Disseminated Infection Due to *Mycobacterium chelonae* with Scleritis, Spondylodiscitis and Spinal Epidural Abscess

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Mycobacteria other than tuberculosis (MOTT) have a low incidence as pathogens in human pathology. The most frequent clinical expression is the disseminated disease in subjects with compromised cellular immunity. Bacteriological characteristics in culture can generate confusion with other pathogens, which delays the appropriate diagnosis and treatment. We present a case of a disseminated infection due to *Mycobacterium chelonae* with scleritis, spondylodiscitis and spinal epidural abscess in a man with a medical background of cellular immunity deficit induced by therapeutic drugs. The antibiotic scheme of twenty-one weeks, during the follow-up period, controlled the infection, however, the optimum duration of treatment has not been established.
Key-Words: *M. chelonae*, scleritis, spondylodiscitis, spinal epidural abscess.

The environmental non-tuberculous mycobacteria (NTM), previously known as atypical mycobacteria or mycobacteria other than tuberculosis (MOTT), constitute a group of pathogens widely spread in nature. There are a wide variety of probable sources of these infections, although there is no evidence of transmission between human beings. The most frequent clinical form is the disseminated disease which generally involves subjects with compromised cellular immunity [1]. It is hard to assert a definitive diagnosis because of the low index of recovery shown in the bacteriological studies and laboratory cultures, as well as the bacteriological characteristics that can generate confusion with other pathogens. The optimum time of treatment has not been established yet, as it has to be focused through bacteriological susceptibility [2].

We reported a case of a patient who developed a disseminated infection due to *Mycobacterium chelonae* with scleritis, spondylodiscitis and spinal epidural abscess.

Case Report

A 67 year-old man, with a medical background of severe medullar hypoplasia treated with interleukin-2, blood transfusions, Erythropoietin, colony stimulating factor and thalidomide in doses of 150-mg/per day, was admitted with dorsal pain and fever. Ten months prior to admission, he had presented a nodular necrotizing scleritis in his left eye. Presumptive diagnosis of infection due to *Nocardia* spp. was made and a treatment with trimethoprim-sulphamethoxazole, amikacin and corticosteroids was started. Culture of the material obtained from the ocular lesion developed Gram-positive bacilli of slow growth, with no growth in Thayer-Martin plus antibiotic medium.

At admission, the physical examination revealed a fever (38.5ºC), dorsal pain with sensitivity at D7-D8 and the presence of scleritis in his left eye with abscesses of the lachrymal gland. A computed tomography scan of the dorsolumbar spinal region was performed and showed a compromise in the bone structure at the D7-D8 level with a partial collapse of the last vertebral body. Magnetic resonance imaging (MRI) showed the replacement of the bone tissue between D7-D8, with compromise of the intervertebral disc and the medullar channel. Bone scintigraphy showed an abnormal concentration of the radioisotope in the affected vertebrae.

Samples were taken from the eye abscesses and the vertebrae segment was stabilized with titanium rods. The histopathology of the tissue obtained by surgery revealed the existence of granulomas with Gram, Giemsa and Ziehl-Neelsen stains negative. The culture of ocular material and that of the vertebrae showed the development of *Mycobacterium chelonae*, resistant to ciprofloxacin, vancomycin, rifampicin, ethambutol and imipenem and sensitivity to doxycycline, amikacin and clarithromycin.

The patient was treated with doxycycline 200 mg t.i.d., clarithromycin 500 mg every 12 hours, rifampicin 600 mg per day, and amikacin 7.5 mg/kg t.i.d. over the course of 3 weeks. Maintenance therapy was continued with the first two, with the same dosage for four and a half months. The patient had a good clinical and ophthalmological response. No evidence of neurological sequelae was observed during the thirty month follow up period.

Discussion

The NTM belong to mycobacterial species other than *M. tuberculosis* complex or *M. leprae*. *M. chelonae* together with *M. fortuitum* and *M. abscessus* are within the environmental mycobacteria of rapid growth, in accordance with the Runyon Classification [1]. Since 1986 significant changes have been made in the taxonomy of this group of mycobacteria. As a result of DNA-DNA hybridization and restriction fragment length polymorphism (RFLP) studies, it is possible to detect the different mycobacteria that compose this group and their sensitivity/reaction to different antibiotics [2].

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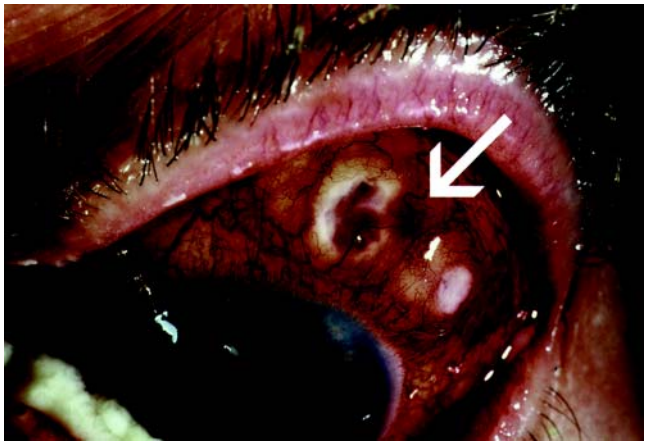
Figure 1. Abscess with necrotizing scleritis in the left eye.



Transmission of infection due to NTM occurs by inhalation of aerosols or by inoculation, but normally it is not transmitted from person to person [3].

The incidence of NTM symptomatic disease will probably increase as the number of immunosuppressed patients continues to rise [3-6].

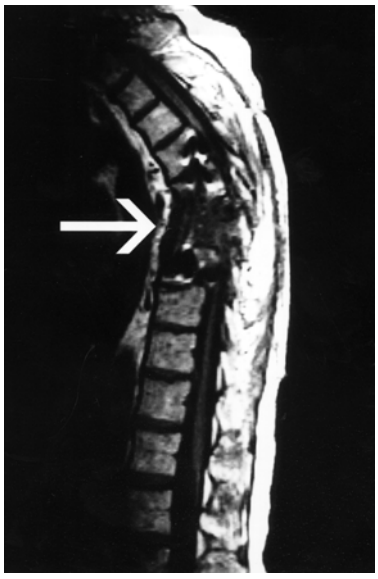
The clinical spectrum of NTM disease depends on the characteristics of NTM species. Clinical manifestations include surgical infections of the dermis and soft tissues, lung involvement, post-traumatic and catheter related infections [7,8]. Generally speaking, *M. fortuitum* is isolated mainly from post-surgeries (osteomyelitis of the sternum, breastbone postthoracotomy) [9], while *M. chelonae* and *M. abscessus* cause skin/dermis and soft tissues infections [10]. Additional communications report cases of keratitis caused by *M. fortuitum* and *M. Chelonae* [11,12].

The infection incidence of *Mycobacterium chelonae* remains low (1%) although its identification has increased since the appearance of the AIDS pandemic and the use of immunosuppressive treatments. The incubation process of this illness ranges from 1 to 3 weeks and the clinical manifestations become evident 4 to 6 weeks later. They generally appear in the skin and tissues as pyogenic abscesses and can develop slowly into subacute or chronic swellings, ulcers and fistulae as in the patient referred. Recurrence is frequent if only local treatment is applied [11,13].

Ryup Sup Kim et al. [13] published a case of osteomyelitis and tissue infection in a previously healthy patient whose poor clinical, microbiological and histopathological expression caused an 8-month delay in confirming diagnosis.

The referred patient presented D7-D8 spine pain at a sensitive level, 10 months after the ocular compromise with no remission of the symptoms or signs of this localization despite empiric treatment. These findings are consistent with spondylodiscitis and epidural abscess due to *Mycobacterium tuberculosis*, and are more frequent among patients with diagnosis of disseminated tuberculosis [14].

Figure 2. Dorsal backbone MRI. Replacement of the bone tissue between D7-D8, with compromise of the intervertebral disk and the medullar channel.



Various authors reported keratitis by non-typical quick growth mycobacteria (*M. chelonae* and *M. fortuitum*) associated to eye surgery and contact lens use. Less frequent cases of blepharitis, scleritis, endophtalmitis, dacryocystitis, and orbital localizations have also been reported [11,12,15].

The referred patient presented a form of necrotizing and nodular long-term scleritis, which coincides with the finding of *M. chelonae* in the tissue compromise referred to in the literature [5,6,11,15].

We must suspect the involvement of quick growth mycobacteria in an immunocompromised host, whose biopsy material shows acid-fast bacilli and/or granulomatous inflammation [16]. Histopathology studies show this inflammation in chronic infections or polymorphonuclear infiltrations, micro abscesses, and necrosis in acute infections. Unlike tuberculosis, caseosis is rarely found [6]. The negative Ziehl-Neelsen stain in the samples obtained from the injuries of the patient, delayed the diagnosis. The final diagnosis requires isolating and identifying the microorganism. The recovering rate is low (bacterial isolation is only possible in a third of samples) making it necessary to take several samples to obtain it [6,11]. In this patient, a differential diagnosis between *M. chelonae* and *M. fortuitum* was made by phenotypic identification. It was based on the rate of growth, temperature of growth, production of pigment and biochemical tests, including Lowenstein-Jensen medium with NaCl to a final concentration of 5%, nitrate reduction test and iron uptake.

The *M. chelonae* bacteriological characteristics in cultures can be confused with *Nocardia* spp. and *M. fortuitum*'s, which in many recorded cases delayed the appropriate diagnosis and treatment [6,11]. Sophisticated molecular diagnostic methods are available to identify a great number of NTM

species. Biochemical characteristics of *M. chelonae* isolation are: growth in MacConkey positive arylsulphatase medium in 3 days, negative iron uptake and a negative nitrate reduction test. *M. fortuitum* isolates grow in MacConkey medium at 42ºC and in Lowenstein-Jensen 5% NaCl, show a positive arylsulphatase test in 3 days, positive nitrate reduction activity and a positive iron uptake test [3,17].

The anti-NTM drug susceptibility pattern is often typical of different species. *M. chelonae* is resistant to antituberculous drugs, so sensitivity tests must be carried out first. Clarithromycin is one of the usually chosen drugs for atypical mycobacterial infections, due to its long plasmatic life and good tissue penetration, but amikacin is also effective. Treatment must last from between 4 weeks to 6 months after the resolution of the clinical signs, even though the duration of the therapy has not been determined. In cases of tissue compromise, surgical debridement must be performed [3,18-21].

The therapeutic scheme based on doxycycline, clarithromycin, rifampicin and amikacin for three weeks followed by a suppressive therapy with the first two for a further 18 weeks, complemented by the removal of the affected tissue at the eye and osteoarticular level, achieved biological healing.

The finding of *M. chelonae* at an osteoarticular level in the referred patient is rare according to the consulted literature.

To conclude, we must point out the importance of considering a high rate of infection by quick growth mycobacteria in patients with immunological compromise when carrying out the bacteriological investigation [22]. This consideration becomes relevant due to the fact that the bacteriological characteristics in cultivation make it possible that, in non-specialized laboratories, *M. chelonae* could be confused with other pathogens, especially *Nocardia* spp. This leads to a delay in the diagnosis and treatment in many reported cases, as in the referred one [3,4,22]. The therapeutic scheme, oriented by the antibiogram, is a basic condition to obtain a favorable clinical outcome and to improve the prognosis of these patients. Moreover, since the ideal duration of treatment has not been established, the period used in the referred case seems to ensure the control of the infection during the time the patient was under observation. The medical management of a spinal epidural abscess included neurological and radiological localization of the fluid collection, surgical drainage, the identification of the etiological agent and, finally, the specific antibiotic therapy.

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