppressed hosts.[8] Biopsy for culture remains the definitive diagnosis. Polymerase chain reaction has become widely used in diagnosis. It should be used with caution because the organism is ubiquitous in the environment and false positive results can occur.[9] Tissue inhibitors can also lead to false negative results.

Specific treatment of *M chelonae* infection usually involves a combination of chemotherapy and surgical debridement. The lack of consensus on treatment is a reflection of the paucity of data from clinical trials. Another problem is the paucity of effective microbiological agents. *Mycobacterium chelonae* is resistant to most standard anti-tuberculosis drugs, and treatment should be based on laboratory sensitivity. Good results have been achieved in some case series with macrolides, and clarithromycin is the drug of choice. However, monotherapy with clarithromycin leading to resistance has been reported.[10] Accumulated experience in the literature supports multidrug therapy.[11] Apart from the macrolides, sensitivity to ciprofloxacin and doxycycline is variable; therefore, amikacin and imipenem are the parenteral agents of choice. Anecdotal evidence suggests that treatment should be given with a minimum of two agents, including clarithromycin, for at least 6 months. This reduces relapse rates and prevents the emergence of resistance. In immunocompromised patients, treatment may have to be longer. Multidrug-resistant, rapidly growing mycobacteria have been increasingly reported, for example in Taiwan.[12] New agents against *M chelonae* include linezolid and tigecycline. Linezolid has proven in-vitro activity and there are case reports of clinical success.[13] The potential adverse effects of its prolonged administration are gastro-intestinal upset, tongue discolouration, taste disturbance, and marrow suppression. Linezolid is a reversible, non-selective inhibitor of monoamine oxidase. A serotonin syndrome may occur if serotonergic agents are used concomitantly. The in-vitro susceptibility to tigecycline is also very good.[14]

Panniculitis is inflammation of the subcutaneous fat. It can be primary or secondary to a disease process such as vasculitis, malignancy, infection, or endocrine disorder. Pathologically, there are two broad categories—mostly septal or mostly lobular—and most lesions are nonetheless a mixture of both. A histopathological classification of panniculitis and the associated disease entities have been proposed (Table 2).[15] Despite the histopathological differences, the external appearances of lesions are the same. They manifest as raised subcutaneous tender erythematous nodules, usually on the extremities.

Panniculitis caused by atypical mycobacterium belongs to the category of infective panniculitis that is characterised by lobular panniculitis with neutrophilic infiltration. Suppurative granulomas, abscess formation, and acid-fast bacilli may be present.[8,15]

Erythema nodosum is a prototype of septal panniculitis. It is an immune-related reaction associated with many disease entities such as infection, tuberculosis, medications, and connective tissue diseases. Lobular panniculitis may be seen in systemic lupus erythematosus and pathologically is termed 'lupus erythematosus profundus'. It is a chronic recurrent panniculitis that appears in approximately 1% to 3% of patients with systemic lupus erythematosus, and more frequently occurred in women. The lesions have a predilection for the upper arms, shoulders, face, and buttocks. These are areas infrequently involved by other variants of panniculitis. The lesions are deeply seated cutaneous nodules that may appear as classic discoid lupus erythematosus or may appear as normal skin. They regress with depressed lesions of lipoatrophy. Histopathologically, it is characterised by mostly lobular panniculitis with predominately lymphocyte infiltration. Epidermal and dermal changes of discoid lupus erythematosus are present in half of the cases.[15]

Panniculitis is less frequent in dermatomyositis. One series reported a prevalence of 6.8%.[16] Histopathological findings of panniculitis are similar to lupus erythematosus profundus: a mostly lobular panniculitis with lymphocyte and plasma cell infiltration.[15] Solans et al[16] summarised 19 cases from the literature and reported that patients having panniculitis associated with dermatomyositis seemed to have good prognosis. No increase in incidence of malignancy was observed, and the panniculitis responded well to corticosteroid therapy.

Mycobacterium chelonae is a rapid-growing mycobacterium that causes opportunistic infection.

Table 2. Histopathological classification of panniculitides

Mostly septal panniculitides	
With vasculitis	
Small vessels	
Venules	Leukocytoclastic vasculitis
Large vessels	
Veins	Superficial thrombophlebitis
Arteries	Cutaneous polyarteritis nodosa
No vasculitis	
Lymphocytes and plasma cells mostly	
With granulomatous infiltrate in septa	Necrobiosis lipoidica
No granulomatous infiltrate in septa	Scleroderma
Histiocytes mostly	
Granulomatous infiltrate	
With mucin in the centre of palisaded granulomas	Subcutaneous granulosa annulare
With fibrin in the centre of palisaded granulomas	Rheumatoid nodule
With large areas of degenerated collagen, foamy histiocytes, and cholesterol clefts	Necrobiotic xanthogranuloma
Without mucin, fibrin, or degeneration of collagen, but with radial granulomas in septa	Erythema nodosum
Mostly lobular panniculitides	
With vasculitis	
Small vessels	
Venules	Erythema nodosum leprosum Lucio's phenomenon Neutrophilic lobular (pustular) panniculitis associated with rheumatoid arthritis
Large vessels	
Arteries	Erythema induratum of Bazin Crohn's disease
No vasculitis	
Few or no inflammatory cells	
Necrosis at the centre of the lobule	Sclerosing panniculitis
With vascular calcification	Calciphylaxis Oxalosis
With needle-shaped crystals in adipocytes	Sclerema neonatorum
Lymphocytes predominant	
With superficial and deep perivascular dermal infiltrate	Cold panniculitis
With lymphoid follicles, plasma cells, and nuclear dust of lymphocytes	Lupus panniculitis (lupus erythematosus profundus)
With lymphocytes and plasma cells	Panniculitis in dermatomyositis
Neutrophils predominant	
Extensive fat necrosis with saponification of adipocytes	Pancreatic panniculitis
With neutrophils between collagen bundles of deep reticular dermis	α_1-Antitrypsin deficiency
With bacteria, fungi, or protozoa identifiable by specialised stains	Infective panniculitis
With foreign bodies	Factitial panniculitis
Histiocytes predominant (granulomatous)	
No crystals in adipocytes	Subcutaneous sarcoidosis Traumatic panniculitis Lipoatrophy
With crystals in histiocytes or adipocytes	Subcutaneous fat necrosis of the newborn Poststeroid panniculitis Gout panniculitis Crystal-storing histiocytosis
With cytophagic histiocytes	Cytophagic histiocytic panniculitis
With sclerosis of the septa	Postirradiation pseudosclerodermatous panniculitis

Disseminated cutaneous disease occurs more commonly in an immunocompromised host. The infection is associated with direct inoculation, and skin lesions may mimic vasculitis and panniculitis. Diagnosis depends on tissue histology and culture, and tissue polymerase chain reaction may be helpful. Treatment consists of a clarithromycin-based multidrug regimen for at least 6 months and surgical debridement of

infected tissue. Multidrug resistance is an increasing concern. New agents such as linezolid and tigecycline show promise in the treatment of multidrug-resistant isolates.

References

1. 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(Suppl):1S-25S.
2. Wallace RJ Jr, Brown BA. Onyi GO. Skin, soft tissue, and bone infections due to *Mycobacterium chelonae*: importance of prior corticosteroid therapy, frequency of disseminated infections, and resistance to oral antimicrobials other than clarithromycin. J Infect Dis 1992;166:405-12.
3. Woo PC, Leung KW, Wong SS, Chong KT, Cheung EY, Yuen KY. Relatively alcohol-resistant mycobacteria are emerging pathogens in patients receiving acupuncture treatment. J Clin Microbiol 2002;40:1219-24.
4. Wallace RJ Jr, Musser JM, Hull SI, et al. Diversity and sources of rapidly growing mycobacteria associated with infections following cardiac surgery. J Infect Dis 1989;159:708-16.
5. Meyers H, Brown-Elliott BA, Moore D, et al. An outbreak of *Mycobacterium chelonae* infection following liposuction. Clin Infect Dis 2002;34:1500-7.
6. Haas SR, Hodge MB, Duncan RA. Cushing's syndrome presenting as disseminated cutaneous *Mycobacterium chelonae* infection. Clin Infect Dis 2001;33:e51-3.
7. Gordon MM, Wilson HE, Duthie FR, Jones B, Field M. When typical is atypical: mycobacterial infection mimicking cutaneous vasculitis. Rheumatology (Oxford) 2002;41:685-90.
8. Bartralot R, Pujol RM, Garcia-Patos V, et al. Cutaneous infections due to nontuberculous mycobacteria: histopathological review of 28 cases. Comparative study between lesions observed in immunosuppressed patients and normal hosts. J Cutan Pathol 2000;27:124-9.
9. Collina G, Morandi L, Lanzoni A, Reggiani M. Atypical cutaneous mycobacteriosis diagnosed by polymerase chain reaction. Br J Dermatol 2002;147:781-4.
10. Driscoll MS, Tyring SK. Development of resistance to clarithromycin after treatment of cutaneous *Mycobacterium chelonae* infection. J Am Acad Dermatol 1997;36:495-6.
11. Wallace RJ Jr, Tanner D, Brennan PJ, Brown BA. Clinical trial of clarithromycin for cutaneous (disseminated) infection due to *Mycobacterium chelonae*. Ann Intern Med 1993;119:482-6.
12. Yang SC, Hsueh PR, Lai HC, et al. High prevalence of antimicrobial resistance in rapidly growing mycobacteria in Taiwan. Antimicrob Agents Chemother 2003;47:1958-62.
13. Wallace RJ Jr, Brown-Elliott BA, Ward SC, Crist CJ, Mann LB, Wilson RW. Activities of linezolid against rapidly growing mycobacteria. Antimicrob Agents Chemother 2001; 45:764-7.
14. Wallace RJ Jr, Brown-Elliott BA, Crist CJ, Mann L, Wilson RW. Comparison of the in vitro activity of the glycylcycline tigecycline (formerly GAR-936) with those of tetracycline, minocycline, and doxycycline against isolates of nontuberculous mycobacteria. Antimicrob Agents Chemother 2002;46:3164-7.
15. Requena L, Sánchez Yus E. Panniculitis. Part I. Mostly septal panniculitis. J Am Acad Dermatol 2001;45:163-83.
16. Solans R, Cortes J, Selva A, et al. Panniculitis: a cutaneous manifestation of dermatomyositis. J Am Acad Dermatol 2002; 46(5 Suppl):148S-150S.