Reversible cerebral vasoconstriction syndrome

Reversible cerebral vasoconstriction syndrome (RCVS), AKA Call-Fleming syndrome, [1] a group of disorders sharing the cardinal clinical and angiographic features of reversible segmental multifocal cerebral vasoconstriction with severe headaches, focal ischemia, and/or seizures. May present as a hemorrhage restricted to a cortical sulcus

Epidemiology

RCVS has been reported to occur more frequently in women aged 20 to 50 years.

Etiology

Several mechanisms have been postulated involving transient deregulation of cerebral arterial tone, small vessel endothelial dysfunction, biochemical factors, hormonal deregulation, oxidative stress, and genetic predisposition. All these mechanisms and triggers are related with sympathetic over-activation which eventually produce vasoconstriction. RCVS is distinguished by acute severe recurrent thunderclap headaches with or without other neurological symptoms. However, the diagnosis can be challenging and most likely underdiagnosed requiring a high level of suspicion from the clinician [2].

Clinical features

Reversible cerebral vasoconstriction syndrome (RCVS) has emerged as the most frequent cause of thunderclap headache (TCH) in patients without aneurysmal subarachnoid hemorrhage, and as the most frequent cause of recurrent TCHs.

The typical TCHs of RCVS are multiple, recurring over a few days to weeks, excruciating, short-lived, and brought up by exertion, sexual activities, emotion, Valsalva maneuvers, or bathing, among other triggers. All these triggers induce sympathetic activation. In a minority of cases with RCVS, TCH heralds stroke and rarely death. Early diagnosis of RCVS in patients who present with isolated headache enables proper management and might reduce the risk of eventual stroke [3].

Outcome

Ischemic stroke affects nearly 25% of patients with RCVS and is associated with adverse clinical outcomes. RCVS patients with cerebrovascular risk factors might have a higher predisposition for developing ischemic lesions during the disease process [4].

Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by severe headache and diffuse segmental constriction of cerebral arteries that resolves spontaneously within a few months.

Although manifestations of stroke are not included in diagnostic criteria of RCVS, it is known that some cases may be associated with stroke, including intracerebral hemorrhage, subarachnoid hemorrhage, or cerebral infarction.

Intracerebral hemorrhage is the most common vascular complication in hospitalized RCVS patients, resulting in longer hospitalizations with more invasive procedures and higher healthcare expenditure. However, overall outcomes are excellent regardless of types of ICH, with no inpatient mortality observed in patients with hemorrhagic RCVS. Female sex and middle to older age-group are associated with higher odds of ICH. [5)].

Case series

162 patients with RCVS. Clinical, brain imaging, and angiography data were analyzed.

The mean age was 44±13 years, 78% women. Hemorrhages occurred in 43% including 21 patients with intracerebral hemorrhage (ICH) and 62 with convexal subarachnoid hemorrhage (cSAH). The frequency of triggers (eg, vasoconstrictive drugs) and risk factors (eg, migraine) were not significantly different between hemorrhagic and nonhemorrhagic RCVS or between subgroups (ICH versus non-ICH, isolated cSAH versus normal scan). Hemorrhagic lesions occurred within the first week, whereas infarcts and vasogenic edema accumulated during 2 to 3 weeks (P<0.001). Although all ICHs occurred before cSAH, their time course was not significantly different (P=0.11). ICH and cSAH occurred earlier than infarcts (P≤0.001), and ICH earlier than vasogenic edema (P=0.009). Angiogram analysis showed more severe vasoconstriction in distal versus proximal segments in all lesion types (ICH, cSAH, infarction, vasogenic edema, and normal scan). The isolated infarction group had more severe proximal vasoconstriction, and those with normal imaging had significantly less vasoconstriction. Multivariable analysis failed to uncover independent predictors of hemorrhagic RCVS; however, female sex predicted ICH (P=0.048), and angiographic severity predicted infarction (P=0.043).

ICH and cSAH are common complications of RCVS. Triggers and risk factors do not predict lesion subtype but may alter central vasomotor control mechanisms resulting in centripetal angiographic evolution. Early distal vasoconstriction is associated with lobar ICH and cSAH, and delayed proximal vasoconstriction with infarction [6)].

Case reports

A rare case of RCVS in the setting of mild SARS-CoV-2 respiratory infection successfully treated with nimodipine and aspirin. SARS-CoV-2 attacks the Angiotensin-converting enzyme 2 receptors, which are expressed in various body organs including the lungs, kidneys, and blood vessels. Vasoconstriction can result from down-regulation of the ACE2-receptors that can lead to sympathetic hypertonia of the cerebral blood vessel walls and/or over-activation of the renin-angiotensin axis [7)].

2018

Reversible Cerebral Vasoconstriction Syndrome Without Typical Thunderclap Headache Complicated by Intracranial Hemorrhage and Posterior Reversible Encephalopathy Syndrome:A Case Report [8].

Al-Mufti et al. from the Rutgers New Jersey Medical School, describe a case of medically refractory Reversible cerebral vasoconstriction syndrome (RCVS) that required treatment with intra-arterial (IA) verapamil and subsequent nimodipine, resulting in both angiographic and clinical improvement after failing to respond to hemodynamic augmentation.

They also supplement a description of the case with a review of other case studies and case series in which IA calcium channel blockers were used to treat RCVS. They propose that the case they outline demonstrates that neurointerventional management with IA verapamil is appropriate and effective as an early intervention of medically refractory RCVS.

Using PubMed and Google Scholar, they performed a search of the English language literature with several combinations of the keywords “intra-arterial”, “calcium channel blockers”, “reversible cerebral vasoconstriction syndrome”, “RCVS”, “nimodipine”, “verapamil”, “milrinone”, and “nicardipine” to identify studies in which RCVS was treated with IA calcium channel blockers.

They identified eight case studies and case series that met our inclusion criteria. Eighteen patients are encompassed in these eight studies.

IA administration of calcium channel blockers has been shown to return cerebral vessels to their normal caliber in patients with medically refractory RCVS. However, there are no randomized controlled trials of the treatment of RCVS, and further studies are needed to elucidate the optimal treatment protocol for medically refractory RCVS [9].

Gonsales et al., present an unusual case of an 18-year-old female who developed RCVS after embolization of a dural arteriovenous fistula with onyx embolic material. A cerebral angiogram was performed and verapamil was administered intra-arterially demonstrating slight improvement of the constricted vessels with clinical improvement. The patient was maintained on oral verapamil during hospitalization. At 7-month follow-up, the patient was neurologically stable and a cerebral angiogram demonstrated no signs of vasoconstriction.

Endovascular procedures are a rare trigger for the development of RCVS and may be misdiagnosed. Prompt recognition of symptoms and diagnosis with treatment are necessary to reduce the risk of stroke. The management should follow the premise of discontinuing precipitating drugs and administering CCBs [10].

2016

A 19-year-old woman had a thunderclap headache, followed by left hemiparesis and left homonymous hemianopsia. Laboratory tests showed no signs of infection and immunological test results were unremarkable. MRI revealed a cerebral infarction in the right posterior cerebral artery territory, and digital subtraction angiography(DSA)showed right posterior cerebral artery stenosis on day 2. The first

follow-up DSA demonstrated an irregular, bead-like appearance on day 9, but the stenotic lesion returned to normal on day 21. Reversible cerebral vasoconstriction syndrome should be suspected in cases of rapid resolution of symptoms [11].

2014

Ishi et al. present three cases of RCVS associated with various types of stroke, and then review the literature. Case 1:A 49-year-old woman presented with a headache followed by left hemiparesis and dysarthria. One month before the onset, she was transfused for severe anemia caused by uterus myoma. CT images revealed intracerebral hemorrhages in the right putamen and right occipital lobe. Angiography revealed multiple segmental constrictions of the cerebral arteries. One month after the onset, these vasoconstrictions improved spontaneously. Case 2:A postpartum 38-year-old woman who had a history of migraine presented with thunderclap headache. Imaging revealed a focal subarachnoid hemorrhage in the right postcentral sulcus and segmental vasoconstriction of the right middle cerebral artery. One week after the onset, this vasoconstriction improved spontaneously. Case 3:A 32-year-old woman who had a history of migraine presented with headache followed by left homonymous hemianopsia. Imaging revealed a cerebral infarction of the right occipital lobe and multiple constrictions of the right posterior cerebral artery. These vasoconstrictions gradually improved spontaneously [12].

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