



The Case | Posttransplant upper limb inflammatory nodules

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Article type : Make your diagnosis

The Case | Post-transplant upper limb inflammatory nodules

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Running head: Post-transplant upper limb inflammatory nodules

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The Case | Post-transplant upper limb inflammatory nodules

A 38-year-old man with Denys-Drash syndrome received a second ABO-incompatible kidney transplant from a living-related donor without anti-HLA donor-specific antibody. His past medical history also included autoimmune erythroblastopenia due to azathioprine, which was successfully treated with intravenous immunoglobulin and steroids. Induction therapy included a combination of low-dose steroids, rabbit antithymocyte globulin, rituximab, and plasmapheresis. Maintenance therapy included a combination of tacrolimus, mycophenolate mofetil (MMF) and prednisone. The patient had immediate renal function with a serum creatinine (SCr) level of 80 $\mu\text{mol/L}$ on day 5. On post-transplant day 12, his SCr level increased to 110 $\mu\text{mol/L}$, and kidney biopsy showed thrombotic microangiopathy. He received three additional plasma exchanges.

One month later, he presented with several progressive inflammatory nodular skin lesions on his left upper extremity. He had no systemic symptoms, including fever, chills, sweats, cough or weight loss. Physical examination revealed mild swelling of the left upper extremity with multiple painful cutaneous erythematous nodules of sizes ranging from 1 to 3 cm on his left hand, forearm, elbow, and axilla. He reported a finger wound one month before transplantation when cleaning his fish tank (Figure 1). Blood tests revealed a white blood cell count of 8.6 G/L, with a neutrophil count of 7.9 G/L, and a lymphocyte count of 0.2 G/L. The patient's hemoglobin level was 8.9 g/dL, and he had a C-reactive protein level of 24 mg/L with normal liver enzyme values, a SCr level of 105 $\mu\text{mol/L}$ and a tacrolimus trough level of 6.6 ng/mL.

What is the diagnosis?

The Diagnosis | Disseminated *Mycobacterium marinum* infection in a renal transplant recipient

Histological analysis of skin biopsy showed noncaseating granulomatous infiltrate consisting of histiocytes and neutrophils with large necrotic abscesses. Ziehl-Neelsen staining revealed numerous elongated bacilli within the inflammatory infiltrate (Figure 2). Blood cultures were positive for acid-fast bacilli, and body scan was normal. The patient was treated with imipenem, rifampicin, clarithromycin, and tobramycin for presumptive nontuberculous mycobacterial (NTM) infection. One week later, ribosomal 16S-23S internal transcribed spacer (ITS) amplification and sequencing analysis performed on the skin biopsy identified *Mycobacterium marinum* (*M. marinum*). Antibiogram realized from the cultures showed susceptibility to rifampin, rifabutin, ethambutol, amikacin, clarithromycin, linezolid and moxifloxacin. The patient then received a combination of rifampin and clarithromycin, and MMF was tapered down. Clinical follow-up at 9 months post-treatment showed a reduction in the size of the skin lesions. Antibiotic therapy will be maintained for 2 additional months after complete resolution of symptoms.

M. marinum is distributed in aquatic environments such as nonchlorinated swimming pools, salt or fresh water reservoirs, and fish tanks. The incidence of *M. marinum* infection is reported as 0.05-0.27 per 100,000 inhabitants per year. Unlike other opportunistic NTM, *M. marinum*, along with *M. ulcerans*, are pathogenic in non-compromised patients, and these two species are genetically closely related to *M. tuberculosis* (1). Infection is acquired from a soft tissue wound in an aquatic environment and is commonly called “swimming pool granuloma” or “fish tank granuloma”. Cutaneous disease can remain localized at the inoculation site with a single papulonodular lesion, which is usually on an extremity (60%), or it can spread continuously throughout the lymphatic system (25%). As *M. marinum* optimally grows at 30°C, infection is usually localized to the skin, but it can spread to joints and bone (20-40%), or regional nodes (15%). Systemic dissemination is exceptional, affecting only immunocompromised patients (2). The diagnosis is suspected by the mode of infection and confirmed by isolation in 7 to 21 days of *M. marinum* from tissue specimens. Smear microscopy is positive for acid-fast bacilli in 30% of cases, and culture in 70-80% of cases. Molecular biology techniques, such as amplification and sequencing of the 16S-23S ITS, can be performed directly on tissue specimens or on a positive mycobacterial culture. Of note, tuberculin skin testing and interferon gamma release assay can be positive because of cross-reactivity with *M. tuberculosis* (1). Guidelines recommend treatment with two active antibiotics, such as cyclins or clarithromycin and rifampin, at least 2

months after resolution of symptoms, and usually 3 to 6 months in total (3). Surgical debridement may be indicated for joint and bone infections or after antibiotic therapy failure.

In conclusion, our case report highlights the need for a detailed patient interview and systematic biopsy for histopathologic examination and microbiological cultures in cases of opportunistic infections, including NTM infections.

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Figures

Figure 1 | Cutaneous lesions of the left upper limb. (A) Initial ulcerated wound on the forefinger. (B) Ascending spread of the erythematous skin nodules on the forearm, elbow and axilla.

Figure 2 | Skin biopsy. Acid-fast bacilli in the inflammatory infiltrate of the deep dermis (Ziehl staining, ×400).



