

# REMISSION OF REFRACTORY CHRONIC CLUSTER HEADACHE AFTER WARFARIN ADMINISTRATION

## Case report

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**ABSTRACT** - Isolated reports of a possible positive effect of anti-coagulant drugs, among them heparin, warfarin and acenocumarol, in migraine prophylaxis are found in the literature. We report the case of a 37 years old man suffering from refractory chronic cluster headache that presented remission with the administration of warfarin for the treatment of deep venous thrombosis associated to arterial thrombosis. We did not found any case like that in the literature.

**KEY WORDS:** cluster headache, warfarin.

### **Remissão de cefaléia em salvas crônica refratária após administração de varfarina: relato de caso**

**RESUMO** - Alguns relatos isolados na literatura referem-se a um possível efeito profilático de drogas anti-coagulantes, entre elas a heparina, varfarina e acenocumarol na profilaxia da migrânea. Apresentamos o caso de um homem de 37 anos com cefaléia em salvas crônica refratária que obteve remissão total das crises após a administração de varfarina para o tratamento de trombose venosa e arterial. Não encontramos nenhum relato semelhante na literatura consultada.

**PALAVRAS-CHAVE:** cefaléia em salvas, varfarina.

Isolated reports of a possible positive effect of anticoagulant drugs, among them heparin, warfarin and acenocumarol, in migraine prophylaxis<sup>1-5</sup> are found in the literature. We do not know references to a prophylactic action of these same drugs on cluster headache. We report the case of a patient suffering from chronic cluster headache, up to this point refractory to the treatment and that presented remission with the administration of warfarin for the treatment of deep venous thrombosis associated to arterial thrombosis.

### **CASE**

A 37 years old white man, salesman, searched medical care due to headache complaint, for the first time, on December 1997. At that time, he reported that the headache had started about two months ago and, since then, he experienced pain with a frequency of one to two crises a day. Headache was described as very strong, obligating the patient to interrupt all and any activity. The pain was invariably located on the left orbit, periorbital and temporal regions, and never changed side. Du-

ring crises, the patient used to be unquiet, walking around, with the hand open against the painful eye. Together with the headache, the patient presented conjunctival injection, eyelid ptosis, nasal congestion and excessive tearing, only on the pain side. These manifestations lasted a time varying from 45 min to 120 minutes. About a third of pain crises occurred during the sleeptime, awakening the patient. The patient was previously healthy and never presented a similar picture before. He also had never been subjected to recurring headache. Neurological examination revealed only a left Horner's syndrome. Blood pressure was normal (130 X 80 mmHg).

Because a so characteristic manifestation, the diagnosis of cluster headache was established and treatment was started with a course of prednisone (60 mg/day) and verapamil (240 mg/day). In order to abort the crises, we gave a prescription of subcutaneous sumatriptane (6 mg) or the inhalation of 100% oxygen. While the patient was using prednisone, there was a significant reduction of the frequency of crises, but complete remission was not achieved. From then on, several medications were tried, sometimes in monotherapy or in association of up to three drugs, namely lithium carbonate (up to 900 mg/day) dival-

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proate sodium (up to 1,500 mg/day); topiramate (up to 200mg/day); methysergide (up to 4mg/day); indometacin (up to 150mg/day), naratriptan (up to 5,0 mg/day), ergotamine (up to 4 mg/day), however, complete remission of the crises was never achieved. There were periods when the crises became less frequent and others when there was a recrudescence of the pain, returning to the original frequency of one to two crises a day. For the acute care, the best result was achieved with oxygen and patient got used to utilize it at the first sign of pain. A magnetic resonance image of the brain performed was completely normal.

The situation remained unchanged until July, 2002, when, in spite of the use of multiple drugs, there was a new increase of the crises frequency that, by that time, started responding less to the use of oxygen and sumatriptane. We prescribed again prednisone, in the dose of 60 mg, what gave him a significant relief. Any try to reduce prednisone, however, caused the return of the pain with an intolerable frequency and the patient became *corticoid-dependant*. On December 2002, we suggested the surgical treatment, but this was not possible due to personal reasons, and the patient continued the self-medication with the corticoid, in addition to keep the use of verapamil and divalproate sodium with medical prescription. He returned to our office in March, 2003, in a deplorable psychological status, still having frequent crises of headache and with several side effects of corticotherapy: cushingoid aspect; systemic blood hypertension and diabetes mellitus. We suggested again the surgical treatment and he agreed.

During the weeks prior to surgery, the patient broke the left ankle in an accident and evolved with deep venous thrombosis and acute arterial occlusion in the same member, being admitted in the hospital in May 23, 2003, when enoxaparin started to be given in the dose of 80 mg each 12 hours. While he was at the hospital, prednisone (60 mg/day) verapamil (720 mg/day) and divalproate sodium (1,500 mg/day) was maintained and, spite of the many analgesic used for the treatment of pains related to arterial occlusion (codein, tramadol, meperidine and injectable antiinflammatory medications), the crises kept occurring, and relief was only partially achieved with oxigen inhalation. He was submitted to an embolectomy in May 30, 2003 and, once again, in June 04, due to reocclusion of the vessel. From July 07 on, warfarin started to be given, in the initial dose of 5 mg/day. With the start of oral anticoagulant, there was a reduction in the frequency of cluster headache crises. They were no longer daily, but the complete remission was not achieved. On July 11, as the INR was still of 1.8, warfarin was increased to 10 mg/day, obtaining a INR  $\geq$  2.5. From then on, the patient did not present headache. Prednisone and divalproate sodium were gradually reduced and, finally, discontinued, and verapamil (480 mg/day) was maintained with no recurrence of the crises.

On October, 2003, the patient presented arterial occlusion again, requiring another vascular surgery. During hospital time, warfarin was replaced by heparin, and crises compatible with cluster headache returned. After the new surgery, the use of warfarin was reestablished, and the remission of crises was achieved again. Now (March, 2004) more than four months after the return to warfarin, the patient takes no longer prednisone or divalproate sodium. He takes verapamil 240 mg/day as anti-hypertensive drug and has no longer crises. INR has been kept around 2.5.

## DISCUSSION

In the present case, it is necessary to consider the possibility of coincidence, but the patient had presented cluster headache crises for more than six years, with no effective control, spite of being in use of suitable medications. With the use of warfarin and achievement of INR 2.5, there was the remission of crises. When it was necessary to replace warfarin with heparin, the crises returned and, once more, they have ceased with the return to oral anticoagulant.

An important datum is that the patient was a smoker, and consumed about 20 cigarettes a day, and the relief during the first hospital admission could be attributed to the smoking habit interruption. However, during the second hospital admission, when the warfarin suspension produced the return of crises, the patient had not smoked for months and the crises remitted only when the use of warfarin was returned.

Our evaluation is that, as it occurs for some patients with migraine, warfarin may have a preventive effect on the cluster headache.

This is the first case in the literature, as far as we know, of a patient with chronic cluster headache refractory to treatment presentig complete remission of the crises following administration of warfarin for another purpose.

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