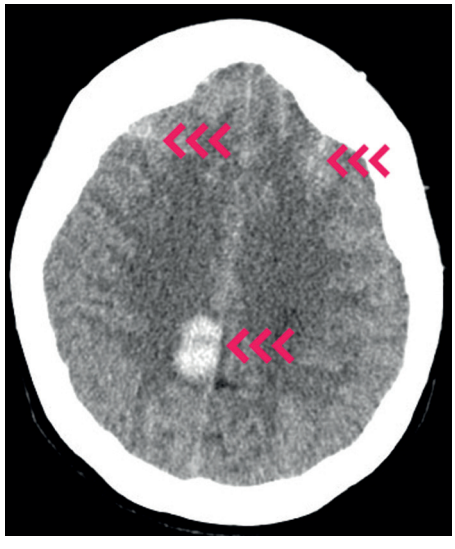
Reversible cerebral vasoconstriction syndrome after sudden caffeine withdrawal

Introduction

Reversible cerebral vasoconstriction syndrome is a rare cause of sudden thunderclap headache, with several potential precipitating factors. Treatment is focused on avoiding any identified precipitants. The prognosis is generally good. This article discusses a middle-aged woman who presented with severe sudden onset frontal headache which began very soon after abruptly stopping caffeine tablets. She was also taking sertraline and citalopram. Her neuroimaging demonstrated diffuse subarachnoid haemorrhage with irregularity of her middle cerebral arteries on angiography. Subsequent scanning revealed normalisation. She recovered well. A clinical diagnosis of reversible vasoconstriction syndrome was made.

Caffeine withdrawal has not previously been described as a precipitant of reversible cerebral vasoconstriction syndrome. Although the patient was taking two selective serotonin-reuptake inhibitors known to be associated with reversible cerebral vasoconstriction syndrome, the timing of her presentation suggests caffeine withdrawal as the cause.

Figure 1. Non-contrast computed tomography scan of the head on admission demonstrating right parafalcine haematoma with diffuse bilateral cortical subarachnoid haemorrhage.



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Discussion

Reversible cerebral vasoconstriction syndrome is characterized by severe headaches, with or without other acute neurological syndromes, and diffuse segmental constriction of cerebral arteries that resolves spontaneously after 3 months (Ducros, 2012). Thunderclap headache is

CASE REPORT

A 57-year-old woman presented to the emergency department with a sudden onset of frontal headache, sharp in nature, made worse on sneezing and vomiting. She had no photophobia. She had vomited 12 times the day before admission. She also complained of left leg weakness which came on at the same time as her headache. She stated that she had felt confused, agitated and unable to walk. There were no visual symptoms. She had no previous history of headaches or migraines.

She had been taking 900 mg (18 tablets x 50 mg) of ProPlus tablets (caffeine anhydrous sulphate) daily for the past 6 months because of stressors in the family, and had abruptly stopped them 3 days previously as she was unable to afford them. She took metoclopramide, thiamine and fentanyl, as well as amitryptiline, citalopram and sertraline for lumbar spondylosis and depression. Dual prescription of selective serotonin-reuptake inhibitors is not recommended and the reasons for this treatment regimen are unclear. She smoked 15 cigarettes a day, did not drink alcohol and did not take any illicit drugs. There was no family history of intracerebral haemorrhage.

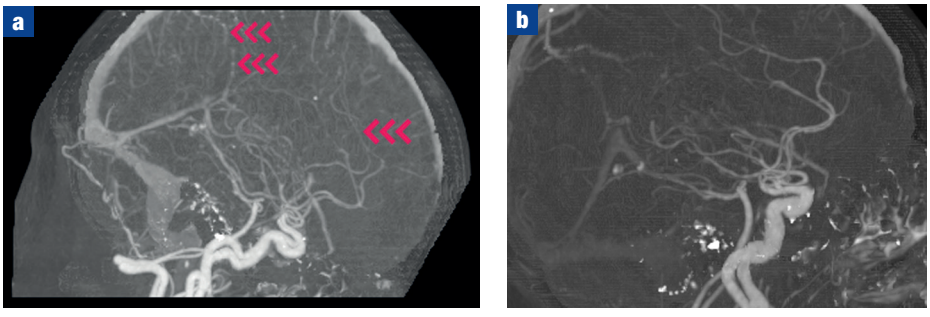
On examination, she had reduced power 3/5 in her left lower limb, and power 4/5 in her left upper limb, coordination was normal, reflexes were equal and reactive bilaterally, with upgoing plantars on the left and equivocal on the right. No cranial nerve abnormalities were found. Blood pressure was 128/63 mmHg. Her modified Rankin score was 3.

Routine haematological and biochemical blood tests were normal. Computed tomography brain scan revealed diffuse cortical subarachnoid haemorrhage, with a right precuneus haemorrhage (*Figure 1*). Computed tomography angiography of her intracranial vessels showed bilateral irregularity of the distal middle cerebral artery branches suggesting stenosis or spasm but no intracranial aneurysm (*Figure 2a*). Repeat imaging 3 months later showed resolution of the middle cerebral artery branch irregularities, suggesting spasm as the cause (*Figure 2b*). Magnetic resonance imaging including blood-sensitive sequences and magnetic resonance venogram demonstrated no evidence of amyloid angiopathy or cerebral venous sinus thrombosis.

The patient was admitted to the stroke unit. She was treated with nimodipine 60 mg 4-hourly for 3 weeks as empirical treatment for suspected intracranial arterial spasm, and her sertraline and citalopram were stopped.

Following multidisciplinary therapy review, the patient was referred for early supported discharge and left hospital after 1 week as an inpatient. On review in clinic 3 months later, she was still complaining of headaches (5–6/10 in terms of severity) without any associated features. These occurred mainly in the morning, and responded to paracetamol. These were thought to be medication overuse headaches, so paracetamol was discontinued. Her leg and arm weakness had resolved.

Figure 2. **a.** Computed tomography angiogram on admission showing irregularity and spasm of right middle cerebral artery, and **(b)** repeat computed tomography angiogram 3 months later showing resolution.



usually the first symptom and can typically recur in the 1–2 weeks after presentation (Miller et al, 2015a,b).

The pathophysiology of reversible cerebral vasoconstriction syndrome is poorly understood but has many potential precipitating factors (*Table 1*). Aetiological hypotheses involve a transient disturbance in the control of cerebral vascular tone. It is unclear if the angiographic abnormalities trigger the headaches or result from the severe headaches. Anatomically, both the vasoconstriction and headaches result from innervation of cerebral blood vessels with sensory afferents from the trigeminal nerve (V1) and dorsal root of C2. There is a likely overlap of pathophysiology with posterior reversible encephalopathy syndrome (Singhal et al, 2011).

There is no proven treatment for reversible cerebral vasoconstriction syndrome. Calcium-channel blockers are sometimes used empirically to reduce vasoconstriction, although there is no randomized controlled trial evidence of benefit (Call et al, 1998; Singhal et al, 2011). Glucocorticoids worsen outcome in patients with reversible cerebral vasoconstriction syndrome (Singhal et al, 2011). Avoiding precipitating factors is recommended. Complete resolution is common, one study showing an excellent outcome of modified Rankin score 0–1 after 90 days in 78% of their patients (Singhal et al, 2011).

Evidence for caffeine-related reversible cerebral vasoconstriction syndrome is limited. Costa et al (2017) highlighted a case of a 50-year-old woman who developed reversible cerebral vasoconstriction syndrome after ingesting herbal supplements containing green tea. Grant et al (2016) reported an intracranial arterial catheter-induced spasm associated with excessive caffeinated energy drink in the context of aneurysmal subarachnoid haemorrhage. Use of more than one selective serotonin-reuptake inhibitor is associated with the serotonin syndrome. The presentation in this case was not felt to be consistent with this because of the lack of seizures, hyperthermia or hyperreflexia. Although this patient was taking two selective serotonin-reuptake inhibitors, the acute nature of the headache after stopping the caffeine tablets suggests a causal role for the caffeine withdrawal in this case. **BJHM**

Table 1. Precipitating factors for reversible cerebral vasoconstriction syndrome

Factor	Examples
Postpartum	
Exposure to drugs, alcohol, medications and blood products	Cannabis, cocaine, ecstasy, amphetamine derivatives, binge alcohol drinking, selective serotonin-uptake inhibitors, nasal decongestants, tacrolimus, nicotine patches
Catecholamine-secreting tumour	Phaeochromocytoma, bronchial carcinoid tumour
Miscellaneous	Hypercalcaemia, porphyria, head trauma, spinal subdural haematoma

adapted from Ducros et al (2007)

LEARNING POINTS

- Reversible cerebral vasoconstriction syndrome is a rare cause of (usually recurrent) thunderclap headache with specific diagnostic criteria and imaging findings.
- The pathophysiology of reversible cerebral vasoconstriction syndrome remains unclear.
- Caffeine withdrawal has not been previously reported as a precipitant of reversible cerebral vasoconstriction syndrome.
- There is no specific treatment for reversible cerebral vasoconstriction syndrome, although calcium-channel blockers have been used in some cases. Avoidance of precipitants is also advisable.
- Prognosis is generally good.

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