Fatal Disseminated *Mycobacterium chelonae* Infection in an Immunocompromised Host – A Unique Presentation

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**Abstract**

Disseminated disease due to rapidly growing non tuberculous mycobacteria especially in the immunocompromised host is being increasingly reported. The usual manifestations of disease being skin and soft tissue infection, post operative wound infection and pulmonary disease.

We present a case of a disseminated infection due to *Mycobacterium chelonae* with features of chronic meningitis and knee joint arthritis in a patient with systemic lupus erythematosus on systemic steroids and mycophenolate. *M chelonae* was isolated from both synovial and cerebrospinal fluid and anti microbial therapy was initiated as per sensitivity results. However the patient’s clinical condition continued to worsen and she succumbed to her illness.

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**Introduction**

Rapidly growing mycobacteria are organisms that are ubiquitous in the environment. In the immunocompetent host they cause post operative wound infections, skin and soft tissue infections and pulmonary disease whereas they cause disseminated disease in the immunosuppressed host. Meningitis is an uncommon manifestation of this disease and to date there are no reports of *Mycobacterium chelonae* being isolated from the cerebrospinal fluid (CSF). These rapidly growing mycobacteria can be readily identified and differentiated from the other non tuberculous mycobacteria by their ability to grow on solid media within 7 days and their inherent resistance to first line anti-tuberculous drugs. The treatment of meningitis is particularly challenging as many of the drugs used routinely have poor penetration into the CSF.

We describe a case in a young lady, recently diagnosed with systemic lupus erythematosus on steroids and mycophenolate who presented with chronic meningitis and knee arthritis. *Mycobacterium chelonae* was identified from both the CSF and synovial fluid by the eighth day. She was initiated on appropriate treatment but progressively worsened and finally succumbed to her illness.

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**Case Report**

A thirty year old housewife from South India, presented with complaints of high grade intermittent fever with chills and holocranial headache of four weeks duration. She also had complaints of progressive altered sensorium of one week duration. She did not have vomiting, seizures or loss of consciousness. Two weeks prior to admission she had also noticed pain and swelling in the right knee joint. There was no history of trauma to the affected knee joint in the recent past.

She had been diagnosed to have systemic lupus erythematosus six months earlier and had been on prednisolone (initially 1 mg/kg/day and then tapered) and mycophenolate.
Fig. 1: Smooth non chromogenic colonies of rapidly growing non tuberculous mycobacteria seen on the Lowenstein Jensen Medium

She was not known to have diabetes, HIV or any other immunosuppressive state. There was no history of animal contact or recent travel and she had no addictions.

On physical examination she was febrile with a temperature of 101°F, tachycardic with heart rate of 108 beats/min and a blood pressure of 110/70 mm Hg. Neurological examination revealed that she was drowsy but arousable and had bilateral upper motor neuron signs in the form of hyperreflexia and bilateral extensor plantar response. She had nuchal rigidity and signs of meningeal irritation. Examination of the musculoskeletal system revealed a swollen tender and red right knee joint. She did not have any skin or mucosal lesions. The rest of the systemic examination was normal.

On admission her haemoglobin was 12 g/dL and total count was 5,700 cells/mm³ with a normal differential and platelet count. Biochemical parameters revealed normal renal and hepatic functions. However she did have a hyponatraemia of 120 mmol/L. She was euglycaemic and serological tests for Hepatitis B, C and HIV were negative. Her erythrocyte sedimentation rate was 108 mm at the end of 1 hour and CRP 126 mg/L. She had a subnephrotic range proteinuria and the anti nuclear antibody was speckled positive. Magnetic resonance imaging of the brain and a chest radiograph were both normal.

A right knee joint synovial fluid aspiration revealed a cell count of 11,500 cells/cu mm with 90% lymphocytes. The fluid was sent for bacterial and fungal cultures which were negative. The fluid that was sent for mycobacterial culture showed acid fast bacilli (AFB).

A cerebrospinal fluid (CSF) analysis showed a lymphocytic pleocytosis (70%) with increased protein of 71 mg% and reduced sugar of 27 mg%. CSF bacterial and fungal cultures were negative. The CSF mycobacterial smears were negative.

A presumptive diagnosis of a disseminated mycobacterial infection with chronic meningitis and right knee joint arthritis was made and the patient was started on standard four drug anti tuberculous therapy with intravenous steroids as per Thwaites protocol.19

On the eighth day, both the synovial and CSF mycobacterial cultures grew smooth non chromogenic colonies of rapidly growing non tuberculous mycobacteria (Figure 1).

The mycobactria grew on Maconkey media and Lowenstein Jensen media with 3% sodium chloride but not on ferrous sulphate containing media. It produced arylsulphatase in 3 days and did not produce nitrate. Based on the above reactions it was identified as M chelonae.

The isolate was susceptible to amikacin, azithromycin and linezolid and resistant to ofloxacin, tetracycline and trimethoprim sulphamethoxazole.

Following this the patient was switched to a regime of Inj Amikacin 15 mg/kg once a day, Tab levofloxacin 750 mg once a day and Tab clarithromycin 500 mg twice a day with an aim to continue therapy for a minimum duration of 12 months in view of the disseminated disease and underlying immunosuppression. However the patient’s neurological condition progressively worsened and she succumbed to her illness on the 14th day of hospital admission.

Discussion

Mycobacterial species other than M. Tuberculosis complex and M. leprae are classified as non tuberculous mycobacteria (NTM). These are widely distributed in the environment and can be found in soil and water, including both natural and treated water sources. As per the Runyon classification used for classifying mycobacterial species, M chelonae is classified as a rapid grower along with M abscessus and M fortuitum.1

The spectrum of clinical manifestations produced by rapidly growing mycobacteria (RGM) ranges from localised to disseminated disease depending on local predisposition and degree of immunosuppression.2 In non-HIV patients, RGM’s may cause localised pulmonary disease with or without adenopathy, skin and soft tissue infections,3 prosthetic joint infections,
multifocal osteomyelitis, bursae and skin ulcers. Most of these syndromes except for lung disease commonly develop following trauma. M. Chelonae has also been reported to produce post LASIK keratitis (laser-assisted in situ keratomileusis).4 Rare manifestations include isolated lymphadenitis and endocarditis. Disseminated disease usually with widespread skin and soft tissue lesions occurs almost exclusively in the immunocompromised setting. AIDS, solid organ transplant and immunosuppressive drugs are the common settings for disseminated disease.2 A retrospective analysis of 100 M. Chelonae isolates over a 10 year period showed that 62% of the patients with the infection were receiving corticosteroids.5

Surgical site infections are well described with the RGM’s particularly with cardiothoracic surgery, cosmetic surgery and augmentation mammoplasty. M. Fortuitum and M. chelonea produce post thoracic surgery sternal wound infections, osteomyelitis and mediastinitis.6

M chelonea surgical site and wound infections are frequently associated with contaminated tap water. Nosocomial infections have also been associated with contaminated gentian violet used for skin marking in plastic surgery.7 Other sources of nosocomial M chelonea infections include implanted devices (e.g., catheters) and injection site abscesses. A hospital outbreak in India was associated with the water used to rinse endoscopes for laparoscopic surgery, resulting in 145 wound infections in 35 patients. Pseudo-outbreaks have been associated with contaminated endoscopes.8 No human-to-human transmission has been documented.

RGM’s causing central nervous system (CNS) disease is uncommon. A review of 19 cases of CNS disease caused by RGM’s showed that the commonest organism isolated was M. Fortuitum (13 out of 19 cases) followed by M. Abscessus and M. mucogencicum (3 cases each). There were no reports of M. Chelonae causing CNS disease.9 Most of the reported cases had disseminated disease or occurred following surgical procedures or penetrating trauma.

Musculoskeletal disease caused by RGM’s is usually in the form of osteomyelitis following surgical wound infection or trauma and prosthetic joint infections. Chronic monoarthritis following trauma has also been reported.10

The recommended laboratory diagnosis of NTM includes phenotypic and genotypic methods. As per the British thoracic society guidelines 2007 for laboratory diagnosis of NTM, the RGM’s (especially M. chelonea, M. abscessus, and M. fortuitum) should be identified to the species level using a recognised acceptable methodology, such as PCR restriction analysis (PRA) or biochemical testing,11,12 M fortuitum may produce similar microbiological characteristics and delay diagnosis. M fortuitum can be differentiated from M chelonea based on rate of growth, and biochemical tests, including growth on Lowenstein-Jensen medium with NaCl to a final concentration of 5%, positive nitrate reduction test and positive iron uptake,7,13

Susceptibility of RGM to eight agents, including amikacin, cefoxitin, clarithromycin, ciprofloxacin, doxycycline, linezolid, sulphamethoxazole, and tobramycin, can also be used indirectly to facilitate identification of M. abscessus, M. chelonea, and M. Fortuitum. M chelonea being inherently resistant to conventional anti tuberculous agents, drug susceptibility is always recommended. Isolates of M. chelonea are susceptible or intermediate in susceptibility to tobramycin (100%), clarithromycin (100%), linezolid (90%), imipenem (60%), amikacin (50%), clofazimine, doxycycline (25%), and ciprofloxacin (20%). For M.chelonea, tobramycin is more active in vitro than amikacin. Imipenem is preferred to cefoxitin because M. chelonea isolates are uniformly resistant to cefoxitin.14

The recommended treatment for RGM’s is usually combination therapy except for minor skin infections where doxycycline or ciprofloxacin can be used for M. Fortuitum infections and clarithromycin can be used for M.chelonea infections. Quinolones should never be used as single agents because of the risk of developing resistance.15 Combination therapy is required for more serious infections with the use of at least one parenteral agent. These patients may be switched to oral therapy once the infection is resolving. The treatment for CNS disease is even more challenging as the usual drugs used such as clarithromycin and amikacin have very poor CNS penetration.16 Carbapenems, quinolones, cotrimoxazole and doxycycline have better CNS penetration. To overcome this problem of poor CNS penetration, intraventricular and intrathecal administration of antibiotics have been attempted and are advised if there is no improvement with the conventional route of antibiotic administration.17

The usual duration of treatment in severe or disseminated disease is usually a minimum of 1 year. Longer therapy or suppressive therapy may be needed in certain situations. Linezolid and tigecycline are two newer agents with particularly good activity against the RGM’s. Linezolid has excellent CNS penetration and can be given orally but long term use may result in bone marrow suppression.18 Tigecycline is only available as an injectable agent but is more effective than the other tetracyclines. However it has a very poor CSF penetration.

The role of adjunct corticosteroids and interferon gamma has not been studied.
Conclusion

RGM’s can cause a wide range of infections particularly in the immunocompromised host. Our patient had SLE and was on steroids and mycophenolate. We diagnosed her to have disseminated *M chelonae* infection, presenting with a chronic meningitis and a right knee joint arthritis. To the best of our knowledge there have been no reports of *M.chelonae* meningitis.

A high index of suspicion is warranted in patients with advanced immunosuppression for early diagnosis and treatment of the disease in order to prevent disease associated mortality, as evident from the fatal outcome of this case. Our patient was receiving conventional anti-tuberculous therapy till the culture reports were ready. Species identification of RGMs with antibiotic susceptibility is the cornerstone of management. Anti microbial therapy as per sensitivity results should be given for a minimum duration of 12 months in patients with disseminated disease or immunosuppression. CNS disease requires drugs with adequate CSF penetration and a combination of carbapenems, linezolid and cotrimoxazole/quinolones may be a suitable option.

We submit this case for its unique presentation – there are no reports of *M.chelonae* being isolated from the CSF, and also to highlight the increasing incidence of non tuberculous mycobacterial disease particularly in the immunocompromised host. The diagnostic difficulties and management challenges are also discussed.

References