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Non-Tuberculous Mycobacterial Infection in AIDS Patients: A Detailed Description of 4 Cases, Including Histopathological Finding

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Infección por micobacterias no tuberculosas en pacientes con SIDA: Una descripción detallada de 4 casos con datos histopatológicos

ABSTRACT

Non tuberculous mycobacteria (NTM) are important opportunistic infection in patients with AIDS. ***Aim:*** *To present 4 cases of disseminated infections by NTM in patients with AIDS.* ***Results:*** *These cases were associated with prolonged symptoms of fever, weight loss, diarrhea or cough, with hepatosplenomegaly, anemia and thrombocytopenia. None were receiving prophylaxis, had a low CD4 lymphocyte count (median 20/mm^3), and three had discontinued their antiretroviral therapy (ART). The diagnosis was established by culture in bone marrow, sputum or bronchioalveolar lavage samples and in two cases also by PCR. Histological features included foamy histiocytes and positive acid fast bacilli in tissues. The species identified were Mycobacterium avium in 3 cases and M. genavense in the remaining case. Patients were treated with combinations of ethambutol, macrolides, quinolones, amikacin or rifampicin on a long-term basis (median 19 months) and even parenterally for severe diarrhea. Three patients survived and one died from disseminated Kaposi's sarcoma. Multiple complications were observed including severe malnutrition, renal failure, calcium and phosphorus metabolism disorders, healthcare-associated infections, co-infections, and neoplasms. All required readmissions and ART adjustments to compensate for interactions with rifampicin.* ***Conclusions:*** *NTM infections in patients with AIDS generate a prolonged morbidity, frequent readmissions, require an extended combination treatment that may present interactions with ART, and are associated with different complications, including calcium and phosphorus*

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disorders. Its diagnosis is complex in the absence of special blood cultures, requiring a microbiological study in multiple samples and with different techniques, including the support of histopathology.
Keywords: *AIDS; Diagnosis; Nontuberculous Mycobacteria; Pathology; Therapy.*

RESUMEN

Las infecciones oportunistas por Mycobacterias no tuberculosas (MNT) son importantes en pacientes con SIDA. ***Objetivo:*** *Describir 4 casos de infecciones diseminadas por MNT en pacientes con SIDA.* ***Resultados:*** *Estos casos se asociaron a cuadros prolongados de fiebre, pérdida de peso, diarrea o tos, con hepatoesplenomegalia, anemia y trombocitopenia. Ninguno estaba recibiendo profilaxis, tenían un bajo recuento de linfocitos CD4 (mediana 20/mm^3), y tres habían abandonado su terapia antirretroviral (TARV). El diagnóstico fue establecido por cultivo en muestras de médula ósea, esputo o lavado bronquioalveolar y en dos casos además con PCR para MNT. Los hallazgos histológicos incluyeron histiocitos espumosos bacilos ácido-alcohol resistentes en tejidos. Las especies identificadas fueron Mycobacterium avium en 3 casos y M. ganevense en el restante. Los pacientes fueron tratados con combinaciones de etambutol, macrólidos, quinolonas, amikacina o rifampicina en forma prolongada (mediana 19 meses) e incluso por vía parenteral por diarrea severa. Tres pacientes sobrevivieron y uno falleció por Sarcoma de Kaposi diseminado. Se observaron múltiples complicaciones incluyendo desnutrición severa, falla renal, trastornos graves del metabolismo del calcio y fósforo, infecciones asociadas a la atención de salud, co-infecciones y neoplasias. Todos requirieron reingresos y ajustes de la TARV para compensar las interacciones con rifampicina.* ***Conclusiones:*** *Las infecciones por MNT en pacientes con SIDA generan una morbilidad prolongada con reingresos frecuentes, requieren un tratamiento combinado prolongado que puede presentar interacciones con la TARV, se asocian a diferentes complicaciones, incluyendo trastorno del calcio y fósforo. Su diagnóstico es complejo en ausencia de hemocultivos especiales, requiriendo un estudio microbiológico en múltiples muestras y con diferentes técnicas, incluyendo el apoyo de la histopatología.*
Palabras clave: *Diagnóstico; Micobacterias no Tuberculosas; Patología; SIDA; Terapia.*

Opportunistic infections due to atypical or non-tuberculous Mycobacteria (NTM) affect patients with AIDS with advanced stages of immunosuppression. Although the epidemiology, risk factors and prognosis for these infections are well described in the literature[1,2,3,4,5,6,7,8] there is little detailed literature on their clinical aspects, including difficulties to reach an adequate diagnosis in the absence of mycobacterial blood cultures, complications, compounds used in the real clinical scenario including parenteral therapies, response to treatment and the value of histopathology in

their study. In this work we present 4 cases of NTM infections in patients with AIDS with a detailed description of their diagnosis, therapy, complications and outcome. The expansion of the epidemic of patients with HIV in Chile and the high percentage of patients who debut with AIDS (>40%), make this publication timely and necessary[9].

Patients and methods

Cases were identified from personal files of treating physicians at the Valdivia Base Hospital in Southern Chile. All known cases from years 2016 to 2023 were included. A standardized data extraction template was used from the Hospital's electronic records or medical records. Extraction focused on the clinical picture, immunosuppression situation, diagnosis, therapy, complications, histological studies and evolution. The study was approved by the Scientific Ethics Committee of the Los Ríos Health Service.

Results

Four cases were identified between years 2016 and 2023, all of them male, with a median age of 31.5 years (range 27-38) (Table 1). The infections were identified between 2016 and 2019. One of the patients was under treatment and the other 3 had abandoned antiretroviral therapy. The median HIV viral load was 291,210 copies/uL and median CD4 lymphocyte counts was 20 (range 1 to 101/uL). None of the patients were receiving NTM prophylaxis (Table 1).

Clinical Picture. Three patients presented the triad of fever or diaphoresis, diarrhea and weight loss, quantified between 10 to 20 kg. The other patient presented with cough with weight loss and pneumonia but without fever or diarrhea (Table 1). Laboratory parameters demonstrated severe anemia in 3 (median 6.3 g/dL), marked leukopenia in 2 (median 3610/uL) and thrombocytopenia in all cases (median 99000/uL). Likewise, all presented visceral malnutrition (median serum albumin 1.79 g/dL) (Table 1). The evolution time was from 2 weeks to 2 months prior to the first admission. Liver biochemical tests did not present major alterations (Table 1). Imaging studies indicated hepatosplenomegaly, polyadenopathy, and abdominal or thoracic lymphadenopathy. Two patients had pulmonary involvement, one with bilateral apical cavities lesions. Two patients presented herpetic infections and another had disseminated Kaposi's sarcoma (Table 4). The latter was hospitalized previously in another region and had negative blood cultures for Mycobacteria.

Diagnosis. The Hospital does not have mycobacterial blood cultures, so the diagnosis was made by alternative methods and included a bone marrow (BM) aspirate in all cases (Table 2). All cases had a positive AFB stain in at least one site and were confirmed with a positive culture on liquid medium at the hospital level and then at species level in the National Reference Laboratory. Bone marrow (BM) culture yield was 75% (3 of 4 cases; Table 2). Positive cultures were also obtained in samples of bronchoalveolar lavage (BAL), ascitic fluid, and sputum (Table 2). AFB staining was positive in a wider range of samples: BAL, BM and expectoration. The molecular study was carried out in 2 cases with positivity for NTM (Table 2). The result of the molecular test does not discriminate between different Mycobacterium species so information on the species involved was not available at first hand (Table 2). The species identified in the Reference Laboratory corresponded to *M. avium* in 3 cases and to *M. genavense* in the remaining patient (Table 2). The diagnosis of NTM infection was obtained with a median of 35.5 days since sampling (range 14 to 62 days). In all these cases, a disseminated infection with 2 or more sites was confirmed according to culture, PCR or a positive stain for AFB in different compartments.

Histological study. All cases had a histological study in a variety of tissue samples (1-3 per patient) (Table 3). In 3, granulomas without a defined architecture were detected. Necrosis was absent. The most frequent findings were foamy histiocytes (in 4 out of 7 samples) and the presence of AFB (5 out of 7 samples). Histiocytes filled with mycobacteria were detected in 3 cases (Table 3, Figure 1).

Treatment. All patients received treatment with

Table 1. Main features of 4 AIDS patients with NTM infections, Hospital Base de Valdivia, Chile.

Variable	Case 1	Case 2	Case 3	Case 4
Gender, age in years	Male, 38	Male, 27	Male, 31	Male, 32
Main clinical features, time of evolution/	Fever, weight loss (10 Kg), diarrhea, abdominal pain, cough. Two weeks	Fever, weight loss (20 Kg), diarrhea. Two months	Diaphoresis, weight loss (10 Kg), diarrhea, abdominal pain. Two months	Pneumonia, weight loss. Two months
CDC HIV Stage, Viral load, CD4 lymphocyte count	C3; 71 copies/mL; 101 CD4/uL	C3: 452,000 copies/mL; 30 CD4/uL	C3; 745,000 copies/mL; 1 CD4/uL	C3; 131,033 copies; CD4 10 CD4/uL
Antiretroviral therapy, MAC prophylaxis	Receiving ART; No prophylaxis	ART abandonment (1 year); No prophylaxis	ART abandonment (>1 year); No prophylaxis	ART abandonment (1 year); No prophylaxis
Liver-spleen enlargment	Yes	Yes	Yes	Yes
Thoracic and abdominal lymph node enlargement	Yes	Yes	Yes	No
Lung /intestinal involvement	Bilateral lower lung infiltrates, bronchiectasis /enterocolitis	No	No	Bronchiectasis, Bilateral upper lung cavities
Hemoglobin g/dL	5.08	7.1	5.5	13.2
Leukocytes /uL	5,080	2,480	2,680	4,540
Platelets /uL	92,000	125,000	36,000	11,000
Serum albumin g/dL	0.8	1.67	1.9	3.3
Alkaline phosphatase IU/L	Normal	Normal	Normal	1.5 times over upper normal limit
Serum Creatinine/BUN mg/dL	0.23/17	0.58/10	6.95/125	1.45/44

Table 2. Diagnostic microbiological features among 4 AIDS patients with NTM infections, Hospital Base de Valdivia, Chile.

Variable	Case 1	Case 2	Case 3	Case 4
Positive acid fast bacilli site	Bronchoalveolar	Bone marrow lavage, Bone marrow	Bone marrow	Sputum
Positive PCR site (RealAccurate® Quadruplex Mycobacteria PCR Kit; PathoFinder®, Maastricht, The Netherlands)	Colonic mucosa	Bone marrow aspirate	Not done	Not done
Time to Mycobacterium positive culture, site and species	14 days, Bronchoalveolar lavage, *Mycobacterium avium*	35 days, Ascitic liquid and bone marrow, *Mycobacterium avium*	62 days, Bone marrow, *Mycobacterium genavense*	36 days, Sputum and bone marrow, *Mycobacterium avium*

Table 3. Main histological findings in 4 AIDS patients with NTM infections, Hospital Base de Valdivia, Chile.

Case	Biopsy site	Granuloma and architecture	Necrosis	Caseum	Palisading cells	Giant cells	Foamy histiocytes	AFB* and distribution
1	Bone marrow	Yes, Not well-organized	No	No	No	No	No	Yes Mycobacterium -filled histiocytes
1	Colon	No	No	No	No	No	Yes	No
1	Duodenum	No	No	No	No	No	Yes	Yes Few
2	Colon	No	No	No	No	No	Yes	Yes Mycobacterium-filled histiocytes
3	Bone marrow	Yes, Not well - organized	No	No	No	No	Yes	Yes Few
3	Lymph node	No	No	No	No	Yes, no Langhans type	No	Yes Mycobacterium-filled histiocytes
4	Bone marrow	Yes, Not well organized	No	No	No	No	No	No

*:AFB Acid fast bacilli.

Table 4. Antiretroviral adjustments, complications and outcome of 4 AIDS patients with NTM infections, Hospital Base de Valdivia, Chile.

Variable	Case 1	Case 2	Case 3	Case 4
Antiretroviral adjustment	Initial therapy with tenofovir-emtricitabine-darunavir/ritonavir was changed to tenofovir-emtricitabine-raltegravir to avoid protease inhibitors	Raltegravir dose was increased twice	Maraviroc dose increased twice	Raltegravir dose was increased twice
Hematological	Anemia secondary to bone marrow hypoplasia and a mild autoimmune hemolytic component (Direct Coombs test positive) Transfusional requirements Normal vitamin B12 levels	Myelodisplasic anemia with a mild autoimmune hemolytic component (Direct Coombs test positive) treated with prednisone. Transfusional requirements Normal vitamin B12 levels	Anemia secondary to renal insufficiency and an autoimmune hemolytic component (Direct Coombs test positive) treated with prednisone and transfusions	
Renal			Renal failure with dialysis requirement. Acute over chronic interstitial nephritis reported by kidney biopsy	
Nutritional	Severe undernutrition (Body Mass Index 16 Kg/m^2) with ascitis Prolonged parenteral nutrition required with multiple readmissions			

...continuación tabla 4.

Variable	Case 1	Case 2	Case 3	Case 4
Calcium-phosphorus metabolism	Hypercalcemia at onset (11.4 mg/dL) with low parathormone levels (8 pg/mL; reference 15-65). Later, symptomatic hypocalcemia-hypophosphatemia due to vitamin D deficiency (< 0.3 ng/mL) with secondary hyperparathyroidism (455 pg/mL)		Hypercalcemia (14.2 mg/dL) with low parathormone levels.	
Hospital-acquired infections/others	Catheter-related bloodstream infection Bell´s paralysis Catheter-related venous thrombosis		Chronic abdominal pain that required alcoholic celiac plexus neurolysis	
Coinfections / Neoplasms	Cytomegalovirus disease Herpes oftalmicus	Disseminated Kaposi´s Sarcoma		Pneumococcal bacteremia, herpetic stomatitis, oral candidiasis
Number of hospital admissions, accumulated days	10 admissions, 334 days	3 admissions, 74 days	5 admissions, 144 days	2 admissions, 40 days
Evolution and Follow up	Alive 44 months of therapy No relapses at 26 months of follow up	Died at 8 month of therapy by disseminated Kaposi´s sarcoma (skin, lymph nodes and retroperitoneal mass) despite chemotherapy	Alive 21 month of therapy No relapses at 40 months of follow up	Alive 17 months of therapy No relapses at 72 months of follow up

different combinations and dissimilar duration (Figure 2A and 2B). The compounds used were ethambutol, rifampicin, macrolides, moxifloxacin and amikacin. No cases treated with linezolid were recorded. The most commonly used compounds were ethambutol (median 19 months), macrolides (median 16 months) and rifampicin (median 14.5 months). The median treatment with moxifloxacin and amikacin were shorter (medians of 6 and 2.5 months, respectively). The whole group was treated between 8 and 44 months (median 19 months) and between 17 and 44 months among the 3 surviving patients. The most used combination was ethambutol with macrolides (median 14.5 months; Figure 2B), rifampicin-ethambutol and macrolides (median 12.5 months), and ethambutol-macrolides and moxifloxacin (median 5.5 months). Three patients received part of their treatment by parenteral route for 1 to 6 months, with either IV amikacin, moxifloxacin or clarithromycin. There were no antimicrobial susceptibility studies. Antiretroviral treatment was adjusted in all cases and included doubling the dose of raltegravir in 2 patients, increasing the dose of maraviroc in another case, and replacing darunavir/ritonavir with raltegravir in the remaining patient. All of these adjustments were made for the concomitant use of rifampicin (See discussion).

Evolution and complications. Three of the 4 patients survived the NTM infection and one died from disseminated Kaposi's Sarcoma (Table 3). The survivors have not presented relapses after the end of treatment with a median of 40 months of follow-up (26 to 72 months). Morbidity was prolonged, requiring readmissions (2 to 10 times) for various causes and totaling 592 bed days with a median of 109 days (range 40 to 334 days). Complications detected at admission or during follow-up included hematological, renal, nutritional, calcium-phosphorus related issues, coinfections, or healthcare-associated infections. Three patients presented anemia of multifactorial cause with an autoimmune hemolytic component, requiring transfusions and corticosteroids in 2 cases (Table 4). One patient presented renal failure requiring dialysis due to interstitial nephritis confirmed by histology. Furthermore, 2 patients presented hypercalcemia with low parathyroid hormone (PTH) values, suggesting that intestinal granulomatosis provoked this complication (see discussion). In one of these cases, severe symptomatic hypocalcemia associated with hypophosphatemia with low vitamin D values was subsequently observed with secondary hyperparathyroidism. This phenomenon was attributed to chronic diarrhea, the use of rifampicin (see discussion) and/or malnutrition. This patient required prolonged parenteral nutrition with several hospitalizations (case 1, Table 4).

The anemia had a slow recovery (Figure 3), taking about 6 months to reach values close to 8 g/dL. In contrast, platelet recovery was

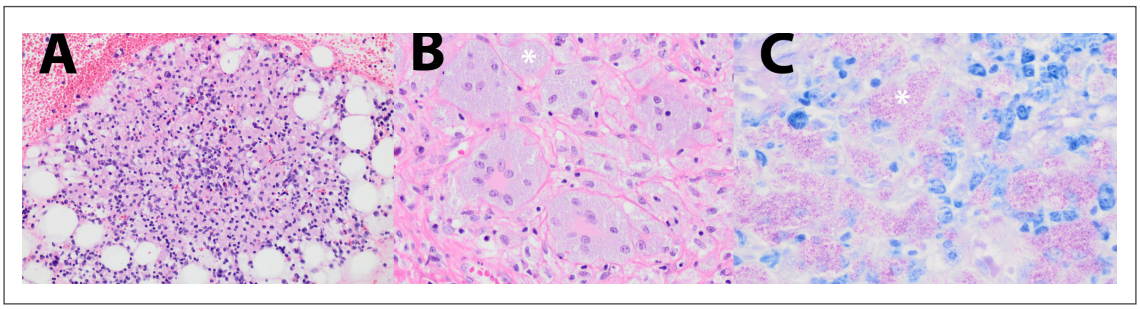

Figure 1: *Some histological findings in patients with AIDS and disseminated NTM infection. Panel A. A non-well formed granuloma is observed in a bone marrow biopsy, Hematoxilin-Eosin 20X. No necrosis, caseum, palisading cells o Giant cells are observed. Panel B. Foamy histiocytes present in a lymph node biopsy (one is marked by an asterix), Hematoxilin-Eosin 20X. Panel C. Histiocytes full loaded with mycobacteria (asterix) in a lymph node biopsy after Ziehl-Neelsen staining. Hematoxilin-Eosin 40X.*

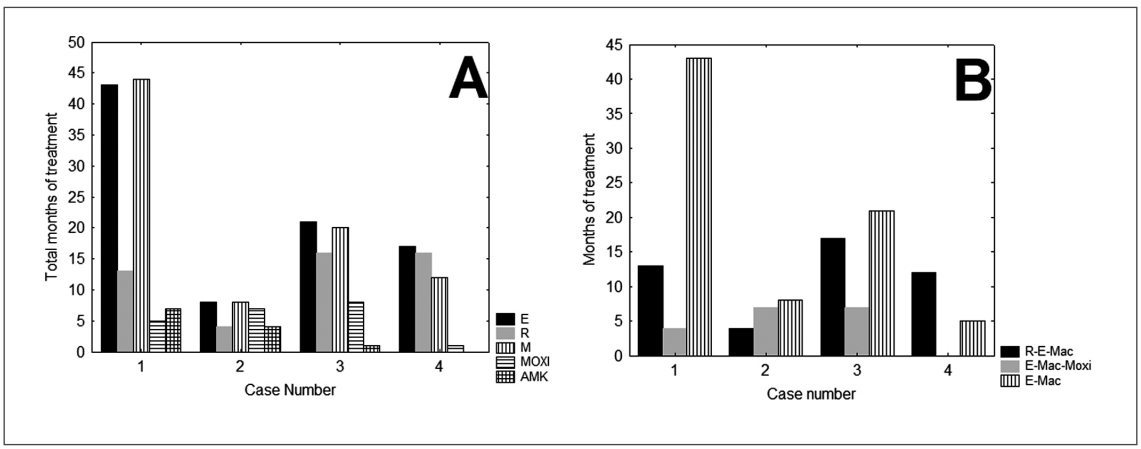

Figure 2: *Distribution of months of treatment with specific compounds used in the treatment of disseminated NTM infections in 4 patients with AIDS (Panel A). The most frequent combination was ethambutol-macrolides with or without other compounds (Panel B). E ethambutol; R: rifamycin; M: macrolides; MOXI: moxifloxacin; AMK: amikacin; R-E-Mac: Rifampicin-ethambutol-macrolides; E-Mac-Moxi: ethambutol-macrolides-moxifloxacin; E-Mac: ethambutol-macrolides.*

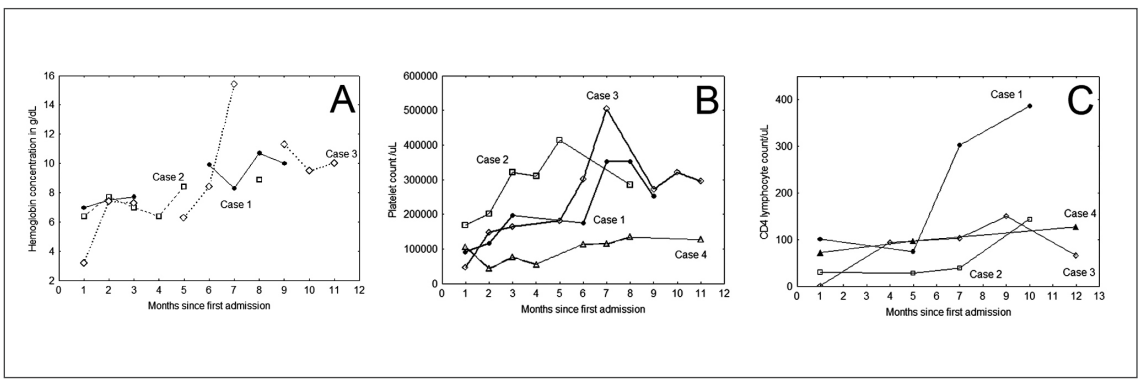

Figure 3: *Panel A. Trends in recovery from anemia in 3 cases of disseminated NTM infections over a period of 12 months after admission. A slow recovery of hemoglobin levels is observed. Panel B. Evolution of platelet counts in 4 patients with disseminated NTM infection. All patients had thrombocytopenia upon admission and one worsened it in the second month with a slow subsequent recovery. In the other 3 cases, recovery was faster with normal levels by the third month. Panel C. Evolution of CD4 lymphocyte counts. A slow increase is observed, achieving values > 100/uL in 3 cases at 6 months and at 10 months in the remaining case shortly before death. For figures 3B and 3C curves were fitted by locally weighted scatterplot smoothing (Lowess) using the software package Statistica 8.0 StatSoft, Inc.*

achieved in approximately 3 months except in one patient. Patients achieved a progressive but slow increase in CD4 lymphocyte counts with values >100 CD4/uL about 8 months after admission (Figure 3). None of our patients had a pre-NTM infection CD4 lymphocyte count and the first measure was the lowest registered in their evolution. Three patients achieved undetectable viral loads (<20 copies/mL) between 4 and 9 months from admission and the other maintained levels <50 copies/mL during the 12 months following admission.

Discussion

This clinical series demonstrates that NTM infections are capable of producing a prolonged morbidity in patients with AIDS, with long hospitalizations, frequent readmissions and a variety of associated complications. Patient's recovery and clinical stabilization was slow and reached periods that exceed one year from diagnosis.

The association of fever, prolonged diarrhea, weight loss, anemia, thrombocytopenia and hepatosplenomegaly in patients with AIDS, suggests disseminated NTM infections, but they are unspecific due to the wide differential diagnosis associated with each of them and also by their imperfect sensitivity because not all patients have all of these components. Except in cases where direct microbiological samples can be obtained, i.e. lung infections, the diagnosis of NTM infections in patients with AIDS can be challenging and frustrating despite an extensive microbiological fishing. The diagnostic performance of disseminated NTM infections has improved with blood cultures treated by lysis-centrifugation either with local procedures or using commercial MycoF/Lytics bottles (Becton Dickinson®) and has allowed a peripheral detection of the problem[10]. Blood cultures in liquid media have improved sensitivity in some experiences, shortening days to diagnosis, allowing also the recognition of bacteremia due to *M. tuberculosis* and have increased the diagnostic performance at regional levels[11,12]. Its sensitivity is higher than bone marrow aspirate cultures (100 vs 57% in one report)[10,13]. Unfortunately, this technology is not locally available nor is it widely widespread in Chile, which maintains the diagnostic problem. Its sensitivity is also not ideal since one of our cases was not detected with this method before being transferred to our region. In our series, the diagnosis was possible only after a systematic search for NTM in different compartments and using stains, PCR, cultures and the support of histopathology. The PCR platform used locally does not discriminate between different NTM species but it advances diagnosis. A classical clue for suspecting NTM infection is the finding of a positive AFB staining with a negative *M. tuberculosis* PCR test. Due to locally available resources, we currently use PCR platforms (either XpertMTB/RIF® or RealAccurate® Quadruplex Mycobacteria PCR Kit) in suspicious cases along with the other strategies mentioned. As comparative data, in the same period of these cases (2016-2019), we observed 5 patients with HIV/AIDS and tuberculosis in our hospital, suggesting a similar frequency for both groups of mycobacterial infections[14]. As in our work, in cases with confirmed NTM infections in patients with AIDS, the most frequent findings correspond to dispersed infiltrates of epithelioid histiocytes filled with mycobacteria[13,15]. The presence of granulomas, necrosis, palisade cells or giant cells occurs in no more than a third of the samples. Histologically, infections by atypical mycobacteria in patients with AIDS are distinguishable, in most cases, from those associated with tuberculosis and in this manner, can help to the differential diagnosis.

There are no guidelines in Chile for the treatment of NTM infections in patients with HIV/AIDS and their treatment is based on recommendations from other latitudes, randomized controlled trials and published experiences[16,17,18,19,20]. Most NTM infections in patients with AIDS are associated with the *M. avium complex* (MAC), which is made up of several species and subspecies, with *M. avium* being the most common species. In *M. avium* infections, macrolides (azithromycin or clarithromycin) improve symptoms and reduce the bacterial count in the blood slowly, after several weeks of use but are associated with the development of resistance if used as monotherapy (>40%)[18]. Coupled to ethambutol, azithromycin or clarithromycin achieve the same results in microbiological control and overall survival but with lower resistance rates[19]. On the other hand, the addition of a third drug (rifabutin in the original study) allows survival to be increased and is associated with a trend toward a lower relapse rate[20]. Thus, it is recommended that patients with infections with high bacterial loads (for example when detected in blood cultures), severe or disseminated infections by the *M. avium Complex*, receive treatment with 3 drugs: ethambutol, a macrolide (clarithromycin or azithromycin) and rifampicin or rifabutin[17]. This approach was used

in all of our patients for varying periods of time (Figure 2B). Long treatment periods are recommended due to the slow recovery of cellular immunity and delayed microbiological sterilization. Microbiological eradication during treatment can be verified by sputum or blood culture samples if these are available. In its absence, only good clinical judgment can guide the duration of therapy. In our patients, up to 5 drugs were used simultaneously, including parenteral therapies with quinolones or amikacin due to absorption problems associated with diarrhea. The most active drugs against MAC correspond to macrolides, amikacin, quinolones and to a lesser extent rifabutin[2]. Except for the latter all were applied.

With the new currently available antiretroviral therapies (ART), the addition of rifampicin does not offer major enzymatic interactions. However, our patients did not have this advantage and in all, adjustments to ART had to be made, which included the replacement of protease inhibitors or an increase in integrase inhibitors or maraviroc doses to compensate for their greater metabolism secondary to the enzymatic induction caused by rifampin[21]. The adjustment in the case of raltegravir is questionable, since comparative studies have not demonstrated a higher rate of virological failure with standard doses compared to higher doses[22]. *M. genavense* infections are very rare, without specific treatment guidelines and are associated, as in our case, with prolonged and difficult to treat abdominal pain[23].

Unexpectedly, we detected relevant calcium-phosphorus disorders (hypercalcemia or hypocalcemia-hypophosphemia). Cases of hypercalcemia associated with NTM infections in patients with AIDS have been progressively described and may occur at the time of diagnosis or after the start of treatment, as in our series. Depending on their severity, they can be treated with hydration, corticosteroids and/or bisphosphonates[24,25]. They appear to originate from an increased conversion of 25 OH-vitamin D to 1,25 OH-vitamin D in extrarenal tissues, monocytes or granulomas. They are associated with low PTH values. In none of our patients was there central nervous system compromise due to this cause. We also observed a case with severe symptomatic and prolonged hypocalcemia, difficult to manage and secondary to severe hypovitaminosis D, probably due to chronic diarrhea and the contribution of rifampicin to the metabolism of this vitamin with reductions in the levels of 25- and 1,25- OH-vitamin D[26].

It has been proposed that it is not necessary to prescribe primary prophylaxis for NTM infections in patients who start their ART and have CD4 lymphocyte counts <50/mm^3 due to a low incidence rate in the groups without prophylaxis, which is similar to those that receive prophylaxis[27,28]. We disagree with this suggestion due to the devastating and complex consequences, demonstrated in this work, of NTM infections in our local reality. Furthermore, other reports indicate a benefit even in patients on ART[29]. Considering the current expansion of the epidemic of patients with HIV in Chile, with a high percentage of cases diagnosed at AIDS stage, the risk of NTM infection cannot be easily ruled out. Our group systematically applies NTM prophylaxis to all patients with low CD4 counts even when they start their ART.

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