CASE REPORT

Non-tuberculous mycobacteria mimic of MDR-TB infection in Pott's disease

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SUMMARY

A 34 year-old woman presented with history of progressive back pain which was diagnosed as Pott's disease with recurrent paravertebral abscess, and had received a total of 23 months of antitubercular treatment for lumbar infection. The patient was non-responsive to treatment and was referred to a higher centre where the infection was finally identified as non-tuberculous mycobacterium (*Mycobacterium fortuitum*) by genotypic testing. The drugs were initiated according to results of drug susceptibility testing by the broth microdilution method. We describe here an unusual case of *M. fortuitum* infection that presented as Pott's disease identified by molecular test which was followed by treatment and successful cure of the disease.

BACKGROUND

Non-tuberculous mycobacteria (NTM) are ubiquitous microorganisms in the environment and are a common but easily overlooked, as a cause of invasive disease in immunocompetent individuals.¹ NTM are often resistant to disinfectants and antibiotics, including those drugs used to treat *Mycobacterium tuberculosis* complex (MTBC) as they are impermeable to nutrients which makes it resistant.^{2–3} More than 150 different species of NTM (ie, *Mycobacterium avium* complex (MAC), *Mycobacterium kansasii*, *Mycobacterium abscessus*, *Mycobacterium chelonae*, *Mycobacterium fortuitum*) are known and treatment of species may differ from each other.^{4–5} In India, accurate identification of NTM to the species level is not a part of routine laboratory practice. Many isolated mycobacteria species are treated empirically with antituberculosis drugs.⁶ NTM infections have also been described in patients with osteoarthritis and other bone infections but infections of the spinal cord have been reported only in few cases until now. We report and describe an unusual case of Pott's disease with NTM. We also describe the clinical manifestations of NTM infection in this patient, differential diagnosis, investigations, treatment and outcome.

CASE PRESENTATION

A 34-year-old woman, a housewife and residing in northern part of India presented to the neurosurgery department of a premier institute situated in North India with history of persistent and chronic radiating back pain since 2 years. On examination power was 4/5 in bilateral lower limbs, with mild spinal tenderness. The patient was a known case of Pott's spine at L1–2 levels with recurrent

paravertebral abscess. She had received multiple courses of antibiotics and antitubercular treatment (ATT) since 2 years; she had received isoniazid, rifampicin, streptomycin, pyrazinamide and ethambutol for 4 months followed by isoniazid, rifampicin and pyrazinamide for about 19 months but without any improvement in lower limb power. There was no history of any spinal surgery, disease or injury to the patient prior to 2 years of illness. Before coming to our centre, she had undergone laminectomy of the lumbar vertebrae for spinal stenosis 14 months back. The patient was then referred to our centre, as a case of drug-resistant *M. tuberculosis*. The patient was admitted, and on examination it was found that the vitals were stable, bulk of lower limbs was adequate, tone was normal, power was decreased in bilateral lower limbs but there was no sensory deficit. There was no history of any pulmonary disease, diabetes or hypertension. The patient had not been pregnant since 5 years and was G₁+P₁+0. The routine haematological and clinical chemistry parameters were normal (haemoglobin 12.6 g/dL, total leucocyte count 7500/mm³, platelet count 245 000/mm³, alanine transaminase 58 U/L, aspartate aminotransferase 32 U/L, alkaline phosphatase 66 U/L, serum creatinine 1.2 mg/dL) except for a raised erythrocyte sedimentation rate which was 66 mm/hour. HIV test was non-reactive to both rapid tests and ELISA. Chest X-ray posteroanterior and lateral films were obtained and results showed that there was no signs of active diseases in either of the lungs. Cardiac shadow, mediastinum and pleural spaces were normal. Sputum samples were tested for the *Mycobacterium* and aerobic bacterial infection by microscopy and culture but results remained negative on various occasions. The MRI showed altered marrow signal intensity of L1 and L2 vertebra, with involvement of intervening disc that appeared hypointense on T1-weighted image and heterogeneous hyperintense on T2-weighted image. The differential diagnosis based on clinical and radiological findings (granulation tissues compressed the thecal sac) were suggestive of Pott's disease, tumorous pathologies with secondary infections and septic arthritis. The patient was then advised CT-guided fine-needle aspiration (FNA) for mycobacterial culture and susceptibility testing and also to rule out cancer and other infections. The tests were performed on the pus sample collected by CT-guided FNA and a final diagnosis was made on basis of test results. There was positive response to specific anti-NTM medication which was evidenced by series of MRIs.

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INVESTIGATIONS

Microbiological tests

The CT-guided FNA pus specimen was collected in a sterile container by lumbar puncture. Smear microscopy was performed by Ziehl-Neelsen staining and culture was performed by the BacT/ALERT three-dimensional (3D) system⁷ and conventional Lowenstein-Jensen (LJ) method.⁸ Smear microscopy for acid-fast bacilli was negative. The culture was monitored continuously by the BacT/ALERT 3D system. After 4 days, the vial signalled positive growth which was then confirmed by smear microscopy. LJ culture also turned out to be positive in 6 days. The isolate was initially labelled as rapidly growing mycobacteria by its rate of growth. The isolate was suspected to be *M. chelonae* or *M. fortuitum* by its growth pattern in paranitrobenzoic acid, and MacConkey's agar, as well as an inability to form any pigment on LJ medium, tolerance to 5% NaCl, positive nitrate reduction and a positive arylsulphatase test (within 3 days). The *M. tuberculosis* protein 64 antigen test was also performed to detect *M. tuberculosis* complex-specific antigen and the test results were negative.

Molecular methods

The isolate was presumptively identified as a rapid grower, probably; *M. chelonae/fortuitum* by conventional methods. When the isolate was tested with the genotype common mycobacteria as per the manufacturers' protocol, it was identified as a strain of *M. fortuitum*. Antibiotic susceptibility tests were performed for amikacin, cefoxitin, ciprofloxacin, moxifloxacin, clarithromycin, doxycycline, imipenem and linezolid by the broth micro-dilution method as recommended by American Thoracic Society guidelines. It was found to be sensitive to amikacin, clarithromycin, linezolid, doxycycline, moxifloxacin and ciprofloxacin.

TREATMENT

The patient had received prior antitubercular drugs isoniazid, pyrazinamide, ethambutol and rifampicin with suspicion of Pott's disease due to *M. tuberculosis* for 23 months before being referred to our centre. After *M. fortuitum* was identified in two separate pus samples by the culture and molecular methods the therapeutic regimen was changed to amikacin (1 g intramuscular once a day), clarithromycin (500 mg once a day) and moxifloxacin (400 mg once a day) which were continued until 18 months according to the antibiogram. The patient was also given linezolid (300 mg two times a day) initially for 1 month.

OUTCOME AND FOLLOW-UP

For this patient, the radiological assessment was carried out by a follow-up MRI at the end of 6 months (figure 1A), 12 months (figure 1B) and at the termination of the treatment after 18 months (figure 1C). The first MRI fulfilling the criteria of suspected Pott's disease was compared with the MRI after initiation of ATT, and then series of MRIs were performed to follow radiological resolution of the spinal lesion. Her neurological symptoms and radiological findings improved gradually with anti-NTM medication. At the time of publication, the patient had recovered quite well and had been living a normal life.

DISCUSSION

Pott's disease is one of the oldest diseases affecting humans⁹ and continues to be a significant health burden in developing countries such as India and accounts for about 2% of all tuberculosis

Figure 1 (A) Contrast MRI sagittal cut showing variable destruction of two vertebral bodies along with disc and vertebral enhancement. The granulation tissues are compressing the thecal sac. (B) Contrast MRI sagittal cut after 6 months, showing localisation of granulation tissue along with features suggestive of healing after chemotherapy (antitubercular treatment) (the patient had clinically improved) enhancement still present. (C) Contrast MRI sagittal cut after 18 months follow-up showing a significant healing and redefinition of the collapsed vertebral bodies and disappearance of granulation tissue. The thecal sac is free from compression.

(TB) cases diagnosed.¹⁰ Pott's disease is commonly associated with poor outcomes because of delay in diagnosis due to various reasons. The morbidity and mortality of this disease continues to pose a challenge to the treating physicians and surgeons. Paraplegia is the most serious complication which usually develops when cases remain undiagnosed or untreated until late during the natural progress of the disease.^{10 11}

Our country too echoes the common mentality of other developing nations, that if the initial treatment is unsuccessful, the clinician usually suspects it to be a multidrug resistant (MDR) case.¹² It is suggested that MDR-TB should be suspected when a patient of pulmonary or extrapulmonary TB fails on the category (CAT) I (2–3 months of initial treatment with isoniazid, rifampicin and ethambutol followed by 4 months of treatment with isoniazid and rifampicin on alternate days) or CAT II (2 months of initial treatment with isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin and then 1 month with isoniazid, rifampicin, ethambutol, pyrazinamide followed by 5 months with isoniazid and rifampicin on alternate days) treatment for tuberculosis as per the DOTS protocol.¹³ In this case, the patient was given multiple courses of ATT despite improvement and was eventually suspected to be a case of MDR-TB (therapeutically refractory case) on the basis of clinicroadiological failure of treatment. On the basis of history of disease persistence, the treating physician advised for repeat MTB culture and drug susceptibility testing.

In this case culture growth indicated a rapid growing isolate, in all likelihood a NTM isolate. Overall NTM infections are rare in the spinal cord and very little information is available about the infection and its management. Duttaroy *et al*¹⁴ found *M. fortuitum* in Pott's disease, as a solitary case and Metta *et al*¹⁵ found *M. chelonae* infection in the spinal cord and proposed diagnosis and management.

The conventional biochemical tests used to identify different mycobacterial species are complex and time consuming.¹⁶

WHO emphasises the need to reduce the time for culture, identification and drug resistance for MTB detection by employing the use of rapid methods such as line probe assays.¹⁷ The GenoType Mycobacterium common mycobacteria/additional species (CM/AS) assay (Hain's Life Sciences, Nehren Germany) is a commercially available kit developed to differentiate and identify different species of NTM from cultures.¹⁸ The GenoType Mycobacterium CM/AS assay is found to be an accurate and reliable test for the identification of mycobacterial species.¹⁹ The strain typing of *M. fortuitum* in the present case was carried out by using the genotype CM/AS assay.

The approach to therapy depends on factors such as the species of NTM isolated, the site of infection, drug susceptibility testing and the patient's underlying conditions. Many strains of NTM are relatively resistant to antituberculosis drugs.²⁰ Based on the antibiotic susceptibility tests the patient was administered clarithromycin, amikacin and moxifloxacin for 18 months and linezolid initially for 1 month. According to American Thoracic Society the therapy of extrapulmonary disease caused by *M. fortuitum*, *M. abscessus* and *M. chelonae* should include drugs such as amikacin and clarithromycin, based on in vitro susceptibility tests.²¹ The patient responded to treatment which was observed in series of MRIs.

We suggest the need for documentation of such unusual cases by the physicians so that proper strategies can be formulated to tackle them. The health authorities in tropical countries must ensure the need for easy accessibility to specialised laboratories for accurate bacterial identification in such cases. When the initial treatment fails with standard ATT then physicians can also consider NTM or MDR infection as a probable cause of Pott's diseases.

Learning points

- ▶ Non-tuberculous mycobacteria (NTM) can also be a causative agent of Pott's disease in the tropical settings even in immunocompetent individuals.
- ▶ Lack of early identification of NTM can lead to diagnostic delay and patients are usually then managed empirically as drug-resistant cases based on the clinical criteria alone.
- ▶ When initial treatment fails it should provoke thought towards NTM infection. This may save the patient needless and superfluous multidrug therapy, which comes with side effects and some potentially dangerous ones also.

Competing interests None declared.

Patient consent Obtained.

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