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SPONTANEOUS ARTERY DISSECTION IN A PATIENT WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

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ABSTRACT - *Background:* The relationship between human immunodeficiency virus infection and stroke may be attributed in some cases to an underlying vasculopathy such as in spontaneous cervical arteries dissections. *Case report:* We report the case of an HIV-infected patient who developed a Wallemberg's syndrome due to a vertebral artery dissection. Screening laboratory exams showed hyperhomocysteinemia and also high C-reactive protein plasma levels. *Conclusions:* This is the first case describing the association between arterial dissection (AD) and HIV-infection. We suggest that AD should also be remembered as a possible mechanism of ischemic stroke in HIV-infected patients.

KEY WORDS: HIV, stroke, vertebral artery dissection.

Dissecção arterial espontânea em paciente com infecção pelo HIV

RESUMO - *Introdução:* A relação entre AVC e infecção pelo vírus da imunodeficiência humana (HIV) pode ser atribuída em alguns casos a uma vasculopatia subjacente, assim como ocorre nas dissecções arteriais cervicais espontâneas. *Relato do caso:* Relatamos o caso de um paciente com infecção pelo HIV que desenvolveu uma síndrome de Wallemberg devido a dissecção da artéria vertebral. Os exames laboratoriais revelaram aumento da homocisteina sérica e proteína C reativa. *Conclusão:* Este é o primeiro caso na literatura descrevendo a associação entre dissecção arterial e infecção pelo HIV. Sugerimos que o diagnóstico de dissecção arterial deve ser lembrado como um possível mecanismo de AVC isquêmico em pacientes com infecção pelo HIV.

PALAVRAS-CHAVE: HIV, AVC, dissecção artéria vertebral.

Current evidence supports the relationship between human immunodeficiency virus (HIV) infection and stroke, although the exact neuropathology of this association is not fully understood[1-5]. Spontaneous cervical arteries dissections (sCAD) are thought to be related to an underlying structural defect of the arterial wall, although the exact type of arteriopathy remains obscure in most cases. Increased plasma homocysteine levels were observed in patients with sCAD when compared to atherothrombotic strokes. A recent history of a respiratorytract infection is also a risk factor for spontaneous carotid and vertebral arteries dissection. The possibility of an infectious trigger is supported by the seasonal variation in the incidence of sCAD[6]. The relationship between HIV-related vasculopathy, carotid or vertebral artery dissections has not been described yet.

We report a case of an HIV-infected patient who developed a Wallemberg's syndrome due to a vertebral artery dissection.

CASE

A 50-year-old white man was admitted to our hospital with a three-day history of sudden right-sided neck pain initiated during physical effort. The cervical pain was followed by an ipsilateral pulsatile parietal headache. Forty minutes before admission he was also complaining of right arm and leg weakness, constant fallings and difficulty in swallowing. He had HIV-infection diagnosed five years earlier and has never taken antiretroviral medications. His last viral load, one year ago, was not detectable and he had CD4 lymphocyte percentage of 1000/μL. Hypertension and diabetes were not found in his prior medical history. General physical examination was not relevant and his neurological findings were suggestive of a Wallemberg's syndrome.

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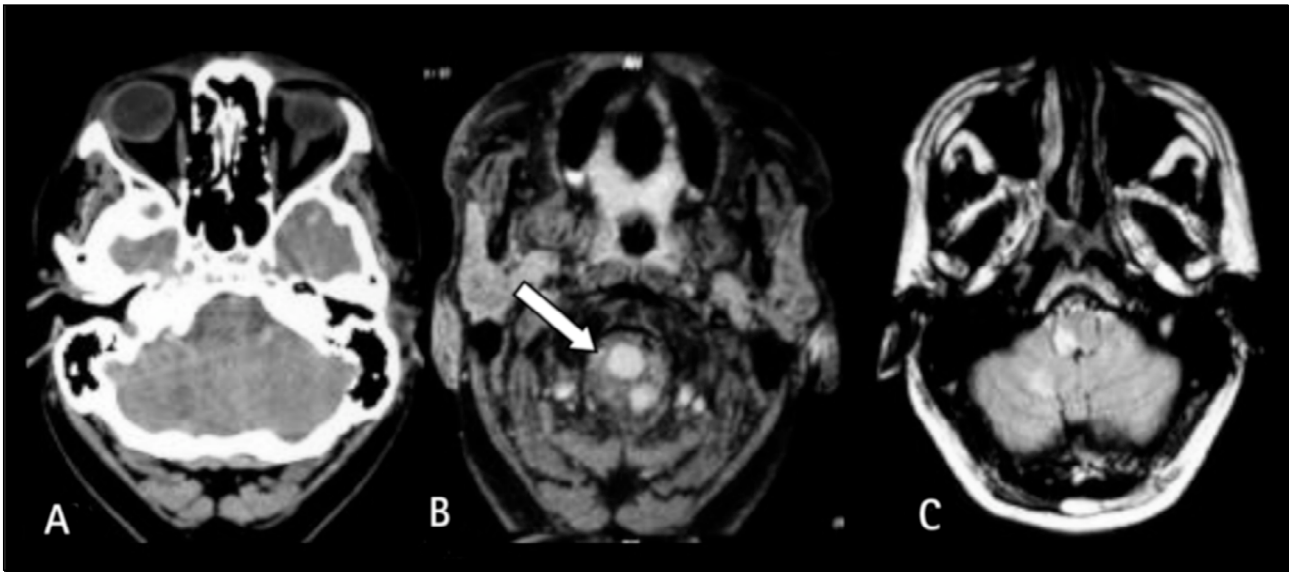

Fig 1. A) CT scanning: right hypodense cerebellar area. B-C) MRI: right medullar and cerebellar hyperintense signals on FLAIR. On T_1-weigthed image the lumen of the right vertebral artery is almost occluded by an intramural hematoma (white arrow).

CT scanning showed a right hypodense cerebellar area. MRI revealed right medullar and cerebellar hyperintense signals on FLAIR, T_1 and T_2-weighted images (Fig 1). The lumen of the right vertebral artery was almost completely occluded by an intramural hematoma. On MR angiography there was absence of right vertebral artery sign.

Laboratory tests, including coagulation studies were unremarkable, except for a level of plasma homocysteine= 15 μmol/L (Reference Value, RV: 5-10 μmol/L) and C-reactive protein=0.53 mg/dL (RV: <0.11). A screening for autoantibodies was negative. Serum complement was normal. New HIV viral load (VL) and CD4 lymphocyte percentage were: VL= 467 copies, CD4=1509 (CD4/CD8=1.18). Serologies for syphilis, Chagas disease, B and C hepatitis viruses and HTLV-1 and 2, cytomegalovirus (CMV) and *T. gondi* were negative. Viral and fungal immunological reactions on CSF were negative (Herpes virus type I and II, *Varicela zoster,* CMV, *P. brasiliensis, C. albicans, H. capsulatum, A. fumigatus, C. neoformans*) such as CSF polymerase chain reaction for Varicela zoster and Herpes simplex I and II.

The patient was given anticoagulant therapy with non-fractionated heparin with neurological improvement receiving warfarin and was discharged from our hospital with Rankin=1.

Informed consent was signed by one of his relatives allowing data publication.

DISCUSSION

Cerebral infarction in an HIV-infected patient may result from many sources such as cardiac origin, vascular changes, abnormalities of coagulation, cerebral opportunistic infection or neoplasm, injection drug use and other associations[1,3,4,7,8]. Reviews of neuropathology have documented cerebral infarction in 4% to 29% of HIV infected patients[1]. Among the common opportunistic infections that take part into blood vessel changes and may lead to ischemic strokes are tuberculosis, toxoplasmosis, aspergillosis, varicella-zoster, herpes simplex and cytomegalovirus infections, hepatitis B, syphilis, cryptococcosis, candidiasis and others[3,4,8-10].

HIV-related vasculopathy is regarded as one of the most important mechanisms of stroke in these patients nowadays[3]. Vascular lesions are usually characterized by hyaline small-vessel thickening, perivascular space dilatation, rarefaction, and pigment deposition, with vessel wall mineralization and perivascular inflammatory cell infiltrates without definitive evidence of vasculitis. These vascular changes are similar to those found in cases of cerebral arteriosclerosis in elderly, diabetic and hypertensive patients[1,11-13].

In the past decade, raised plasma total homocysteine level has emerged as a potential risk factor for the development of vascular disease. Mild hyperhomocysteinemia may result from nutritional and genetic factors. Several biological mechanisms might explain the association between increased levels of plasma homocysteine and arterial dissection. A link between hyperhomocysteinemia and abnormalities in the elastic components of the arterial wall has been described. In vitro studies demonstrated that high levels of plasma homocysteine result in a decrease in the elastin content of the arterial wall[14-15].

Micronutrient deficiency is frequent in HIV infected adults. Folate and cobalamin deficiency have been

specifically described in these patients, although it does not seem to be a common finding. Plasma total homocysteine increases considerably when there is an intracellular deficiency of folate or cobalamin, as it is a sensitive marker of suboptimal vitamin concentrations[16,17].

Stroke may occur in the context of a wide range of systemic inflammatory or infectious conditions. Cervical artery dissection has a significant association between recent infection. Current evidence also support that plasma C-reactive protein (CRP) concentration is elevated in patients with acute stroke with or even without infection[18]. Whether the interplay between HIV-infection and associated inflammation played a role in the case reported is difficult to assure but these mechanisms should be taken into account mainly if we consider that other causes were excluded.

Protease inhibitors (PI) are another possible reason for the occurrence of cerebrovascular diseases in HIV-infected patients. It is believed that the use of these medications lead in a long-term period to accelerated atherosclerosis[3]. This could be the effect of the metabolic abnormalities produced by PIs: dyslipidemia and insulin resistance. It is important to emphasize that, while the association between PIs and dyslipidemia is well documented, the risk of clinically important premature atherosclerosis remains to be established[19]. In the case we reported HAART was never introduced.

Although the exact process leading to sCAD in our case remains elusive, increased plasma homocysteine levels due to cobalamin or folate deficiency related to HIV infection may have played a role in the mechanism of vascular injury.

As far as we know, there is no previously described association between vertebral or carotid dissection and HIV-infection. Since a casual relationship between these two conditions in the case reported could not be established, other clinical observations specially focusing on neuropathological features are necessary to provide further information on the role of HIV related vasculopathy and dissection of cervical arteries. Our report is also important to remind that cervical arteries dissections should be considered as a possible mechanism of ischemic stroke in HIV- infected patients, regardless of the causal relationship of these two conditions, once most of these patients are young and free of traditional vascular risk factors.

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