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Case Report

Reversible cerebral vasoconstriction syndrome secondary to chronic cocaine abuse: Case report ☆

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ABSTRACT

We describe the case of a 36-year-old male patient with a history of chronic headache who came to the emergency room due to an intense global headache, associated with a tonic-clonic episode and loss of consciousness. A cranial computed tomography revealed subarachnoid hemorrhage without apparent aneurysms and a left temporal hyperdense lesion suggestive of intraparenchymal hematoma on the follow-up computed tomography. Cerebral angiography showed irregularities in the right internal carotid artery, including a pseudoaneurysm and multiple stenoses in pial arteries, which were related to chronic cocaine use. The final diagnosis was reversible cerebral vasoconstriction syndrome, a rare but potentially serious condition, triggered in this case by cocaine use. Early diagnosis, through imaging studies such as cerebral angiography, is crucial to prevent serious complications like hemorrhages or ischemic events. This case highlights the importance of imaging in the diagnosis of reversible cerebral vasoconstriction syndrome and its relationship with triggers such as sympathomimetic drugs.

Introduction

Cocaine is a widely used sympathomimetic drug worldwide, and its production and consumption have increased in recent years, predisposing individuals to the development of multiple pathologies associated with this practice. One of them is reversible cerebral vasoconstriction syndrome, characterized by stenosis caused by cerebral arterial vasoconstriction. The development of imaging techniques has improved the diagnosis of this condition, allowing for appropriate approaches to its management.

☆ Competing Interests: We have no conflict of interest.

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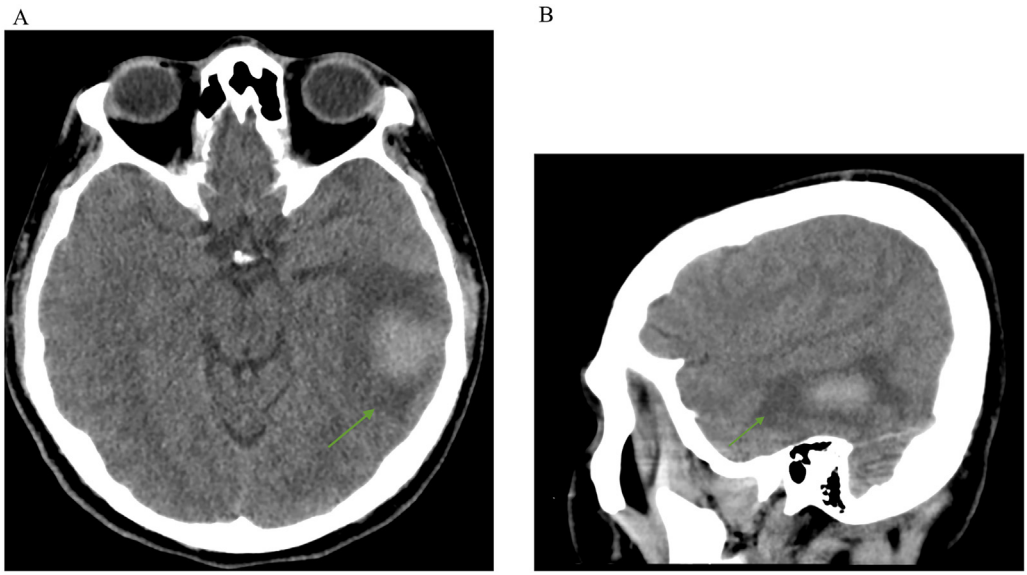

Fig. 1 – (A and B) Axial and sagittal view of cranial CT identifying left temporal intraparenchymal hemorrhage with marked perilesional hypodense vasogenic edema indicated by the arrow.

Case description

A 36-year-old male patient with a history of chronic headache presented to the emergency department due to worsening symptoms, including a global headache, with an intensity of 10/10, associated with a tonic-clonic episode in the right upper limb, blurred vision, and loss of consciousness, without sphincter relaxation in the postictal state. On initial physical examination, he was alert, hypertensive, and showed no signs of neurological focalization. A noncontrast cranial CT scan revealed Fisher II subarachnoid hemorrhage, without apparent related aneurysmal dilations. A follow-up CT showed a left basal temporal subcortical intra-axial supratentorial lesion, hyperdense, likely related to an intraparenchymal hematoma with a hypodense halo suggesting perilesional vasogenic edema (Figs. 1A and B).

Subsequently a cerebral panangiography was performed to rule out vasculitis or any arteriovenous malformation, identifying irregularities in the contours of the right cervical internal carotid artery, with a 5 mm lateral pseudoaneurysm and slight distal stenosis. (Fig. 2). Additionally, multiple areas of stenosis were observed in the medium and small caliber pial arteries across all vascular territories, as well as an old dissection of the right cervical internal carotid artery (Fig. 3). Autoimmune pathology was ruled out with normal extractable nuclear antigen antibodies (ENA) and complement levels. The findings were associated with chronic cocaine use, which the patient initially omitted from his history upon admission.

Fig. 2 – Cervical vessel angiography: Irregularities in the contours of the right cervical internal carotid artery are indicated by the white arrow, showing a 5 mm lateral pseudoaneurysm and slight distal stenosis indicated by the green arrow.

Discussion

Reversible cerebral vasoconstriction syndrome (RCVS) is a set of rare and difficult-to-diagnose disorders resulting from mul-

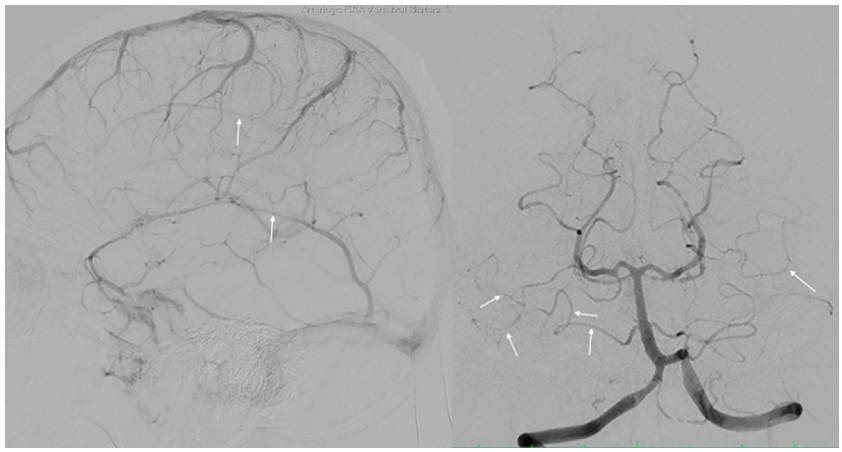

Fig. 3 – Cerebral panangiography: Multiple areas of stenosis in medium and small caliber pial arteries with a beaded appearance or resembling the "Sausage on a string" sign.

tifactorial cerebrovascular dysregulation. There is no precise epidemiological data regarding its frequency; however, some reports show a highly variable incidence, reaching up to 50%, which has increased thanks to the growing understanding of this condition and the support of diagnostic imaging that confirms the findings [1]. It has been described to occur more frequently in women than in men, with a 2:1 ratio, increasing to 10:1 in the postpartum period [2]. The average age of onset is usually around the fifth decade of life, although cases have been reported in childhood, where it affects males more frequently [3].

Regarding the pathophysiology, no single cause has been established for this syndrome. Some proposed mechanisms involve factors such as oxidative stress or endothelial dysfunction caused by multiple agents as contributors to the disease. Cocaine is a sympathomimetic drug; according to Colombian statistics, in 2019, the prevalence of consumption was 2.1% in the population aged 12 to 65 years [4]. Globally, the World Health Organization has reported an increase in production, with cocaine available in up to 90% of countries worldwide. Since 2011, its use in Europe has risen by up to 80% [5]. The active metabolite is benzoylecgonine, a sodium channel blocker that increases sympathetic activity at low doses. In the central nervous system, it blocks presynaptic nerve terminals and inhibits the reuptake of norepinephrine, serotonin, and dopamine [6]. There is an elevation of endothelin-1 in response to stress reducing nitric oxide production and causing sudden vasoconstriction. Additionally, increased dopamine levels trigger cerebral vasospasm.

The most common symptoms are related to the criteria proposed by Singhal et al., showing a specificity of more than 98% and a positive predictive value (PPV) of 98%-100% for suspecting and differentiating it from primary angiitis of the central nervous system (PACNS). These criteria include: recurrent thunderclap headaches, defined as a sudden, global headache that reaches its peak intensity within 60 seconds and may be accompanied by vomiting, neck stiffness, and even altered consciousness of variable duration; or a single thunderclap headache with normal neuroimaging or watershed infarction/vasogenic edema; or no thunderclap headache but abnormal angiographic findings with normal neuroimaging. In primary angiitis, there are always abnormal imaging findings [7].

Vasospasm and prolonged vasoconstriction can trigger ischemic strokes due to reduced arterial flow, as well as subarachnoid hemorrhage resulting from arterial wall rupture caused by increased intravascular pressure from vasoconstriction. Hemorrhage occurs less frequently, in up to 20% of cases [8].

Approximately 70% of patients during the first episode of the syndrome present with neuroimaging that shows no pathological findings. However, after 2 weeks, 70% of those who require hospitalization will experience complications, starting with parenchymal or subarachnoid hemorrhages before cerebral ischemic manifestations. The gold standard for diagnosing this condition is cerebral angiography, where the most common finding is the "string-of-beads" sign, characterized by arterial segments alternating between dilated and narrower segments due to vasoconstriction, primarily affecting medium and large-caliber arteries. This finding tends to normalize within 8 to 12 weeks [9]. Other diagnostic methods such as CT and magnetic resonance imaging are highly useful for evaluating early signs of potential complications. Follow-up is preferably done with transcranial Doppler, a safe, non-invasive, and readily available technique for patients (Table 1) [10].

RCVS has replaced terms for conditions now recognized as subtypes of this syndrome, each characterized by different triggers, such as postpartum cerebral angiopathy, since pregnancy is a prothrombotic state that alters vascular tone. Similarly, migraine-related vasospasm is considered another subtype, though it is not yet fully understood whether it is a risk factor for the syndrome or a manifestation of it. There are also numerous differential diagnoses for this condition, including intracranial atherosclerosis, moyamoya disease, and infectious vasculitis, among others. The condition most often confused with RCVS is PACNS; however, there are imaging characteristics that can help guide the diagnosis (Table 2) [11].

Table 1 – Imaging findings in RCVS [10–12].

Imaging modality	Findings in RCVS
Cerebral angiography	"Sausage on a string' sign in medium and large caliber arteries.
Computed tomography (CT)	• Convexity subarachnoid hemorrhage • Ischemic stroke (watershed infarct) [11] • Lobar intracerebral hemorrhage • Vascular narrowing in CT angiography
Magnetic resonance imaging (MRI)	• **T2/FLAIR:** Sulcal hyperintensities reflecting convexity subarachnoid hemorrhage or vascular hyperintensities (early sign). Cortical hyperintensities related to cortical edema (early sign). Vasogenic edema related to vasoconstriction or cytotoxic causes • **T2/FLAIR C+ (Gd)** Blood-brain barrier disruption • **Resonance Angiography (MRA)** Vascular narrowing • **Diffusion-Weighted Imaging (DWI)** Watershed infarcts (diffusion restriction).
Transcranial Doppler	• Increased basal velocity of the middle cerebral artery (>21 cm/s/day) within 3 days after subarachnoid hemorrhage (SAH) is highly suggestive of vasospasm. • Velocities above 160 cm/s are usually required to produce symptoms. • Lindegaard ratio >3.0 is diagnostic, and ratios >6.0 indicate severe vasospasm) [12].

Table 2 – Differences between RCVS and PACNS in imaging [13].

Features	RCVS	PACNS
Abnormalities in initial CT or MRI	Present in 70% of cases	Exclusively present (100% of cases)
Infarcts	Occur in 28% of cases	Occur in 81% of cases
Vasogenic edema	Typical in RCVS patients	Rare in PACNS
Convexity subarachnoid hemorrhage	Common in RCVS	Rarely observed in PACNS
Hyperintense artery sign on FLAIR	Observed in approximately 61% of patients	Observed in only 7% of patients

Conclusion

The advancement of diagnostic imaging, such as cerebral angiography, and the understanding of the pathophysiology of RCVS have allowed us to improve the timely and effective diagnosis of patients. Radiological signs are essential when there is a relevant clinical context, such as a history of cocaine use, to make the diagnosis.

Patient consent

Consent was received to publish both the clinical history data and the images from the patient. Available upon request.

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