



Case Report/Relato de Caso

HTLV-1 associated myelopathy diagnosed during lepromatous leprosy reaction treatment: a case report

Mielopatia associada ao HTLV-1 diagnosticada durante tratamento de hanseníase virchowiana reacional: relato de caso

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ABSTRACT

Leprosy and human T cell lymphotropic virus type 1 infection are prevalent in Brazil. Coinfection by *Mycobacterium leprae* and HTLV-1 is reviewed and a case is reported. A 59 year-old woman was followed and HTLV-1 associated myelopathy was diagnosed during leprosy treatment. The clinical and neurological aspects of this unusual association were initially reviewed. Immunological markers and the possible prognoses due to the association of the diseases were discussed. The unexpected association of leprosy and **HTLV-1 associated myelopathy** may occur in endemic areas and causes difficulties in determining the correct diagnosis and adequate management of the neurological manifestations.

Key-words: Human T-cell lymphotropic virus type 1. Myelopathy. Leprosy.

RESUMO

Hanseníase e infecção pelo HTLV-1 são prevalentes no Brasil. A associação de hanseníase e infecção por HTLV-1 é revista e é relatado um caso de coinfeção. Paciente feminina de 59 anos teve diagnóstico de mielopatia associada ao HTLV-1 durante o tratamento para hanseníase. Aspectos clínicos e neurológicos desta associação, ainda não descrita, são revistos e os marcadores imunológicos e possíveis evoluções relacionadas com a associação dessas doenças discutidos. A associação de hanseníase e mielopatia associada ao HTLV-1, aparentemente pouco usual, pode ocorrer em áreas endêmicas e trazer dificuldades para o diagnóstico e tratamento das manifestações neurológicas.

Palavras-chaves: Vírus linfotrópico de células T humanas do tipo 1. Mielopatia. Hanseníase.

INTRODUCTION

Leprosy is still endemic worldwide. Brazil has high prevalence rates, with over 1 case/10,000 inhabitants. In 2008, 38,914 cases were diagnosed and the prevalent cases registered were 41,817¹. Infection by human T cell lymphotropic virus types 1/2 (HTLV1/2) is widely distributed in Brazil, which may have the greatest number of cases among endemic countries².

Both leprosy and HTLV-1 infection may course with incapacitating neurological manifestations. In leprosy, the damage is restricted to peripheral nerves and related to acute reaction episodes mediated by immunological alterations³. In HTLV-1 infection, the neurological damage occurs in the central nervous system (CNS), as an inflammatory disease that compromises the spinal cord, denominated HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP)⁴. The risk of HAM/TSP development among asymptomatic carriers is low (lifetime risk ranging from 0.25 to 3%). This myelopathy has a progressive course that is devastating to the affected individual⁴. The association between HTLV-1 infection and leprosy has been reported^{4,5}; however, no reports concerning the association of leprosy with HAM/TSP were found. The difficulties faced in treating the patient, the neurological alterations and the 14 year follow-up deserve attention.

CASE REPORT

A 59 year-old woman from the State of Minas Gerais, Brazil, an endemic area for leprosy, was diagnosed with lepromatous leprosy in 1993, with a bacilloscopy index (BI) of 6.0 and grade 0 disability. Her treatment was multibacillary multidrug therapy (MB-MDT) for 24 months. She developed type 2 reaction a year after being taken off the medication. The patient has been followed at the HC-UFMG (clinical hospital) since 1999, when she presented type 2 reaction with generalized erythema nodosum leprosum, as well as ulnar, fibular and tibial nerve enlargement. At the time, she presented zero BI, grade 1 disabilities in addition to foot insensitivity, controlled type 2 diabetes and a history of alcoholism. Thalidomide was prescribed at a dosage of 100 to 200mg/day. A year later, she reported weakening of the lower limbs and gait difficulty. Physical examination showed diminished muscular strength in extending the toes. Due to the aggravation of her symptoms, thalidomide was withdrawn and aspirin was initiated intercalated with thalidomide during the worse type 2 leprosy reactions.

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For a year, improvement in muscular strength occurred, though the foot insensitivity and diminished amplitude of movements in her toe interphalangeal joints persisted. At that time, HTLV-1 seropositive was verified, when she agreed to take part in a serum-epidemiological survey to evaluate HTLV-1 infection in dermatological patients⁶. She was then submitted to neurological examination, which confirmed that tactile and pain sensitivity was preserved from C2 to L3 dermatomes, with hypoesthesia from L4 to S5. No loss of motor strength had occurred in the myotomes analyzed. Hypopalesthesia of the inferior limbs was verified. Proprioceptive sensation was preserved and muscular tonus was normal. Hoffman's and Babinsky's signs were absent. Gait analysis showed diminished speed and metry and the base was slightly widen, maintaining her eyes focused on the ground. The electroneuromyographic exam was compatible with motor-sensory peripheral polyneuropathy, axonal, predominantly sensory to the lower limbs. The magnetic resonance image of the entire spine showed no alterations, with no changes in the intensity of the spinal cord sign. Ultrasonography of the upper urinary tract was normal and revealed thickening of the vesicle wall, compatible with neurogenic bladder, with significant (11%) post-mictional residue. The clinical impression was of a multifactor polyneuropathy: leprosy, diabetes, history of alcoholism, thalidomide and HAM/TSP. In 2001 she started using a T cane and in 2003 changed to a Canadian cane to assist locomotion.

DISCUSSION

The association of leprosy and HTLV-1 infection has been observed in Japan and África^{7,8}. Decreased survival among coinfecting individuals was previously observed, without correlation with the clinical subtype of leprosy, which was attributed to other infectious diseases⁹. Spastic paralysis and hyperreflexia were described among leprosy inpatients at New Caledonia¹⁰. These neurological alterations were verified in native and European-born individuals and the differential diagnoses among several neurological diseases were emphasized, including the spastic paralysis already described at Jamaica¹⁰. Nowadays, such paralysis is known to be related to HTLV-1^{4,5}.

In the present case, the great difficulty was related to the etiologic diagnosis of the neurological alterations. Several neurological manifestations involving different levels of evidence have been related to HTLV-1 infection. Polyneuropathy is possibly related to HAM/TSP and the patient usually does not show improvement during the course of this myelopathy⁴. Conversely, in polyneuropathy caused by adverse drug reaction, improvement is usually observed following suspension of the drug. The muscular strength improvement after thalidomide suspension provides support for this hypothesis. Nevertheless, some immunological aspects are common in both type 2 leprosy reactions and in HAM/TSP.

In type 2 leprosy reaction, increases in proinflammatory cytokines, such as the tumor necrosis factor- α (TNF- α) and interferon- γ (IFN- γ) in the serum are evidence of cellular immune activation. In addition, increases in the levels of mRNA of these cytokines are observed in biopsies of skin lesions³. In HAM/TSP, high levels of TNF- α and IFN- γ in serum and cerebrospinal fluid are observed⁴. In both conditions, there is an important participation of the Th1 response of the immune system. Whether the immune response pattern induced by HTLV-1 infection induces the leprosy

type 2 reaction, or the contrary, i.e., the presence of chronic type 2 leprosy reaction could aggravate the myelopathy caused by the virus, remains a question to be considered. While type 2 leprosy reaction promptly responds either to steroids or to thalidomide³, in HAM/TSP no reliable proven treatment has been developed, though corticosteroids use is recommended⁴. In the present case, response to specific leprosy treatment with MDT was usual and leprosy type 2 reaction diminished in frequency and intensity, such that it has ceased for the past three years. The patient maintains good control over the diabetes with no signs of background diabetic retinopathy; however, paraparesis gradually worsens and has been attributed to HTLV-1 infection.

In conclusion, the unexpected association of leprosy and HAM/TSP may occur in endemic areas and causes difficulties in determining the correct diagnosis and the adequate management of the neurological manifestations.

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