

EPISODES OF GUILLAIN-BARRÉ SYNDROME ASSOCIATED WITH THE ACUTE PHASE OF HIV-1 INFECTION AND WITH RECURRENCE OF VIREMIA

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ABSTRACT - We report a severe case of Guillain-Barré syndrome (GBS) characterized by flaccid areflexive tetraplegia and signs of autonomic instability related to acute HIV-1 infection, and the occurrence of relapse episodes coinciding with the detection of HIV-1 RNA in blood during the phase of irregular treatment with antiretroviral agents. The patient has been asymptomatic for 3 years and has an HIV-1 load below the limit of detection. The recurrence of GBS in this case may be related to alterations of the immunologic response caused by disequilibrium in the host-HIV relationship due to the increase in HIV-1 viremia.

KEY WORDS: recurrent Guillain-Barré syndrome, HIV-1 infection, AIDS, acute demyelinating neuropathy.

Episódios de Síndrome de Guillain-Barré associados com a fase aguda da infecção pelo HIV-1 e com recorrência da viremia

RESUMO - É reportado um caso grave de Síndrome de Guillain-Barré (SGB) caracterizado por tetraplegia flácida arreflexa e sinais de instabilidade autonômica relacionado com infecção aguda pelo HIV-1, e a ocorrência de episódios de recidivas coincidentes com a detecção do RNA-HIV-1 no sangue, durante fases de tratamento irregular com antiretrovirais. O paciente encontra-se assintomático há 3 anos e com a carga viral do HIV-1 abaixo do limite de detecção. A ocorrência de SGB, neste caso, pode estar relacionada com alterações da resposta imunológica ocasionada por desequilíbrio na relação hospedeiro-HIV devido ao aumento da viremia do HIV-1.

PALAVRAS-CHAVES: síndrome de Guillain-Barré recorrente, infecção pelo HIV-1, AIDS, neuropatia desmielinizante aguda.

Guillain-Barré syndrome (GBS) is an acute peripheral polyneuropathy characterized by symmetrical muscle weakness occurring in the absence of identifiable causes of genetic, metabolic or toxic origin. There are some variants of the disease with distinct presentation, etiology and pathological characteristics, with the most common form being acute inflammatory demyelinating polyneuropathy, which represents about 75% of the cases of the syndrome¹. The characteristic presentation of the syndrome involves symmetrical paresis or paresthesia of an ascending nature, with reduction or loss of deep reflexes and variable autonomic dysfunction. Examination of cerebrospinal fluid (CSF) reveals increased protein and normal or only slightly increased cellularity. The pathogenesis of GBS is not well known, but this is a disease with an important autoimmune component with cel-

lular and humoral activity in which antibodies probably are more involved in the mechanism of demyelination of peripheral nerves. The onset of the disease is associated with a history of infection, mainly of viral origin. There are several reports of the disease affecting HIV-infected patients, in which GBS occurs concomitantly with HIV seroconversion or during the initial phases of infection²⁻⁵. However, there are reports of the disease occurring also during the chronic phase⁶. There is evidence that GBS precedes acquired immunodeficiency syndrome (AIDS) and is not related to immunodeficiency, being usually observed in patients with high CD4⁺ lymphocyte counts. Cases of GBS associated with the immunological reconstitution induced by the use of highly active antiretroviral agents (ARV) have also been reported⁷. We did not detect reports of the occurrence of GBS related

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to the plasma viral load of HIV-1. Recurrent GBS is a rare condition which has been reported to occur at intervals ranging from 4 months to 10 years⁸, with the cases reported being unrelated to HIV.

We report, after written informed consent, a severe case of GBS related to acute HIV infection with recurrent episodes coinciding with the detection of HIV viral load in blood during the phase of irregular treatment with ARV.

CASE

A previously healthy 38-year-old man presented paresthesia and reduced evolute ascending muscle strength in the lower limbs of 4 weeks duration, progressing to involvement of the upper limbs and abdomen, with impairment of locomotion and of arm movements.

He had a history of promiscuous homosexual behavior, although an anti-HIV ELISA test was negative during the month preceding the onset of symptoms. He presented diffuse micropolyadenomegaly, and neurological examination revealed an alert patient with sensitive ataxia and tactile painful hypesthesia up to the root of the thighs, and of the glove type up to the distal third of the forearms. Muscle strength was reduced bilaterally in the upper and lower limbs, with global areflexia. Meningeal signs were absent.

The ELISA test was repeated, with a positive result for anti-HIV-1 antibodies, as confirmed by Western blot. A CD4⁺ lymphocyte count showed 502 cells/ μ L and the CSF contained 8 cells/ μ L, 194 mg/dL protein and 144 mg/dL glucose. At the time, the test for the quantitative determination of plasma HIV-1 RNA was not available. Electromyography revealed muscle action potentials with prolonged latencies, reduced conduction velocity with disperse morphology, partial block of peroneal nerve conduction and "F" waves with prolonged or non-detectable latencies with no signs of axonal damage, findings corresponding to those observed in GBS.

Intravenous immunoglobulin (400 mg/kg/day) was administered for 5 days, leading to progressive improvement of the symptoms. Eight days after the end of this treatment there was recurrence of the initial neurological picture accompanied by dysphagia, dysphonia and respiratory difficulty. Treatment with immunoglobulin was restarted, but the patient rapidly progressed to respiratory insufficiency, flaccid areflexive tetraplegia and autonomic instability characterized by hypertensive peaks, sudoresis, intestinal constipation and urine retention. Mechanical ventilation was necessary and the immunoglobulin cycles were maintained, complemented with plasmapheresis sessions. ARV treatment (zidovudine, lamivudine and indinavir) was started. Electroneuromyography was repeated, revealing the absence of a response in the study of motor conduction of the median, ulnar and peroneal nerves. "F" waves were not detected, suggesting severe axonal damage, with little evidence of re-innervation. A nerve biopsy was compatible with mild to moderate axonal damage. The patient was hospitalized in an intensive care unit for 4 months, present-

ing a slow progressive improvement of signs and symptoms. At the time of discharge from the hospital he had 1045 CD4⁺ lymphocytes/ μ L blood and plasma HIV-1 RNA below the detection limit. During follow-up the patient recovered completely using ARV, always maintaining CD4⁺ lymphocyte counts above 500/ μ L and HIV RNA below 50 copies/mL. Eighteen months after the acute signs and symptoms of GBS, he started to have reduced sensitivity and muscle strength of the extremities of the limbs. He had discontinued the use of ARV 15 days before due to episodes of renal lithiasis. On that occasion he had 570 CD4⁺ lymphocytes/ μ L and 2600 copies/mL of HIV RNA (3.41 log). ARV were reintroduced but were changed to zidovudine, lamivudine and ritonavir due to renal lithiasis. The patient coursed with progressive and rapid improvement of the neurologic symptoms and the HIV-1 viral load became undetectable.

About 31 months after the first episode of GBS, the patient discontinued ritonavir due to intestinal intolerance. About 30 days later he started to present paresthesia and progressive ascending reduction of muscle strength in the limbs, with difficulty in walking. At that time the CD4⁺ lymphocyte count was 677/ μ L and HIV RNA was 380,000 copies/mL (5.59 log). HIV genotyping showed that the virus was sensitive to all ARV. CSF examination showed 1.5 cells/ μ L and a protein content of 72 mg/dL. Electromyography was repeated and revealed alterations corresponding to GBS. The ARV scheme was replaced with zidovudine, lamivudine and efavirenz and treatment with immunoglobulin was started at weekly doses for about 6 months, with total recovery of movements and sensitivity. The patient has been asymptomatic for 3 years on the same antiretroviral scheme, with HIV-1 RNA below the detection limit.

DISCUSSION

Cell-mediated immunity is known to play an important role in the pathogenesis of GBS. The characteristic initial stage of GBS is associated with demyelination related to the action of macrophages, with multifocal distribution in the nerves. The main action of T cells appears to be the impairment of the integrity of the blood-nerve barrier by the action of metalloproteinases. T cells may also influence the recruitment of other cells of the immunologic response such as macrophages, Schwann cells and fibroblasts, resulting in the process of demyelination. Biopsy and autopsy findings have been contradictory regarding the presence or absence of perivascular lymphocyte infiltration in GBS. The fact that no lymphocytes are detected in nerves suggests that the changes mediated by antibodies are important, in agreement with the pathogenetic mechanism proposed for the onset of GBS, which occurs after infections, as is the case for *Campylobacter jejuni* infection⁹.

The mechanisms proposed for GBS in HIV-1-infected patients include a direct action of HIV-1 on the

nerves by neurotropic strains, or of autoimmune mechanisms, with the formation of antibodies against myelin secondary to the abnormal immunoregulation determined by HIV infection¹⁰.

The onset of GBS in this case coincided with the acute retroviral syndrome of HIV, during the phase of serologic conversion, as observed in other cases reported in the literature⁵. Particularly interesting in the case in question was the fact that new episodes of GBS occurred during a late period in relation to the acute picture, with the two recurrence episodes coinciding with periods of exacerbation of HIV-1 viremia due to the interruption of ARV. This fact may suggest the occurrence of peculiar physiopathogenic mechanisms related to lack of control of viremia.

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