# HEMORRHAGIC STROKE AFTER NAPHAZOLINE EXPOSITION

## Case report

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ABSTRACT - Ten percent of all strokes are due to spontaneous cerebral hemorrhages. They are associated to drugs (licit and illicit) in 9.5% of all cases in young adults. This is a case report of a 44-year-old man, without previous morbidities, who presented a sudden onset headache and arterial hypertension 24 hours after use of naphazoline as nasal decongestant. Cranial tomography showed right thalamus hemorrhage. Cerebral angiography showed no aneurisms, vascular malformations or vasculitis. No other risk factors were found during investigation in this patient and the stroke was attributed to naphazoline exposition.

KEY WORDS: hemorrhagic stroke, naphazoline, sympathomimetic drug.

### Acidente vascular encefálico hemorrágico após exposição à nafazolina: relato de caso

RESUMO - Dez por cento de todos os eventos vasculares encefálicos são devido às hemorragias intracerebrais espontâneas, associados a drogas (lícitas e ilícitas) em 9,5% de todos os casos em adultos jovens. Relatamos o caso de um homem de 44 anos de idade, sem doenças prévias, que apresentou cefaléia súbita e hipertensão arterial 24 horas após o uso de congestionante nasal contendo nafazolina. A tomografia de crânio evidenciou hemorragia talâmica. Durante a investigação não foram encontrados outros fatores de risco e a hemorragia foi atribuída à exposição à nafazolina.

PALAVRAS-CHAVE: doença vascular encefálica hemorrágica, nafazolina, droga simpaticomimética.

Cerebrovascular diseases occur more frequently in elderly people. Peak incidence is between 7<sup>th</sup> and 8<sup>th</sup> decades<sup>1,2</sup>. Before age 55, incidence is 10%<sup>3,4</sup> and before 45 it falls to 3.9%<sup>5</sup>.

Ten percent of all cerebrovascular events are due to hemorrhage<sup>6</sup>. Its estimated incidence in United States of America is 0.3/100000 in younger than 35 years old<sup>7</sup>. Main etiologies are vascular malformations, arterial hypertension and exposition to drugs (amphetamines, sympathomimetics and illicit drugs)<sup>8,9</sup>. In young adults, drugs are associated to 9.5% of ischemic and hemorrhagic stroke<sup>10</sup>.

We report a case of exposition to sympathomimetic drug naphazoline followed by thalamic hemorrhage.

#### **CASE**

A 44 year-old previously healthy man, with no history of arterial hypertension, was admitted to the emergency department of Hospital de Clinicas, Federal Uni-

versity of Parana, complaining of headache and left arm weakness. Five days before he had had some flu-like symptoms and naphazoline nasal decongestant was prescribed. In the following day he had a sudden onset headache associated to nausea and vomiting. He then looked for medical attention. Blood pressure was 190/120 mmHg and captopril 50 mg as a single dose was prescribed. A couple of days latter he developed left hemiparesia that made him seek for our emergency department. There was no previous history of thrombotic disorders and there were no familiar stroke cases.

On physical examination vital signs were normal including blood pressure (120/70 mmHg), with no positive signs on cardiopulmonary and abdominal examination. Neurological examination revealed an oriented patient, with intact memory and cognition. Cranial nerve examination showed no positive signs. There was left arm and leg hypotonia and slight weakness (4-/5). Babinski sign was not present. He could stand up by himself and there was no gate disorders or cerebellar signs.

Cranial CT revealed thalamic hemorrhage of 2.1cm

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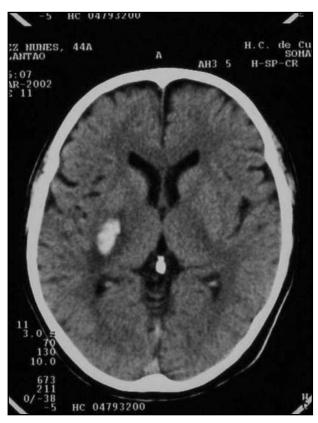


Fig 1. Cranial tomography showing right thalamus hematoma.

x 1.6 cm (Fig 1). The patient was admitted to the Neurologic Unit. Chemical constituents of blood and hematological exams as total cholesterol and fractions, fast glucose, triglycerides, complete blood count, coagulation tests (hypercoagulable states from protein C, free protein S, antitrombin III, lupus anticoagulant and anticardiolipin antibody abnormalities) and inflammatory marks were negative (C-reactive protein, ESR). Electrocardiogram and echocardiogram were normal. Cerebral angiogra-

phy revealed no aneurisms, vascular malformations or vasculitis (Fig 2). No drugs were needed to control blood pressure and the patient was discharged in the 8<sup>th</sup> day after admission with total recovery of the motor deficit.

#### DISCUSSION

Cerebrovascular diseases are an example of medical conditions with multiple risk factors. Complete investigation of predisposing factors and exhaustive laboratory data performance are needed to find their cause. Even these efforts are not always sufficient and the diagnostic conclusion is made by exclusion. In younger patients it becomes more evident once vascular risk factors can be absent most of the time.

Most common causes of hemorrhagic stroke in young adults are vascular malformations, including cavernous angiomas, and arterial hypertension<sup>11</sup>. Risk factors are smoking and hypocholesterolemia. In 1984, Pentel described sympathomimetic drugs exposition as a risk factor for cerebrovascular disease<sup>12</sup>. Most common drugs associated to stroke were phenylpropanolamine, ephedrine, pseudoephedrine and caffeine leading to hypertension, hypertensive encephalopathy and hemorrhagic stroke. Sloan et al. found a positive previous exposition to drugs in 11% of 116 cases of stroke between 1988 and 1989<sup>10</sup>. There was no difference for hemorrhagic or ischemic stroke. Related substances were cocaine, heroine, sympathomimetic drugs and phencyclidine. Most recently, Morgenstern et al. showed association between high doses of Ephedra in over-the-counter products for weight loss and energy enhancement and occurrence of hemorrhagic stroke13.

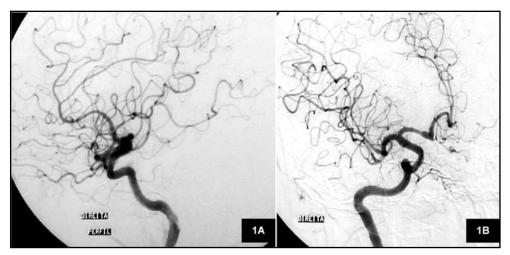


Fig 2. Lateral (1A) and anterior view (1B) of cerebral angiography showing no aneurysms, vascular malformations or vasculitis.

Until 1992, 142 cases of hemorrhagic stroke associated to exposition to phenylpropanolamine as nasal decongestants have been reported <sup>14</sup>. Between 1969 and 1991, there were 22 spontaneous reports of such relation to the FDA.

In order to verify if association of phenylpropanolamine to stroke was true, Kernan et al conducted a prospective study between 1994 and 1999<sup>15</sup>. Association was positive for patients who used it as nasal decongestant for the first time and for woman who used it as appetite moderators. A possible mechanism for cerebral infarction is focal arterial vasoconstriction and occasionally cerebral vasculitis. A likely mechanism for intracranial hemorrhage is acute arterial hypertension. With the exception of endocarditis, management of stroke related to drug abuse is largely supportive, with emphasis on supportive care to prevent stroke complications, physical and occupational therapy, and aggressive addiction rehabilitation.

There are no other risk factors than exposition to naphazoline in the reported case above. No other similar cases were found in medical literature. Our conclusion is that as it is a sympathomimetic drug as phenylpropanolamine, it can lead to the same adverse reactions such as arterial hypertension and stroke.

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