Mycobacterium haemophilum Infection Presenting as Bilateral Cellulitis and Annular Lesion in a Heart Transplant Recipient

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Mycobacterium haemophilum, a recently described pathogen, carries a wide range of dermatologic manifestations and is of importance especially in immunocompromised patients. We describe a case of *Mycobacterium haemophilum* infection in a heart transplant recipient, manifesting as annular plaques and bilateral cellulitis. Our case demonstrates the diversity of dermatological clinical manifestations of *M. haemophilum* and emphasizes the need for a high index of suspicion for this pathogen in immunodeficient patients.

Mycobacterium haemophilum is a slow-growing, fastidious, iron-requiring microorganism first described in 1978 in a woman with a cutaneous ulcerating lesion and Hodgkin disease. More than 120 cases have been described around the world to date, mainly in immunosuppressed hosts, such as patients with hematological malignancies or AIDS and transplant recipients [1]. Although new cases continue to be discovered, the natural habitat of *M. haemophilum* and its mode of infection are still unknown [2].

Clinical manifestations of *M. haemophilum* infection include osteomyelitis, septic arthritis, bacteremia and pneumonitis, in addition to chronic lymph adenitis which was described in immunocompetent children [3]. The most common clinical presentation in adults is cutaneous lesions, which range from nodules, cysts and papules [4] to erythema, cellulitis and annular lesions [5].

M. haemophilum requires unique growth conditions for laboratory isolation, including growth media supplementation with a ferric-containing compound and a lower incubation temperature. Polymerase chain reaction and other molecular biology techniques offer a more rapid option for isolation. Histopathologically, infections with *M. haemophilum* can present with a mix of suppurative and granulomatous reactions but can also present with necrosis, lichenoid inflammation, ulceration, and subcutaneous abscess.

PATIENT DESCRIPTION

A 62 year old man was admitted to our dermatology department with a 1 month history of fever and erythematous plaques on both shins. Medical history included heart transplantation 8 years previously due to ischemic heart disease. His immunosuppressive regimen consisted of cyclosporine (75 mg twice daily), prednisone (5 mg once daily) and mycophenolate mofetil (1500 mg twice daily). In addition, mild chronic renal failure, deep vein thrombosis (methylene tetrahydrofolate reductase homozygote), hypertension, osteoporosis, and esophageal reflux were reported. Three weeks prior to presentation at our department, the patient underwent endoscopic retrograde cholangiopancreatography for investigation of suspected bile duct lithiasis leading to iatrogenic pancreatitis, followed by endoscopic cholecystectomy.

On physical examination, the patient had a temperature of 38.5°C. Warm and tender erythematous plaques with undefined borders were observed on his shins bilaterally [Figure A]. In addition, swelling of the wrists, distal interphalangeal joints and ankles were observed.

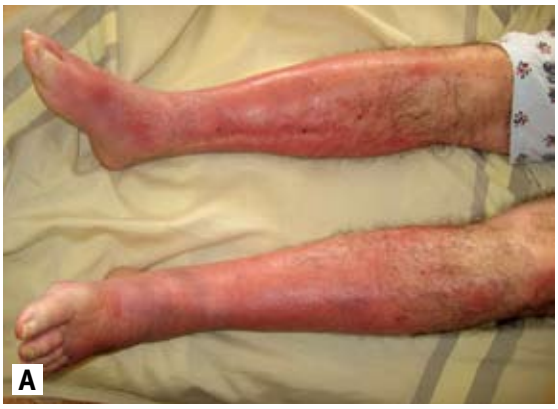
Laboratory studies on admission showed a white blood cell count of 8160 cells/mm^3 (80% neutrophils) and creatinine level of 1.9 mg/dl (normal range 0.6–0.9 mg/dl). Antinuclear factor, complement levels and rheumatoid factor were normal. In addition, cryoglobulin and lupus anticoagulant were within normal range.

Ultrasound and computed tomography scan of the abdomen demonstrated hypodensic masses in the spleen. The differential diagnosis was malignancy, sarcoidosis, or splenic abscesses.

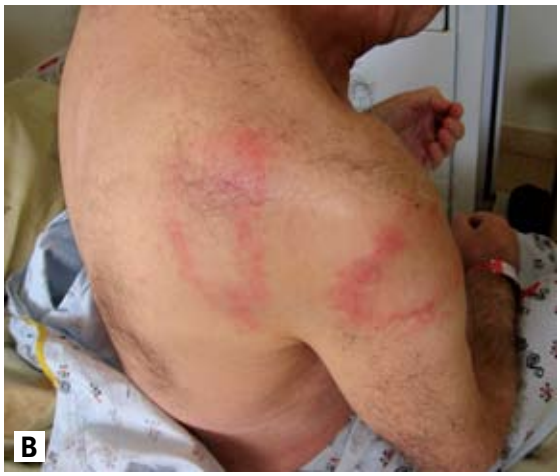
The patient was treated first with intravenous amoxicillin and clavulanic acid for the diagnosis of cellulitis. When no improvement was noticed, his treatment was changed to prednisone 20 mg daily for the diagnosis of vasculitis. Under this treatment, annular erythematous plaques appeared on his right shoulder and waist [Figure B].

Four skin biopsy specimens were taken from the shins and shoulder

[A] Warm, tender, erythematous plaques on both shins



[B] Macular skin lesions forming annular plaques on the right shoulder and scapular region



plaques. Three demonstrated granulomatous dermatitis without acid-fast bacilli and one was interpreted as vasculitis.

The skin biopsy specimens were cultured using liquid medium (Mycobacteria growth indicator tube system, Middlebrook 7H9 broth base, Becton, Dickinson and Company, Sparks, MD, USA) with growth detected 12 days following incubation at 36°C. PCR DNA amplification followed by hybridization assay (Genotype Mycobacterium CM and AS, Hain Lifescience, Nehren, Germany) identified the mycobacterium as *M. haemophilum*. The bacterium was then cultured in Loenstein-Jensen culture plates (Heipha, Eppenheim, Germany) supplemented with hemin at 30°C. No growth was detected at 36°C or in hemin deficient Loenstein-Jensen cultures.

The patient was treated with ciprofloxacin (750 mg twice daily), clarytromycin (500 mg twice daily) and rifampin (600 mg once daily). Regression of skin lesions, decrease in temperature to normal range, and amelioration of bone and joint pain were noted within 3 weeks of starting this treatment. Follow-up skin biopsy and blood cultures were negative for *M. haemophilum* 1 month following treatment initiation.

COMMENT

Special growth and culture requirements make *M. haemophilum* an under-diagnosed pathogen. Since 1978, about 120 cases of infection have been described, mostly in immunosuppressed individuals. Nevertheless, the mode of acquisition and natural habitat of *M. haemophilum* are still unknown. Isolation of the pathogen requires special media supplemented with hemin or ferric ammonium citrate. Optimal incubation temperatures of 28–33°C are compatible with the organism's preference for cooler sites of the body including skin and extremities. Molecular biology techniques, such as PCR (real-time PCR), ribosomal RNA gene, or high pressure liquid chromatography offer a rapid and specific alternative.

Dermatologic manifestations of *M. haemophilum* are varied and range from erythematous plaques and nodules to cysts, scaly plaques, focal paniculitis and annular lesions. In our patient, a combination of cellulitis and annular lesions that tested positive for *M. haemophilum* was observed. To the best of our knowledge, this unique presentation has not been described before. Worth mentioning is the widespread infection in our patient, affecting skin, joints, and possibly the spleen.

Treatment of *M. haemophilum* is based on previous cases and includes ciprofloxacin, clarithromycin and rifampin. Noteworthy are the opposing effects of rifampin and clarithromycin on liver metabolism, which stabilize cyclosporine levels [1].

In summary, clinicians should be aware of the varied clinical manifestations caused by *M. haemophilum*. Accurate diagnosis based on the culture is important because the organism frequently responds to therapy. Additional cases will allow optimization of treatment and the development of prevention methods.

PCR = polymerase chain reaction

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"When I was in the military, they gave me a medal for killing two men and a discharge for loving one"

Leonard Matlovich (1943-1988), a gay Vietnam veteran