Bilateral Peripheral Facial Palsy Secondary to Lymphoma in a Patient with HIV/AIDS: A Case Report and Literature Review

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Neurological complications represent one of the most important causes of morbidity and mortality in patients with HIV/AIDS. However, peripheral neuropathy comprises only 5% to 20% of the total neurological complications and facial nerve palsy, especially when it is bilateral, is a less common manifestation. Peripheral facial palsy has been considered as a possible neurological complication of the early stage of HIV infection but the number of reported cases in the literature is limited. Histological findings of nervous tissue in peripheral facial palsy at an early stage of HIV infection include a degenerative and not suppurative inflammatory process, but its etiology remains obscure. Peripheral facial palsy in the late stage of HIV infection is characterized by an advanced immunological deficit and generally it is secondary to an opportunistic infection of the CNS, such as neurotoxoplasmosis and lymphoma. However, this peripheral attack of the facial nerve is not very common at this late stage of HIV infection. Bilateral peripheral facial palsy as a complication of non-Hodgkin's lymphoma is considered an extremely rare entity. There are no published reports of bilateral peripheral facial palsy secondary to lymphomas or other neoplasms of the CNS in immunosupressed patients. Non-Hodgkin's lymphoma (NHL) has been considered a late and relatively common manifestation of HIV infection, but an exact cause for the higher incidence of this malignant neoplasm in HIV/AIDS patients is still uncertain.
Key Words: HIV, facial palsy, lymphoma.

Neurological complications are among the most important causes of morbidity and mortality in patients with HIV/AIDS [1]. However, peripheral neuropathy comprises only 5% to 20% of the total neurological complications [2,3], and facial nerve palsy, especially bilateral, is quite uncommon [1,4].

Though there have been some reports of facial palsy as a late complication of HIV infection [1], this neuropathy occurs mainly at early stages of virus infection [5]. However, in the specific case of bilateral facial palsy, there is no report of this type of complication late in the course of HIV infection, as found in our patient, who had bilateral facial palsy as a primary manifestation of a non-Hodgkin's lymphoma.

Non-Hodgkin's lymphoma has been considered a late manifestation of HIV infection [6,7], being frequently present in extranodal sites and particularly in the central nervous system (CNS) [8]. We report a case of bilateral facial palsy as a primary manifestation of non-Hodgkin's lymphoma in an HIV/AIDS patient.

Case Report

A 39-year-old homosexual male patient was admitted with a complaint of generalized myalgia, periorbit pain, headache and blotched vision with diplopia. Physical examination demonstrated a bilateral peripheral facial palsy predominantly on the right side (Figure 1).

Received on 21 May 2001; revised 15 February 2002.
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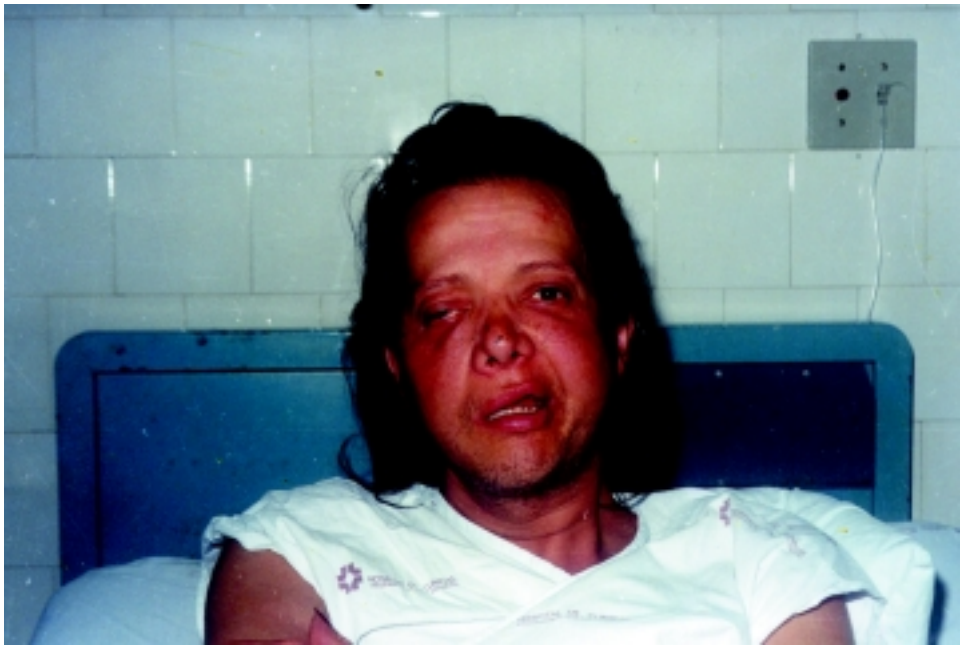
The Brazilian Journal of Infectious Diseases 2002;6(1):50-54

1413-8670

Figure 1. Picture of the patient showing bilateral facial palsy, with predominance on the right side



He had a 10 year-old positive ELISA test for HIV, which had been performed when the patient had a recurrent herpes simplex virus infection. At this time, the patient began the use of zidovudine, stavudine, indinavir and prophylaxis with trimethoprim-sulfamethoxazole. There was a history of marihuana use, but he denied intravenous drug abuse. The CD_4 and CD_8 counts were 175 cells/ml (17.5%) and 573 cells/ml (57.3%) respectively.

Cerebrospinal fluid (CSF) analysis revealed a total cellularity of 175 cells/mm^3, with 75% blasts and 25% lymphocytes. The CSF total protein level was 430 mg/dl and the glucose level was 13 mg/dl. The CSF immunophenotype showed 70% B-lymphocytes and 30% T-lymphocytes (23% CD_3^+ and 7% CD_4^+), with a positive light Kappa chain and a negative light Lambda chain. No organisms were seen on Gram's stain, and cultures were negative for bacterial, fungal, viral, and mycobacterial organisms. The CSF specimen was tested for cytomegalovirus antibodies and herpes simplex virus antigen; both were negative. A computer tomography (CT) scan of the brain was normal. An abdominal ultrasound made after the lumbar puncture revealed retro-peritoneal lymphadenopathy, which was confirmed by a CT of the abdomen. The latter also showed a hepatic steatosis, intestinal wall thickening and a lymphadenopathy of the hepatic hilum.

Because of the hypothesis of non-Hodgkin lymphoma, a weekly cycle of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) was begun, with a partial improvement of the symptoms, including the bilateral facial palsy. However, during the period of clinical observation, the patient worsened and died.

Discussion

Acute peripheral facial palsy can occur at any stage of HIV infection, even preceding the appearance of HIV antibodies, but it seems more common in a healthy HIV carrier than in a patient with AIDS. Thus, peripheral paralysis can be divided into two types according to it's etiology: one related with early stages and another related with late stages of HIV infection.

Early stage of HIV infection. Peripheral facial palsy has been considered as a possible neurological complication of the early stages of HIV infection [9], but there have been few reported cases, especially when we consider peripheral facial palsy related to AIDS, as in our patient.

Histological findings of nervous tissue in the peripheral facial palsy at early stages of HIV infection include a degenerative and non suppurative inflammatory process, but its etiology remains obscure [1]. Recent investigations suggest an infectious origin to this HIV related facial palsy, including principally, herpes simplex virus, adenovirus, mumps virus, rubella virus and, more recently, HIV [10]. Because of the great number of microorganisms involved, some authors support the idea of a common pathogenic mechanism, in which an immunological reaction associated with an infectious event could determinate a generalized cranial neuropathy that involves a compressive and degenerative process of the VII cranial nerve [10]. However, although this physiopathological hypothesis is a result of a long study, and though the predictive value of HIV in peripheral facial palsy reaches 73.63% in African reports [11], there is disagreement about the possibility of this neuropathy being caused by an immunological reaction against HIV or other pathogen. The relation between Bell's palsy and HIV infection may be only a coincidence, especially in the countries where the prevalence of HIV is high. We cannot attribute a direct role of HIV in facial palsy, especially since viral proteins have never been found in biopsies of peripheral nerves acutely compromised in the early stages of retrovirus infections [12,13]. On the other hand, the lack of virus at nerve biopsy in acute cases does not preclude its participation in the neuropathological inflammatory process; this could occur by immunocomplex development, especially because the acute stage of HIV infection is not always accompanied by immunosuppression [2].

We found only three reported cases of bilateral facial palsy in the early stage of HIV infection [4,15,16] and there was no primary pathology that would justify a bilateral attack of cranial nerve VII. Thus, the physiopathological mechanism is probably the same as in a unilateral pathology.

Late stage. Peripheral facial palsy at a late stage of HIV infection is characterized by an advanced immunological deficit and generally it is secondary to an opportunistic infection of the CNS, such as neurotoxoplasmosis and lymphoma. On the other hand, as we have already commented, this peripheral attack of the facial nerve is not very common at this late stage of HIV infection.

It is already known that in the immunocompetent patient, bilateral peripheral facial palsy is frequently associated with a complex of systemic pathology symptoms [17]. Thus, a detailed investigation of any patient with this diagnosis is fundamental.

In non-HIV patients some etiologies of bilateral facial palsy are already well described and they include polyarteritis nodosa, sarcoidosis, Lyme disease, acute or chronic otitis media, bulbar palsy, infectious mononucleosis, syphilis, tetanus, malaria, tuberculosis, leprosy, Melkersson-Rosenthal's syndrome, Guillan-Barre's syndrome, after rabies, poliomyelitis or influenza immunization and other malignant causes, especially acute leukemia [13,17-19]. Bilateral peripheral facial palsy as a complication of non-Hodgkin's lymphoma is considered an extremely rare entity. Ozmenoglu et al. [9] reported a bilateral disorder in the facial nerve associated with a non-Hodgkin's lymphoma in a non-HIV patient. There are no reports of bilateral peripheral facial palsy secondary to lymphoma or other neoplasms of the CNS in immunosuppressed patients.

Non-Hodgkin's lymphoma (NHL) has been considered a late and relatively common manifestation of HIV infection [6,20], but an exact cause for the higher incidence of this malignant neoplasm in HIV/AIDS patient is still uncertain. There are some theories that involve an ongoing infection by Epstein-Barr virus and a release of B-cell proliferation inducing cytokines by T-cells infected by HIV [8,21]. So, NHL associated with AIDS has different clinical and pathological characteristics from that found in the non AIDS-infected individuals. Histologically, many cases are B cell lymphomas, with an intermediate

or high degree of malignance [6,8,22,23], while clinically they are characterized by their predominance at extranodal sites [22,24] particularly in the gastrointestinal tract and the CNS [25].

In the specific case of primary NHL of the CNS, the most common symptoms are dizziness, focal neurological dysfunction, headache and/or cranial nerve palsy [26,27].

Diagnose of brain NHL is based on cytological confirmation by biopsy or cytology of CSF [28]. Radiological evaluation generally demonstrates one or two homogeneous or heterogeneous lesions in parenchyma, and can have an enhanced contrast on CT scan. Otherwise, NHL shows a brain toxoplasmosis-like lesion, which does not permit a definitive diagnosis of this neoplasm using only imaging methods [29,30].

The sensibility of detection methods for finding malignant cells in CSF varies with the neoplasm type, with meningeal involvement and with the extension of this involvement [31-34]. The percentage of primary brain tumor detection in CSF varies from 7.3% to 69.2%, with gliomas and medulloblastomas being more frequently detected [31,35]. In primary lymphomas of the CNS, malignant cells were detected in CSF in about 20% to 30% of the patients [33], as in our patient.

Some factors can help to increase the probability of finding neoplasmic cells in CSF, such as: multiple lumbar punctures, withdrawal of at least 10 ml of CSF, immediate processing of the sample and care at the collection site [36-38]. More sensible and specific methods than cellular morphology are also necessary for adequate identification of malignant cells in CSF. Immunocytochemistry and immunophenotype methods, and tumor biochemistry markers can help in this diagnosis [39-42]. In primary brain lymphoma, the level of soluble CD_{27} is increased in CSF [43,44], and Epstein-Barr virus (EBV) investigation by PCR also has diagnostic value [40,45].

Peripheral facial palsy, including bilateral cases, must always be an alert signal in the HIV-infected patient, considering that this palsy may be an initial manifestation of an NHL, which consequently will compromise the prognosis of HIV/AIDS patients.

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