

## Mycobacterium abscessus lymphadenitis in bone marrow transplant patient

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### Abstract

Non-tuberculous mycobacteria (NTM) are acid-fast bacteria categorized into rapidly growing and slow growing mycobacteria. NTM are more common in transplant patients who are immunocompromised. Here we report the case of a post- bone marrow transplant adolescent male presenting with submandibular swelling and fever. The gland was excised and the histopathology showed chronic granulomatous inflammation. Culture grew *Mycobacterium abscessus* which was sensitive to amikacin, linezolid and clarithromycin. A good response was achieved on therapy.

**Keywords:** Non-tuberculous mycobacteria, *Mycobacterium abscessus*, Rapid growing mycobacteria.

### Introduction

Non-tuberculous mycobacteria (NTM) are environmental organisms with low virulence. Infections caused by NTM take months or years to manifest clinically.<sup>1</sup> There are increasing number of reports of NTM disease in patients with stem cell and solid organ transplantation. It is estimated to affect 0.4% to 4.9% of transplant patients, which is 50-600 times higher than the general population.<sup>2,3</sup>

Pulmonary symptoms may include chronic productive cough, dyspnoea and haemoptysis. Skin and soft tissue infections being second most common form of NTM infection can present as enlarged lymph nodes which may be painful and erythematous subcutaneous nodules on the extremities. Systemic infections occur in severely immunocompromised patients and bacteraemia is almost always associated with catheter-related infections.<sup>4</sup>

Biological specimens such as abscess fluid, synovial fluid, cerebrospinal fluid, bronchoalveolar lavage fluid and biopsy specimens should be submitted to the laboratory for mycobacterial culture and staining. Therapeutic options for NTM infections include medical, surgical or combined treatment. Slow growers usually respond to the first-line antituberculosis drugs as rifampicin and ethambutol. Rapid growers are highly resistant to

antituberculous medicines and often have inducible macrolide resistance mechanisms. Multiple-drug regimen is intended to prevent emergence of drug resistance when treating NTM infections.<sup>3,5</sup>

We present a case of *Mycobacterium abscessus* lymphadenitis diagnosed in a 15 year old bone marrow transplant patient at Aga Khan University Hospital Karachi in 2016.

### Case Report

A 15 year old boy presented with a gradually increasing swelling of the left submandibular region for 3 weeks and fever for 1 day. The swelling had no ulceration or discharge and was not associated with trauma or dental pathology. The boy was a diagnosed case of  $\beta$ -thalassaemia major and had a bone marrow transplant one year back. He was on cyclosporine, cotrimoxazole and acyclovir chemotherapy. There was no associated cough, weight loss, drenching sweats, bone pains and bleeding or bruising. There was no history of animal exposure.

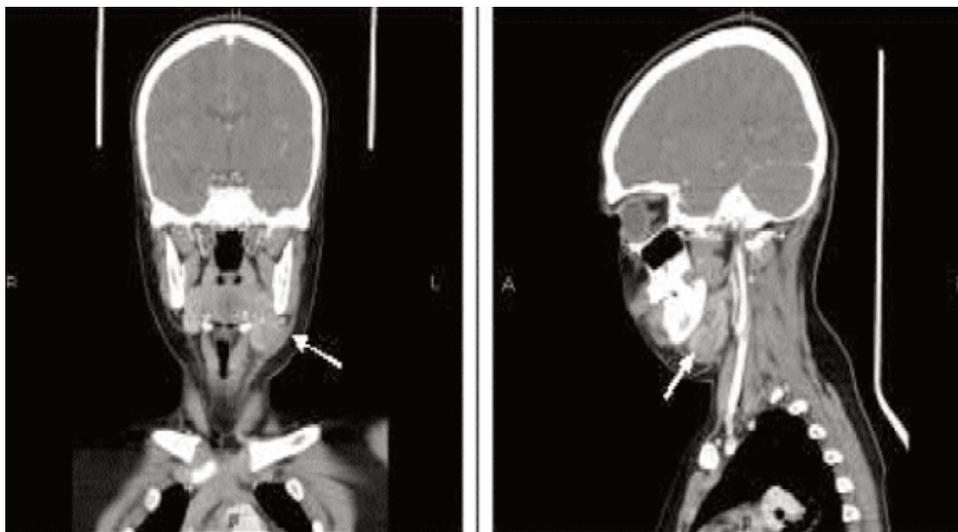
Clinical examination revealed an anxious, febrile boy with a temperature of 101°F. The swelling was warm and tender to touch. It consisted of multiple matted lymph nodes, overlying skin was erythematous, there was no discharging sinus and swelling was not adherent to the bone. Throat and ears were clear on examination and there were no carious teeth. Hepatosplenomegaly, other regional lymphadenopathy or bleeding bruising were not found. Central nervous system, respiratory system and cardiovascular examination revealed no abnormality.

On the basis of history and examination differential diagnosis of infection (nocardia, tuberculosis), haematopoietic (leukaemia) or lymphoid (lymphoma) malignancies were considered.

Initial laboratory investigations revealed Hb 8.3 gm. %, TLC of 7200/mm<sup>3</sup> with 70% neutrophils and 22% lymphocytes, platelets of 163,000 and serum creatinine of 0.4 mg/dl. Peripheral blood smear did not show any evidence of haematological malignancy. Blood cultures remained negative after five days of incubation. CT-head and neck revealed a heterogeneous mass at left mandibular angle displacing the left parotid gland and there was no liquefied abscess formation or collection

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**Figure:** CT-scan head and neck showing heterogeneous density oval shaped mass lesion along the left angle of mandible.

and no bone involvement (Figure-1). Surgical excision of the swelling was done to rule out the possibility of tuberculosis and malignant growth. Specimens were sent for histopathology, culture sensitivity and Xpert MTB/RIF for mycobacterium tuberculosis. Microscopy revealed acid fast bacilli 04/100 fields. Xpert MTB/RIF was negative for *Mycobacterium tuberculosis* and histopathology revealed chronic granulomatous inflammation with necrosis. Bacterial cultures of the specimen remained negative.

As microscopy for acid fast bacilli was positive but Xpert MTB/RIF was negative, the possibility of NTM infection with lymphadenitis was considered and specimen cultures were extended for NTM. Within a week culture grew the colonies *Mycobacterium abscessus* that was fully sensitive to amikacin, linezolid and clarithromycin and intermediate sensitivity to ceftazidime and imipenem. Due to multidrug resistance nature of the organism; patient was started on oral linezolid, clarithromycin and intravenous amikacin. After three weeks of therapy, patient developed signs of renal injury. His creatinine rose to 0.9 mg/dl (> 50 % above baseline). His trough amikacin level were < 10 µg/ml (normal trough levels 5 - 10 µg/ml), complete urine examination was normal and ultrasound abdomen for renal system did not show any abnormality. So rising creatinine was attributed to the nephrotoxic drug (amikacin). The amikacin therapy was stopped, and oral clarithromycin and linezolid was continued with a regular follow-up and monitoring. The creatinine level dropped to baseline one week after stopping amikacin. Patient completed four months of therapy. On follow up patient was doing well with no signs of disease

recurrence.

## Discussion

A total of 160 different species of non-tuberculous mycobacteria (NTM) have been identified to date. Rapidly growing mycobacterial (RGM) species form mature colonies on culture media within seven days and include *Mycobacterium fortuitum*, *chelonae*, and *abscessus*. Slow growing mycobacteria require many weeks to grow and include *Mycobacterium avium*, *kansasii*, and *marinum*. NTM have been increasingly identified as pathogenic cause of disease in transplant

patients with incidence rates ranging between 0.4 and 10%.<sup>6</sup>

Initial septic work-up and ENT examination of our patient remained negative. Complete blood counts and blood smear did not show evidence of leukaemia. His chest X-ray and ultrasound abdomen did not reveal lymph node enlargement of any other region. Surgical excision of the swelling was done, specimens were sent for histopathology (tuberculosis vs. malignancy) and culture sensitivity. Microscopic examination showed 04 acid fast bacilli / 100 fields, histopathology revealed chronic granulomatous inflammation with necrosis and there was no evidence of malignancy. Xpert MTB/ RIF performed on tissue specimen were negative. This gave the clue to non-tuberculous mycobacterial infection. Yellow colonies of *Mycobacterium abscessus* grew on culture in Löwenstein-Jensen (LJ) medium. The isolate was fully sensitive to amikacin, linezolid and clarithromycin and intermediate sensitivity to ceftazidime and imipenem.

*Mycobacterium abscessus* is reported to be the third most frequently recovered respiratory NTM. Other than lungs; *mycobacterium abscessus* causes lymphadenitis, skin and soft tissue infection, bone infection, and otomastoiditis. Affected lymph nodes are usually unilateral, slowly growing and freely movable. An average incubation — period of 4-6 weeks is required before appearance of clinical symptoms. Early non-specific symptoms include loss of weight and appetite with fever occurring in 60 % of children.<sup>7,8</sup>

*M. abscessus* is resistant to the first line antituberculous

therapy. Antibiotics of choice include clarithromycin or azithromycin combined with intravenous medicine (amikacin, cefoxitin, or imipenem) in the treatment of serious skin, soft tissue, and bone infections. Duration of six months of therapy is recommended to treat bone infections due to NTM. Indications for surgery are extensive disease, abscess formation or difficulties in drug therapy due to drug — drug interactions or drug toxicities.<sup>9,10</sup>

Our patient was started on oral linezolid three times daily, clarithromycin twice daily and intravenous amikacin once daily. He was monitored by blood counts (pancytopenia — caused by linezolid) and renal function test (kidney injury — by amikacin) on weekly basis. Rising creatinine levels three weeks after intravenous amikacin were noted in time and managed accordingly. The patient completed four months of treatment with linezolid and clarithromycin. He remained in clinical remission after stopping the treatment.

### Conclusion

Transplant patients are at risk for developing various types of opportunistic infections like in our case; nontuberculous mycobacterial infection. Physicians dealing with post-transplant patients should have a broader vision and Liaison with the microbiologist is of prime importance in accurate diagnosis and therapy. Drug — drug interactions and side effects of long term antimicrobial therapy need to be kept in mind and monitored accordingly. Accurate diagnosis, appropriate therapy and regular monitoring in our patient resulted in successful recovery.

**Approval from Ethical Review Committee:** This case report was approved by the hospital's ethical

review committee.

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**Conflict of Interest:** None.

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### References

1. Keating MR, Daly JS. Nontuberculous mycobacterial infections in solid organ transplantation. *Am J Transplant* 2013; 13 Suppl 4: 77-82.
2. Weinstock DM, Feinstein MB, Sepkowitz KA, Jakubowski A. High rates of infection and colonization by nontuberculous mycobacteria after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant* 2003; 31: 1015-21.
3. Doucette K, Fishman JA. Nontuberculous mycobacterial infection in hematopoietic stem cell and solid organ transplant recipients. *Clin Infect Dis* 2004; 38: 1428-39.
4. Atkins BL, Gottlieb T. Skin and soft tissue infections caused by nontuberculous mycobacteria. *Curr Opin Infect Dis* 2014; 27: 137-45.
5. Esteban J, Ortiz-Perez A. Current treatment of atypical mycobacteriosis. *Expert Opin Pharmacother* 2009; 10: 2787-99.
6. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007; 175: 367-416.
7. Iversen RH, Illum P. Cervicofacial nontuberculous mycobacterial lymphadenitis in children. *Dan Med J* 2012; 59: A4349.
8. Bennett JE, Dolin R, Mandell GL, Blaser MJ, Brown-Elliott BA, Wallace, Jr R. Infections due to nontuberculous mycobacteria other than *Mycobacterium avium-intracellulare*. *Mandell, Douglas, and Bennetts principles and practice of infectious diseases*. 8th. Philadelphia: Elsevier/Saunders; 2015. p. 2844-52.
9. Timmerman MK, Morley AD, Buwalda J. Treatment of nontuberculous mycobacterial cervicofacial lymphadenitis in children: critical appraisal of the literature. *Clin Otolaryngol* 2008; 33: 546-52.
10. Lindeboom JA, Lindeboom R, Bruijnesteijn van Coppenraet ES, Kuijper EJ, Tuk J, Prins JM. Esthetic outcome of surgical excision versus antibiotic therapy for nontuberculous mycobacterial cervicofacial lymphadenitis in children. *Pediatr Infect Dis J* 2009; 28: 1028-30.