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Case Report

Reversible cerebral vasoconstriction syndrome as a cause of thunderclap headache: a retrospective case series study

Abstract

Thunderclap headache is a common emergency department presentation. Although subarachnoid hemorrhage (SAH) should be the first diagnosis to exclude, reversible cerebral vasoconstriction syndrome (RCVS) is an important alternative cause, which may be commoner than appreciated. Reversible cerebral vasoconstriction syndrome is characterized by multifocal narrowing of cerebral arteries, typically manifested by acute, severe headache with or without neurologic deficits.

To compare and discuss the clinical and radiologic characteristics of patients with RCVS.

We report 4 cases of RCVS, presenting at a single unit in 1 year. All presented with thunderclap headache, whereas half of them had additional neurologic symptoms such as right homonymous hemianopia, right-sided weakness, and slurred speech. Brain computed tomography was normal in 2 of our patients, but subsequent cerebrospinal fluid analysis revealed xanthochromia consistent with SAH. The remaining 2 patients demonstrated intracerebral hemorrhage on computed tomography. All of our patients underwent digital subtraction angiography that showed segmental narrowing and dilatation of one or more cerebral arteries without any signs of aneurysm. Repeat digital subtraction angiography after 3 months was entirely normal prompting the diagnosis of RCVS.

Thunderclap headache requires urgent workup to identify the underlying cause. Although SAH is the most important diagnosis to exclude in the first instance, emergency physicians should be aware of other causes and how they present, such as RCVS. Early recognition of this condition is important in order to remove precipitants, avoid unnecessary investigations, and inform patients about their prognosis.

Patients with headache constitute up to 4.5% of emergency department attendances [1]. In many cases, patients present with thunderclap headache (TCH), which requires urgent workup to identify the underlying cause. Subarachnoid hemorrhage (SAH) is the most important diagnosis to exclude and should be the focus of initial assessment, given its significant morbidity and mortality [2]. Another cause that has gained increased recognition in recent years is reversible cerebral vasoconstriction syndrome (RCVS).

Reversible cerebral vasoconstriction syndrome is characterized by acute severe headaches, often thunderclap in nature, with or without additional neurologic symptoms and constriction of cerebral arteries that resolves spontaneously within 3 months [3,4]. The major complications of RCVS are nonaneurysmal cortical-convexity SAH and ischemic or hemorrhagic stroke [5,6]. Conventional cerebral angiography is crucial in the diagnosis of RCVS, showing segmental narrowing and dilatation ("string of beads" or "sausage string" appearance) of one or more arteries [7]. Table lists the diagnostic criteria for RCVS.

Herein we report 4 cases of RCVS presenting to our regional neurosciences unit between December 2012 and December 2013. We study these cases in detail to highlight the clinical and radiologic heterogeneity of RCVS, which we contend is a diagnosis that emergency physicians should be familiar with.

A 41-year-old woman was admitted for evaluation of sudden-onset occipital headache. She had a history of migraine. Neurologic examination revealed mild neck stiffness without any focal neurologic signs. Computed tomography (CT) of the brain was normal, whereas cerebrospinal fluid (CSF) examination demonstrated xanthochromia (consistent with SAH) with normal white cell count, protein, and glucose.

Magnetic resonance (MR) brain showed hyperintense signal in the subarachnoid space over the right occipital lobe suggestive of cortical-convexity SAH (Fig. 1). Direct cerebral angiography revealed multiple small contour irregularities and beading of the distal right middle and right posterior cerebral arteries, but no evidence of aneurysms. Three months later, digital subtraction angiography (DSA) was entirely normal prompting a diagnosis of RCVS to be made.

A 45-year-old man was admitted for evaluation of sudden-onset headache, nausea, and vomiting. His medical history was unremarkable. Neurologic examination revealed mild neck stiffness, but no other abnormalities. Computed tomography of the brain on admission was normal, whereas CSF examination showed xanthochromia (consistent with SAH) with normal white cell count, glucose, and protein. Intracranial CT angiography was normal.

Twenty-four hours later, the patient developed recurrent sudden-onset severe occipital headache and nausea. Repeat CT brain was normal. Digital subtraction angiography revealed focal areas of narrowing in the superior cerebellar arteries bilaterally. The patient was discharged with a possible diagnosis of RCVS, which was confirmed 3 months later after demonstrating normalization of the intracranial vessel appearances on cerebral angiography.

A 56-year-old woman was admitted with TCH in the occipital area during coitus, accompanied by vomiting and visual disturbance. She noticed inability to see images in her right visual field. She had experienced a similar episode during coitus 10 days prior to her admission, but had not sought medical advice at that time. She had a history of migraine. Examination revealed a right homonymous hemianopia. Computed tomography of the brain demonstrated a large intracerebral hemorrhage in the left occipital lobe and a smaller hemorrhage in right occipital lobe (Fig. 2).

Digital subtraction angiography of the brain revealed narrowing of both distal internal carotid arteries with evidence of beading of the proximal and distal middle and anterior cerebral artery branches (Fig. 3a). It also revealed irregularity of the posterior

Table
Diagnostic criteria for RCVS

- Acute severe headache (often thunderclap) with or without focal deficits or seizures
- Monophasic course without new symptoms more than one month after clinical onset
- Segmental vasoconstriction of cerebral arteries shown by indirect (eg, MR and CT) or direct catheter angiography
- No evidence of aneurysmal SAH
- Normal or near-normal CSF (protein concentrations <100 mg/dL, <15 white blood cells/μL, normal glucose)
- Complete or substantial normalization of arteries shown by follow-up angiography (indirect or direct) within 12 wk of clinical onset

Adapted from the International Headache Society criteria for acute reversible cerebral angiopathy and the criteria proposed in 2007 by Calabrese and coworkers [3,4].

and superior cerebellar arteries. Repeat cerebral angiography 3 months later was entirely normal in keeping with the diagnosis of RCVS (Fig. 3b).

A 22-year-old woman was admitted with TCH and vomiting, followed by slurred speech and right-sided weakness. Prior to headache onset, she had been in a friend's house drinking coffee which was later found to have been spiked with recreational drugs (amphetamine-like, Lysergic acid diethylamide (LSD), and ketamine).

Neurologic examination revealed dysarthric speech and a right hemiparesis (Medical Research Council scale (MRC) grade 4/5) with an extensor right plantar response. There was also evidence hypoesthesia affecting the right arm and leg on sensory examination. Computed tomography of the brain revealed an intracerebral hemorrhage in the left basal ganglia with mild midline shift to the right.

Digital subtraction angiography revealed multiple areas of segmental narrowing and dilatation of the left anterior and middle cerebral arteries (Fig. 4a) as well as the right posterior cerebral artery, consistent with drug-induced RCVS. Three months later, the patient underwent cerebral angiography which was normal, confirming the diagnosis (Fig. 4b).

Thunderclap headache necessitates emergency assessment. In approximately 50% of patients, an underlying cause can be identified and 11% to 25% of patients presenting in emergency departments with sudden headache may have SAH. This, therefore, should be the first cause to search for, using noncontrast CT brain followed by CSF analysis (including xanthochromia) if scan is normal, at least 12 hours after headache onset [2,8,9]. Other causes of acute headache detected by noncontrast CT are intracerebral and intraventricular hemorrhage, subdural hematoma, cerebral infarcts, tumors (eg, third ventricle colloid cyst) and

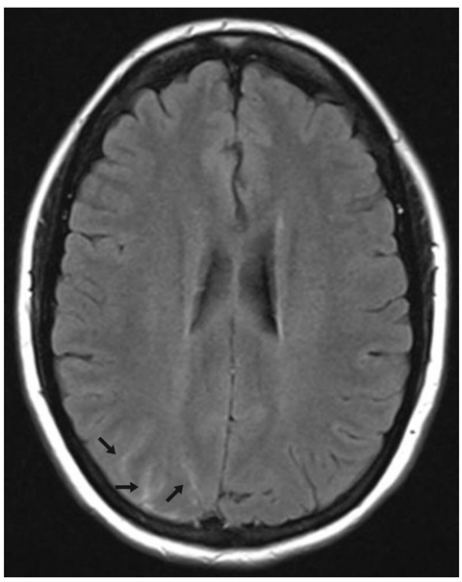

Fig. 1. Axial FLAIR brain MR image demonstrates hyperintense signal in the subarachnoid space over the right occipital lobe (arrows), suggestive of cortical-convexity SAH.

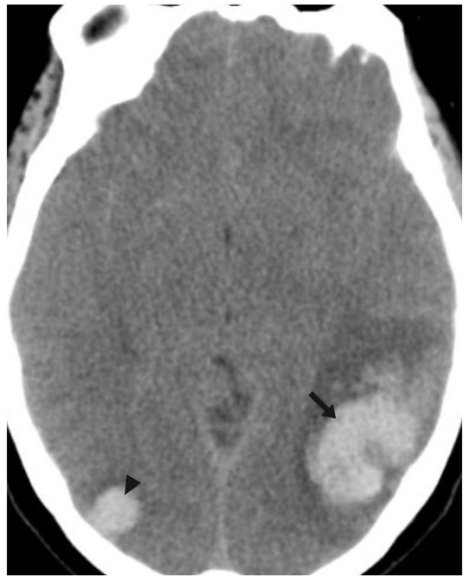

Fig. 2. Brain CT image demonstrates hyperdense lesion in the left occipital lobe (arrow) and a smaller hyperdense lesion in right occipital lobe (arrowhead) in keeping with intracerebral hemorrhages.

acute sinusitis. After a normal CT, CSF analysis can be used to identify SAH or meningitis [9,10]. Many other disorders can present as TCH, with normal CT and CSF analysis, including RCVS, cerebral venous thrombosis, cervical artery dissection, pituitary apoplexy, symptomatic but yet unruptured aneurysms (eg, painful third nerve paralysis), and intracranial hypotension. In these cases, MR imaging and angiography are necessary [2]. Patients with TCH in whom an underlying cause is not found are diagnosed as having primary TCH. Primary TCH is a diagnosis of exclusion, which can be made only after exhaustive assessment for all possible underlying causes [2].

Reversible cerebral vasoconstriction syndrome is characterized by multifocal narrowing of cerebral arteries, typically manifested by acute, severe headache with or without neurologic deficits [8].

All of our cases presented with TCH, whereas half of them experienced recurrence and had additional neurologic symptoms such as right homonymous hemianopia, right-sided weakness, and slurred speech. Reversible cerebral vasoconstriction syndrome has a female preponderance, and occurrence peaks at around the age of 45 years [11].

The incidence of RCVS is unknown, although it is thought to be underrecognized [5]. Ducros et al [5] identified 67 consecutive patients over a 3-year period, at a center with an "emergency headache center" and a department with an established reputation in headache and stroke. Our patients were seen at a Regional Neurosciences Centre, serving a population of between 750 000 (for neurology) and 2 500 000 (for neurosurgery), giving an estimated incidence of between 0.16 and 0.53/100 000 per year. The population served has access to neighboring neurology and neurosurgical facilities in London and Cambridge, so these are likely to be lower estimates.

Our female/male ratio was 3:1, and the mean age was 41 years. Reversible cerebral vasoconstriction syndrome may occur spontaneously, or it may be triggered by various factors in approximately 60% of cases such as sexual activity, postpartum, exposure to various medications (eg, selective serotonin reuptake inhibitors, triptans, bromocriptine, intravenous immunoglobulins, interferon alpha, tacrolimus, cyclophosphamide, blood products, and nasal decongestants), illicit drugs (eg, marijuana, cocaine, methamphetamine, Lysergic acid diethylamide (LSD), and ecstasy), endocrine abnormalities (eg, catecholamine-secreting tumors), neurosurgical procedures, and extracranial or intracranial large artery disorders (such as arterial dissection) [5,8,9,11]. In 2 of our patients, the notable triggers were sexual activity and recreational drugs. Two of our patients had a history of migraine, which has