**CASE REPORT**

# First case of *Mycobacterium haemophilum* infection in an AIDS patient in Italy**

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## ABSTRACT

*Mycobacterium haemophilum*, a strongly acid- and alcohol-fast bacillus belonging to the group of non-tuberculous mycobacteria was first described in 1978 as the cause of cutaneous ulcerating lesions in a woman with Hodgkin's disease. Infection due to *M. haemophilum* is rare but increasing in prevalence in immnunosuppressed subjects, particularly in patients with acquired immunodeficiency syndrome (AIDS) patients. The skin is the most common site of infection with erythematous or violaceous papules and/or nodules that are usually painless at first, but some elements develop into abscesses or ulcers that can become very painful. The incidence of *M. haemophilum* is unknown, but cases of infection have been reported in Australia, Canada, the United States, France, Israel, the United Kingdom and Taiwan; to date no cases have been reported in Italy, thus the case reported here is apparently the first one observed in our country.

**Key words:** cutaneous infection, *Mycobacterium haemophilum*, AIDS

*Received: 27 September 2002, accepted 8 November 2002*

## Introduction

*Mycobacterium haemophilum* was first described in 1978 as the cause of cutaneous ulcerating lesions in a woman with Hodgkin's disease.[1] *M. haemophilum* is a strongly acid- and alcohol-fast bacillus (AFB); it belongs to the group of non-tuberculous mycobacteria (NTM), which represents a large number of mycobacterial species frequently found in environmental habitats and that can colonize and occasionally cause infection in humans and animals. The terms NTM and mycobacteriosis reflect efforts to distinguish these forms from *Mycobacterium tuberculosis*.[2] The natural habitat and means of acquisition of *M. haemophilum* are unknown. Potential routes of transmission include percutaneous inoculation, inhalation or ingestion, and hospital transmission has been suspected.[3]

Infection due to *M. haemophilum* is rare but increasing in prevalence in immnunosuppressed subjects with AIDS, lymphoma, those on long-term high-dose steroids or who have undergone organ transplants.[4] Disease caused by this organism has also occurred in a few healthy children, in whom manifestations are cervical, submandibular, and perihilar adenitis.[5] In adults the skin is the most common site of infection with erythematous or violaceous papules and/or nodules that are usually painless at first, but some elements develop into abscesses or ulcers that can become very painful.[4] Cutaneous lesions are most frequently found on the extremities and less commonly on the trunk and the face. Differential diagnoses considered include other cutaneous *Mycobacterium* infections (*M. marinum*, *M. avium complex*), non-specific bacterial infections and Kaposi's sarcoma. Other features may include arthritis and osteomyelitis, and a few cases of pneumonia have been reported. Although infection due to this organism is rarely fatal, it is a cause of significant morbidity.[6] The incidence of *M. haemophilum* is unknown, but cases of infection have been reported in Australia, Canada, the United States, France, Israel, the United Kingdom and Taiwan; to date no cases have been reported in Italy, thus the case reported here is apparently the first one observed in our country.

**This case report was partially presented at the 11th Congress of the European Academy of Dermatology and Venereology, Prague, 2–6 October 2002.

## Case report

In August 2000 a 51-year-old homosexual Italian male was admitted to hospital for wasting syndrome, oral candidiasis, and a 3-week history of cutaneous erythematous papules and pustules on his extremities. Laboratory tests revealed an HIV infection; the absolute CD4 count was 1/mm$^3$, and the plasma HIV RNA was 500 000 copies/mL. He was administered antiretroviral therapy with zidovudine, lamivudine, indinavir, and oral fluconazole, and amoxicillin/clavulanate. The skin lesions were not subjected to culture or biopsy.

The man's past history revealed syphilis when he was 20 years old and he had undergone rhinoplasty and silicone implants in the upper cheeks and lips 6 years previous to hospitalization in our ward. He had diabetes mellitus for which he had been treated with oral drugs for the past two years. The man lived and worked in Florence and he had no travel history in recent years. He raised birds and had a dog.

In November the skin lesions developed as erythematous or violaceous and fluctuant, painful nodules, ranging in diameter from 1 to 3 cm, and some elements developed into abscesses or ulcers (fig. 1). Biopsy of one leg nodule showed acute inflammation of the dermal layers without evidence of microorganisms using PAS, Giemsa and Grocott stains. Initial culture of aspirate from skin lesions was positive for *Staphylococcus sciuri* and mycobacterium were detected in acid-fast smears while genic amplification for *M. tuberculosis* was negative.

The initial treatment was rifabutin, ethambutol and clarithromycin, but when *M. haemophilum* was recovered, the therapy was modified to ciprofloxacin with ethambutol. In addition to the culture media routinely used in our laboratory for mycobacteria, MGIT, the samples were also inoculated in radiometric vials both unenriched and supplemented with 0.4% bovine haemoglobin.[7] The identification of *M. haemophilum* was obtained with INNO LiPA mycobacteria and was confirmed by high-performance liquid chromatography of cell-wall mycolic acid.[8] After two months during which cutaneous lesions gradually improved, the therapy was changed to rifabutin, azithromicyn and levofloxacin due to adherence problems. The man showed complete regression of the cutaneous lesions after 5 months of therapy and antimicrobial treatment was stopped. He has had no recurrences 7 months after cessation of therapy; his CD4 cell count has in fact risen to 116/mm$^3$ and plasma HIV RNA is undetectable.

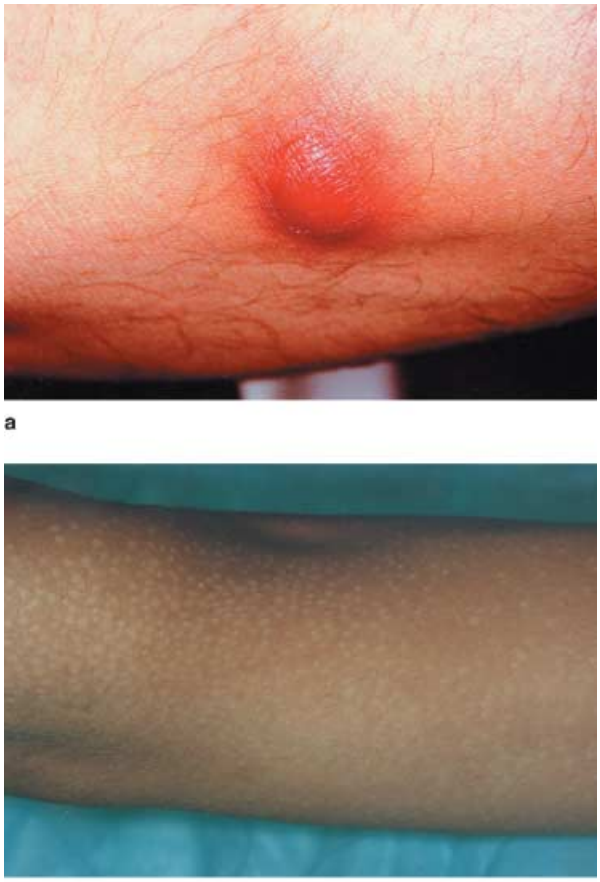

**fig. 1** Erythematous painful nodules over the right leg due to *M. haemophilum* infection.

## Discussion

Atypical mycobacterial infections are major complications in subjects with AIDS, and recently the pathogenetic significance of *M. haemophilum* has been recognized in these individuals.[9] *M. haemophilum*, an organism of low virulence, is emerging as a pathogen in persons who are severely immunocompromised by AIDS infection as well as after renal, bone marrow, and cardiac transplantation, lymphoma, rheumatoid arthritis, and in children with apparently normal immune function. *M. haemophilum* infection should be considered in immunologically compromised hosts who develop multiple erythematous papules or nodules (with a light central area that becomes necrotic) on the extremities and less commonly on the trunk and face, osteomyelitis, and pneumonia of uncertain cause. In our patient, the skin lesions initially occurred as non-follicular pustules that mimicked a bacterial infection, and antibiotic therapy was started. After 2 months subcutaneous nodules appeared, and histological examination did not demonstrate granulomas with the epithelioid and giant cells that are usually found in cutaneous mycobacterial infections but rather an acute inflammatory infiltrate. Staining of a skin preparation showed acid-fast bacilli and specific therapy was initiated, but the treatment was modified 3 weeks later when cultures of biopsy specimens evidenced *M. haemophilum*.

Treatment of *M. haemophilum* includes surgical excision of localized foci of infection and antibiotics. The most common antimicrobial agents administered are the rifamycins, macrolides, chinolones, clofazimine and amikacin; isoniazid shows

some activity, but ethambutol, tetracycline and trimethoprim-sulfamethoxazole are usually inactive.[10] The failure of susceptibility testing could not help us in directing therapy. However, even should it be successful, the interpretation of results of a non-standardized method still remains ambiguous.[11] The outcome of treatment in adults appears to be greatly influenced by the ability to limit the underlying immunosuppression. In our case the use of an optimal antimycobacterial regimen led to cure, certainly influenced by the enhancement of immune system function due to highly active antiretroviral therapy. The man showed marked regression of his skin lesions after only 2 months, and after 5 months of therapy the cutaneous nodules had disappeared, with no recurrence 1 year later.

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