

Ganglionic Mycobacteriosis associated to *Mycobacterium colombiense* in a Seropositive HIV Patient.

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Abstract

Mycobacterium avium complex (MAC) is a heterogeneous group of species found in several environmental sources and that exhibit variable degrees of pathogenicity. Among the MAC members, *M. colombiense* has been related to pulmonary disease and disseminated infection in HIV-infected patients in Colombia. This entity, without adequate treatment; evolves to fatal outcomes. Macrolides should not be used as monotherapy because resistance occurs rapidly. There is currently no consensus concerning the optimal duration of therapy, but several authors recommend approximately 6 months of therapy. Have been reported successful treatment with chemotherapy alone or combined with surgery.

Keywords: *Mycobacterium colombiense*; Ganglionic disease; ELISAP; MAC

Case Report

A man, 39 years of age, single, without profession, alcoholic, single, man who has sex with men (MSM), seroconcordant couple who died of AIDS. He consulted the institution for a clinical picture of 1 month of evolution consisting of subjective, intermittent fever that appears at intervals of 3 to 5 days, associated with chills, asthenia, adynamia and intermittent diarrhea without blood, plus 1 month of onset of cervical and inguinal adenopathies (not susceptible to biopsy), not painful, due to which he consulted at the first level of attention, where they perform studies including presumptive HIV test which is positive and is confirmed with a 4th generation test different from the first and is referred to the HIV AIDS program with a picture compatible with recently diagnosed HIV infection, acute mononucleosis syndrome to study/acute retroviral syndrome documenting HIV viral load of 240,315 copies/m log 5.38 and a CD4 count of 16 cells/ μ l (4.22%). Opportunists were discarded (Table 1) and the antiretroviral regimen was prioritized in a patient with severe diseases including tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) + lopinavir/ritonavir (LPR/r) and primary prophylaxis was indicated with trimethoprim sulfamethoxazole 160/800 mg per day and Azithromycin 1,250 mg per week. He was admitted 2 months later referring to sharp chest pain in the right hemithorax, in addition to fever and night sweats without other associated symptoms. With chest CT scan (Figures 1 and 2) that reported neck lymph nodes (not susceptible to biopsy), axillae and mediastinum, defining a mediastinoscopy with biopsy. The focus was an early inflammatory syndrome immune reconstitution and chronic mononucleosis syndrome under study. The initial direct microbiological studies were negative for MTB, common germs and fungi (Table 1). The final culture report by Lowenstein Jensen and MGIT in the mediastinal ganglion was positive for *Mycobacterium colombiense* and was confirmed by MALDITOF mass spectrometry.

Taking into account the interactions of rifampicin with protease inhibitors (PI), the antiretroviral scheme was rotated to TDF / FTC associated with efavirenz and empiric treatment was started with clarithromycin 500 mg vo/12 h+Rifampicin 300 mg vo/12 h+Ethambutol 1200 mg vo day agreed to 10-12 months. Sensitivity tests for MIC of non-tuberculous mycobacteria revealed sensitivity to claritromizine and moxifloxacin and resistance to linezolid (Table 1). The patient evolved towards improvement, in the absence of fever and adenopathies resigned.

Discussion

Non-tuberculous mycobacteria (MNT) are usually microorganisms that are difficult to isolate, due to the requirement of special culture media, slow growth, and complexity in obtaining representative samples; Therefore, the evolution of diagnostic methods has allowed and improved the diagnostic opportunity.

MNT belong to the Mycobacterium family, which are taxonomically divided into tuberculous, lepromatous and non-tuberculous; The MAC complex (*Mycobacterium avium* complex) is part of this last category, which is usually found in the environment, either in the soil or in the liquid medium. Transmission from person to person has not been demonstrated, unlike what usually occurs in tuberculous mycobacteria.

The majority of infections by this group of mycobacteria have similar clinical findings, in almost all cases they present lymphadenopathy, pulmonary symptoms and in those guests with some type of disturbance of their immune system, disseminated disease is usually seen [1]. The virulence mechanism of the MAC complex is highly conserved between species, being characteristic the intracellular multiplication and the evasion of the immune system to proliferate and cause disease [2].

It is a recently discovered mycobacterium, described in Colombia in 2006 in 4 HIV positive patients with 7 microbiological isolates from blood and respiratory tract [3], the new species presented microbiological characteristics such as bacillus, acid, alcohol, resistant, non-mobile, in a 3-year period. weeks in media such as Lowenstein-Jensen, Ogawa Kudoh, but not growth in MacConkey medium, negative for niacin production and positive for catalase and urease, the latter allows to differentiate it from other species of *Mycobacterium avium*

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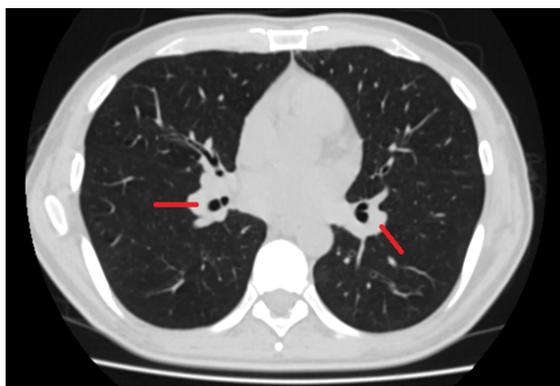


Figure 1: High resolution tomography of the chest (HRTC). Mediastinal adenomegalies (red lines) in relation to an inflammatory process not ruling out lymphoproliferative.



Figure 2: High resolution tomography of the chest (HRTC). Normal (without mediastinal adenomegalies).

Study	Results	Methods
HIV Viral load.	240.315 copies/ml, log 5.38	Real time PCR
CD4 Lymphocytes	16 cells/ μ l (4.22%)	Flow cytometry
Surface antigen Hepatitis B virus	Negative	Chemiluminescent Microparticle Immunoassay (CMIA)
Hepatitis B virus Surface Antigen (Antibodies)	Negative	Chemiluminescent Microparticle Immunoassay (CMIA)
Hepatitis C virus Antibodies	Negative	Chemiluminescent Microparticle Immunoassay (CMIA)
VDRL	Negative	Flocculation
Toxoplasma IgG-IgM	Negative	Enzyme-Linked ImmunoSorbent Assay (ELISA)
PPD	0 mms	
KOH (Cerebrospinal Fluid)	Negative	Direct
Culture Typical germs (Cerebro espinal Fluid)	Negative	Culture Typical germs
Herpes Simplex virus (Cerebro espinal Fluid)	Negative	Real time PCR
Cryptococcus antigen (Cerebro espinal Fluid)	Negative	Latex agglutination
Pathological Anatomy. Sample: Mediastinal Gangly Biopsy.	Chronic Inflammation Granulomatosa with Necrosis Focuses	Pathological Anatomy.
Urinary antigen Histoplasma capsulatum	Negative	Enzyme immunoassay
Serum galactomannan	Negative	Enzyme-Linked ImmunoSorbent Assay (ELISA)
MTB RCP, sample: Mediastinal lymph node biopsy	No detected	Real time PCR
Culture of Mycobacteria, sample: Mediastinal lymph node biopsy	Growth of <i>Mycobacterium colombiense</i> was obtained	Lowestein Jensen y MGIT - MALDI TOF
Non-tuberculous mycobacteria-sensitivity by Minimum inhibitory concentration (MIC)	Clarithromycin Sensitive 2.0 μ g/ml Moxifloxacin Sensible 1.0 μ g/ml Resistant Linezolid 64 μ g/ml	Minimum inhibitory concentration (MIC)

Table 1: Studies performed during hospitalizations.

complex as they do not produce urease in general; however, the main mechanism that was able to differentiate from other species in its family was based on genetic sequencing, a fragment (ITS-1) spacer in rRNA 16S-23S gives it its own characteristics and is the basis of identification [3-5].

Since then there are some but very rare case reports in the literature with isolation of *Mycobacterium colombiense*, in our search we identified 8 previous case reports, with diverse clinical manifestations and involvement in both immunocompromised and immunocompetent, highlighting 2 cases described only as manifestations of lymphadenopathy in children without apparent immunocompromise and with good evolution, [4,6] although cases reported in adults have shown much more aggressive manifestations with dissemination, pulmonary compromise [7-9] cutaneous [10,11] and lymphadenopathy; in 3 of them with fatal results [7-9].

Among the cases evaluated, possible factors that affect the immune system were found (4 cases); all of them in adults, which were respectively: HIV disease [12], immunosuppression by kidney transplant [7], myelodysplastic syndrome [11] and autoantibody disease against interferon gamma [9], in addition there are 2 cases in which primary or secondary immunodeficiencies are not described, but if there is coinfection with hepatitis B chronic or previous history of tuberculosis, so it cannot be excluded that there was an immune alteration not evaluated [8,10]; In this case, our patient presents HIV infection that makes him susceptible to mycobacterial involvement.

In most cases, the diagnosis was made by means of both excisional lymph node biopsy and Fine Needle Aspiration Biopsy (FNAB) and in one case by spontaneous pus secretion from a lymphadenopathy [11] and in another case by culture of the mycobacterium in lung samples by bronchoalveolar lavage [9] in all of them, the microorganism was isolated through culture; in seven of the cases, ZN staining and smear microscopy were negative except for one case in a patient coinfecting with HIV [12], somewhat similar to the findings in our case; It is relevant that in the reports the histological findings in biopsy were consistent granulomas, histiocytosis, necrosis of caseification or lymphocytic infiltrate similar to this case.

The main method of molecular identification for confirmation of Colombian Mycobacterium was the detection by PCR or sequencing of the segment 16S rRNA or detection of the hsp65 gene, except for one case in which the MALDITOF [7] technique was used, but later it was confirmed with the same method of genetic detection by PCR, in our case the confirmation of *Mycobacterium colombiense* was performed by MALDITOF in a similar way to the last case described and suggestive by phenotypic tests, however the degree of compatibility of the test in MALDITOF allows confirming that it is the Mycobacteria in question.

Regarding first line treatment, it is recommended to avoid monotherapy with macrolides and opt for combination schemes that include rifampicin, clarithromycin and ethambutol [13]; however, it is essential to perform sensitivity tests for the probability of therapeutic

failures. Among the reports evaluated, 2 cases of rifampicin resistance were identified that required adjustment in the therapy [8,12], in our case the DST (Drug Sensitivity Tests) revealed sensitivity to macrolides, quinolones and resistance to Linezolid (Table 1).

Conclusion

We describe a case of lymph node disease caused by *M. colombiense* in a patient with evidence of HIV infection, that although it was initially described in this group of patients; there is only one additional reported case of co-infection with the human immunodeficiency virus. It seems that there are additional determinants that can confer risk of infection and develop disease, should be outlined and sustain clinical suspicion; as well as having knowledge of the diagnostic methods available to grant adequate treatment and avoid fatal outcomes.

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