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Superposition of Leprosy and other neglected tropical diseases in the State of Rio de Janeiro: a case series report

DANIEL GARBIN DI LUCA*, PEDRO JOSÉ SECCHIN DE ANDRADE*, ANNA MARIA SALES*, VINÍCIUS MARTINS DE MENEZES*, MARIA CLARA GUTIERREZ GALHARDO**, MARIA INÊS FERNANDEZ PIMENTEL**, MARCELO ROSANKIDKI LYRA** & JOSÉ AUGUSTO DA COSTA NERY*

**Ambulatório Souza Araújo, Laboratório de Hanseníase, Instituto Oswaldo Cruz (IOC), Fiocruz, Rio de Janeiro, RJ, Brazil*

***Instituto de Pesquisa Clínica Evandro Chagas (IPEC), Fiocruz, Rio de Janeiro, RJ, Brazil*

Institution where the work was undertaken: Ambulatório Souza Araújo, Laboratório de Hanseníase, Instituto Oswaldo Cruz (IOC), Fiocruz, Rio de Janeiro, RJ, Brazil

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Summary This is a report on eight non-HIV infected leprosy patients presenting unusual co-infection with other, often neglected, tropical diseases, namely: American tegumentary leishmaniasis (ATL), sporotrichosis, and cryptococcosis. To the best of our knowledge, there have been very few ATL-leprosy co-infection reports in the literature to date and only one previous description of the coexistence of leprosy-cryptococcosis and leprosy-sporotricosis.

Introduction

Leprosy is an infectious disease caused by *Mycobacterium leprae.* There are approximately 220,000 new cases a year distributed among nine high-burden countries, including Brazil, in which nearly 34,000 new cases nationwide and 1,800 in the State of Rio de Janeiro alone were detected in 2011.[1,2]

Correspondence to: Daniel Garbin Di Luca, Laboratório de Hanseníase, Instituto Oswaldo Cruz, Fiocruz, Av. Brasil 4365, Manguinhos 21040-360, Rio de Janeiro, Brazil (e-mail: dilucadaniel@gmail.com)

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Latin America is also an endemic area for several other tropical diseases. However, the association of these conditions in individuals also affected by leprosy appears to be a rare event with few reported cases. Needless to say, these cases require early identification and treatment to prevent further dissemination of either disease.

In the present retrospective study, co-infection by leprosy and three other tropical diseases in non-HIV infected patients was assessed from the database of the Leprosy Outpatient Clinic at Fiocruz, Rio de Janeiro, RJ, Brazil, from 2009-2013. All eight patients included in the study signed their written consent.

Case series report

All eight patients were diagnosed with leprosy by experienced specialists through clinical and slit-skin smear examinations and confirmed via histopathology of a biopsied leprosy lesion.

Two cases of concomitant American tegumentary leishmaniasis (ATL) and leprosy were reported. Patient 1 was a 70 year old male with a past history of borderline leprosy treated in 2000 with multibacillary multidrug therapy (MD MBT). In 2002, he presented a nasal obstruction and epistaxis. Seven years later, he developed nodular lesions in the left arm and forearm (Figure 1), nasal crusting, diffuse infiltration, fetid smell, and hypoacusis. The ATL

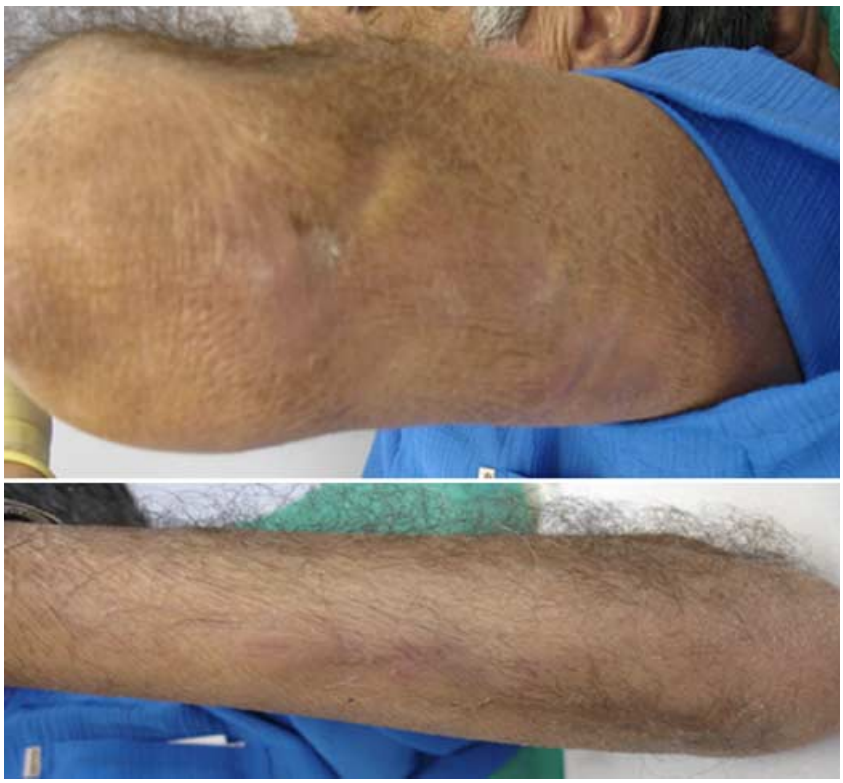

Figure 1. Leishmaniasis lesions located on the arm and forearm in patient 1.

diagnosis was made through a *Leishmania brasiliensis* PCR search of a nasal biopsy. Treatment with meglumine antimoniate (MA) was administered.

The second patient was a 59 year old male whose ATL diagnosis was made in 2006 via culture of a lesion biopsy together with a negative Montenegro skin test. He had ulcerated lesions distributed on both legs and abdomen. Initial treatment regimens followed by two re-treatments were carried out with MA. In 2011, clinical examination revealed an infiltrated lesion with altered sensitivity in the dorsal region. This same patient was then diagnosed with tuberculoid leprosy and treated with paucibacillary multidrug therapy (PB MDT).

Three individuals with a previous diagnosis of leprosy were found to have a sporotrichosis coinfection. All three reported contact with cats, and *Sporothrix schenckii* was confirmed by tissue culture. The patients were then treated with MB MDT and terbinafine and/or itraconazole for sporotrichosis.

The first patient was an 87 year old female who presented a past history of borderline leprosy treated in 2006. In 2011, she was found to have ulcerated lesions and subcutaneous nodes along the lymphatic vessels of the left forearm compatible with lymphocutaneous sporotrichosis.

Patient 2 was a 56 year old male who had successfully completed lepromatous leprosy treatment in 2001. Ten years later, when he presented a nodular ulcerated lesion and lymphangitis in the right arm, lymphocutaneous sporotrichosis was diagnosed.

Lastly, patient 3 was a 39 year old male with a history of leprosy that had been treated 12 years earlier. He presented an ulcerated lesion in the right hand with nodular lesions in the right forearm and arm together with a cystic lesion of the left leg and was diagnosed as having disseminated cutaneous sporotrichosis (Figure 2).

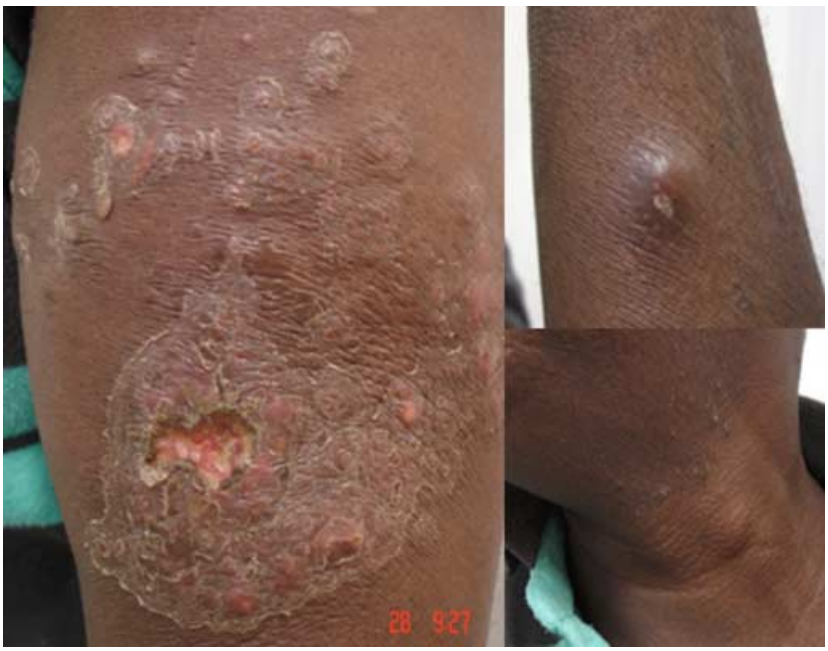

Figure 2. Disseminated sporotrichosis lesions in case 3.

Moreover, three cases of cryptococcosis were found in patients previously treated for leprosy with MB MDT. All diagnoses were made through blood serology, biopsies accompanied by direct examination, and cultures for *Cryptococcus neoformans*.

The first patient was a 55 year old male presenting a unilateral hearing impairment associated with vegetating lesions at the external auditory canal during treatment for an erythema nodosum leprosum (ENL) reaction (2 years after completing leprosy treatment).

Patient 2 was a 36 year old male who, during ENL treatment in 2011 (3 years after completing leprosy treatment), also developed an ulcerating plaque of 1·5 cm in the upper thoracic region with a concomitant upper and lower limb edema, fever, and malaise for 3 months. Both patients were treated with fluconazole; but amphotericin B was added to the treatment of patient 1.

Patient 3 was a 40 year old female who presented a lower limb edema, paresthesia, and subcutaneuos nodes during treatment of ENL reaction (one year after completing leprosy treatment in 2009). She was also seen to have an upper limb edema and hyperpigmented lesions with concomitant face infiltration and was immediately admitted and diagnosed with cryptococcal meningitis. Treatment was with fluconazole during the four months of hospitalization and she is currently being treated with itraconazole. It is important to emphasize that these three patients were taking thalidomide (100-300 mg per day) and prednisone (1 mg per kg per day) for ENL treatment, during a period that varied from 12 to 24 months.

Discussion

Brazil occupies a pivotal role in the study of leprosy since it is an endemic area and also has a generally well-organised health care system that allows for the control and analysis of large quantities of pertinent data. Notwithstanding the disturbing increase in leprosy and HIV co-infection, however, the aim of the present study was to provide information on non-HIV patients, in view of the paucity of published articles in this field and the frequent misdiagnoses in connection with these co-infections.

ATL is a zoo-anthroponosis endemic in the tropical and neotropical regions of the world, with approximately 1·5 million new cases each year.[3] The State of Rio de Janeiro, for example, detected 306 cases from 2007 through 2011,[4] 90% of which was notified by our institution.[5] ATL and leprosy are both caused by intracellular pathogens whose development depends on impaired cell-mediated immunity. Molecular studies show a similar pathway between these two diseases, suggesting a possible inability to mount an appropriate Th 1 response to up-regulate IL-12 receptor expression.[6] In our case series, we observed mucosal lesions, which are considered particularly challenging[7] and are the clinical expression of hyperergic responses.

Sporotrichosis is the most frequently-occurring subcutaneous mycosis in Brazil.[8] The scenario is one of an epidemic fueled by transmission of the disease via infected cats, resulting in the diagnosis and treatment of over 2,000 human cases at IPEC/FIOCRUZ since 1990.[9,10] Between 1998 and 2004, 759 humans and 1,503 cats were diagnosed in our clinic by isolating *Sporothrix schenckii* in biological specimens.[11] Interestingly, in the present case series, one immune-competent patient with a past history of leprosy also exhibited the uncommon condition of a disseminated cutaneous sporotrichosis, which is increasingly seen

in the zoonotic transmission of sporotrichosis. To our knowledge, only two reports on such co-infection have been published to date.[12,13]

Cryptococcosis is a fungal infection affecting about 960,000 patients worldwide in its meningeal form each year.[14] These numbers have been rising due to the high prevalence of HIV. Unfortunately, there are no other official and accurate numbers of the incidence in Rio de Janeiro, despite its being a common diagnosis in specialised centres. It is worth pointing out that all of the patients in the present study were non-HIV infected, but were receiving prednisone and thalidomide treatment for ENL reaction episodes. A plausible hypothesis could be that prednisone immunosuppression leads to a higher susceptibility to this fungal infection, an event reported numerous times in other diseases,[15,16] but only once in association with ENL.[17] Of additional interest is that this well-recognised immunosuppression, due to long-term steroid use for ENL, is often associated with tuberculosis and less commonly so with such intercurrent infections as strongyloides or any other neglected tropical diseases.[18] Clinicians need to be aware of the risks involved and be alert for evidence of locally-common infections among their ENL cases.

In summary, our case series report provides a unique description of eight leprosy-affected patients affected by three other endemic infections, suggesting the existence of diagnostic delay and a scenario of sub-notification. In medical practice, there is often a tendency to make the *a priori* assumption that typical signs and symptoms of leprosy are only due to this condition. However, once aware that this is not always the case, health workers should make an effort to question and reflect on each new patient complaint being put forward, without being distracted by or limiting their medical perspective to the present or past history of the patient. It is imperative that doctors learn to consider and recognise other coexistent infections in leprosy patients originating from endemic areas of these other diseases.

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