Dual Energy Computed Tomography Angiography for the Rapid Diagnosis of Reversible Cerebral Vasoconstriction Syndromes: Report of a Case

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Abstract-

Purpose: Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by segmental vasoconstriction and dilatation of intracranial arteries, typically affecting bilateral medium-sized intracranial arteries and their branches. The diagnosis usually relies both on clinical presentations and cerebral vascular imaging such as magnetic resonance angiography or conventional angiography. Dual energy computed tomography angiography (CTA) could provide high-quality imaging and is usually immediately available for the diagnosis at the emergency department.

Case Report: A 37-year-old previously healthy woman was admitted to the neurology ward for recurrent episodes of headaches within 3 days. She was diagnosed as having RCVS presenting with thunderclap headaches. Dual energy CTA provided high-quality imaging and almost immediately available for diagnosis at the emergency department (ER). CT perfusion showed adequate brain perfusion. Transcranial Doppler disclosed increased arterial velocities at bilateral middle cerebral arteries. We treated the patient with oral diclofenac and nimodipine. After a few days, she had great improvement of headaches. The follow-up CTA 3 months after her initial presentation disclosed complete resolution of the constrictions of these intracranial arteries.

Conclusion: Brain magnetic resonance imaging (MRI) with magnetic resonance angiography (MRA) and MR venography is the choice for initial investigation; however, CTA is an alternative diagnostic tool when MRI is not readily available. Dual energy CTA has the great advantage in providing high-resolution imaging, high speed scanning with a lower radiation dose.

Key Words: Reversible cerebral vasoconstriction syndrome (RCVS), thunderclap headache, CT perfusion, dual energy computed tomography angiography

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INTRODUCTION

Headache is one of the most common primary complaints presenting to the emergency departments. We often encountered different red flags and pitfalls while managing patients with headaches, leading to the mak-

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ing correct diagnosis of headache being challenging.

Thunderclap headache is a hyperacute and severe headache with its reaching maximum intensity within one minute and such characteristic of headache is usually described as a "clap of thunder." Thunderclap headache is a medical emergency because it could be the first symptom of subarachnoid hemorrhage (SAH), unruptured intracranial aneurysm, cervical artery dissection, cerebral venous sinus thrombosis, ischemic stroke, pituitary apoplexy, and intracranial infection[1]. Although SAH is almost the first consideration while encountering patients presenting with thunderclap headache, many differential diagnoses for this headache syndrome have been emphasized. As a medical emergency, the initial diagnostic assessment should be focused on the exclusion of SAH. Non-contrast computed tomography (CT) of head is highly sensitive and specific for the diagnosis of SAH and is usually the first test of assessment. However, after the first 24 hours, the sensitivity of head CT for the detection of SAH decreases. An early CT study in which serial scans were performed on patients with aneurysmal hemorrhage has estimated that the probability of recognizing hemorrhage is 85% after 5 days and 50% after 1 week.[2] Therefore, cerebrospinal fluid assessment with measuring of routine cell counts, protein, glucose, opening pressure and inspection for xanthochromia is needed for patients with thunderclap headache having normal or non-diagnostic CT scans[1].

A subgroup of patients developing reversible and multifocal segmental arterial narrowing involving intracranial arteries are diagnosed as reversible cerebral vasoconstriction syndrome (RCVS). RCVS is characterized by severe and hyperacute headaches with or without additional focal neurological deficits, and evidence of vasoconstriction of cerebral arteries which resolves spontaneously within 1-3 months[3]. Here we present a woman presenting to the emergency department with thunderclap headaches. Dual energy CT angiography disclosed multiple intracranial artery vasoconstriction and spontaneously recovery within 4 months.

CASE REPORT

A 37-year-old previously healthy woman was admitted to the neurology ward for recurrent episodes of severe headaches within 3 days. She had a normal spontaneous vaginal delivery 2 months prior to this admission. Three days before admission, she had an acute onset of explosive, throbbing headaches in the bilateral frontal-temporal region associated with nausea and vomiting. The headaches reached peak intensity within one minute and she had never experienced such headaches before. There was no associated photophobia, neck stiffness, fever, visual loss, limbs weakness, convulsion or loss of consciousness. She received uncertain medication prescribed by local medical doctors and the headache was improved after a sleep. However, another episode of severe explosive headache recurred 2 days later therefore she came to our emergency department. She was afebrile and had a pulse rate of 63 beats per minutes and a blood pressure of 112/66 mmHg. Initial assessment at the emergency department showed a normal neurological examination. Blood analysis showed no significant abnormalities. Since brain MRI was not immediately available at night in our hospital, we directly performed a computed tomography angiography (CTA) with perfusion scan (SOMATOM Definition Flash, dual energy CT; DECT; Siemens, Forchheim, Germany). The CTA of the brain revealed multifocal segmental luminal stenosis but still preserved normal antegrade flow at M2-M3 segments of bilateral middle cerebral arteries (MCA,

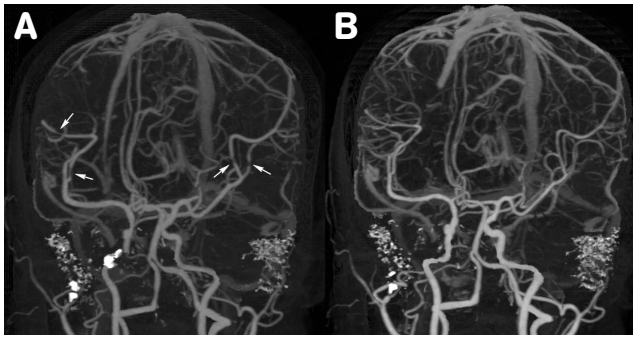

Figure 1. (A) 3D intracranial CTA maximum intensity projection (MIP) technique in different projections shows multifocal segmental vessels luminal stenosis (arrows) but still preserves normal antegrade flow at bilateral M.C.A M2-M3 segments. (B) A follow-up CT angiography 3-4 months later shows no more intracranial focal vessels stenosis or spasm for this reversible cerebral vasoconstriction syndrome patient.

figure 1A). No SAH was seen in the CT imaging. These pictures were consistent with the clinical diagnosis of RCVS. The brain CT contrast perfusion study (with rapid injection method which covered brain tissues from suprasellar cisterns to frontotemporal opercula region and covered mainly both anterior cerebral arteries and MCA cortical territories with a 8mm thickness acquisition) revealed no significant difference in cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT) between left and right hemispheres (Figure 2A). The transcranial color- coded sonography (TCCS) was performed 3 days after symptoms onset and disclosed increased arterial velocities at bilateral MCA (right M2 segment, 166cm/sec; left M2 segment, 155 cm/sec, Table 1).

The patient was treated with oral diclofenac 25mg three times a day, nimodipine 60mg every 6 hours and other medications including propranolol 10mg twice a day. We discontinued nimodipine on the next day because she felt better with diclofenac than nimodipine. At the 4th day of admission she had much improvement in the headaches and was discharged uneventfully. A follow-up brain MRI one month later demonstrated no evidence of cerebral arterial flow disruption in MRA and no hyperintensity lesions in diffusion-weighted image (DWI).

About 3-4 months after the initial symptoms, dual energy CTA was arranged to make sure the complete resolution of vasoconstriction and it showed normal vasculature of cerebral arteries in previous vasoconstriction locations (Figure 1B). Brain CT perfusion study showed no significant difference between the bilateral hemispheres as the previous study did (Figure 2A, 2B). Therefore, the confirmative diagnosis of RCVS with full recovery was made.

DISCUSSION

We reported a patient presented to the emergency department with recurrent thunderclap headaches. Dual energy CT and CTA not only excluded SAH and cerebral aneurysm at the first time but also clearly disclosed the multiple vasoconstriction in bilateral M2-M3 segment of MCA simultaneously. Establishment of the diagnosis is of the utmost importance because further management differs between aneurysmal SAH and RCVS.

According to the diagnostic criteria of International Classification of Headache Disorders, second edition, this syndrome could be classified as “headache attributed to benign (or reversible) angiopathy of the central nervous system” (code 6.7.3, Table 2)[4].

Thunderclap headache refers to the sudden onset of severe headaches that reach the maximal intensity within seconds to a minute. This should always be a red flag

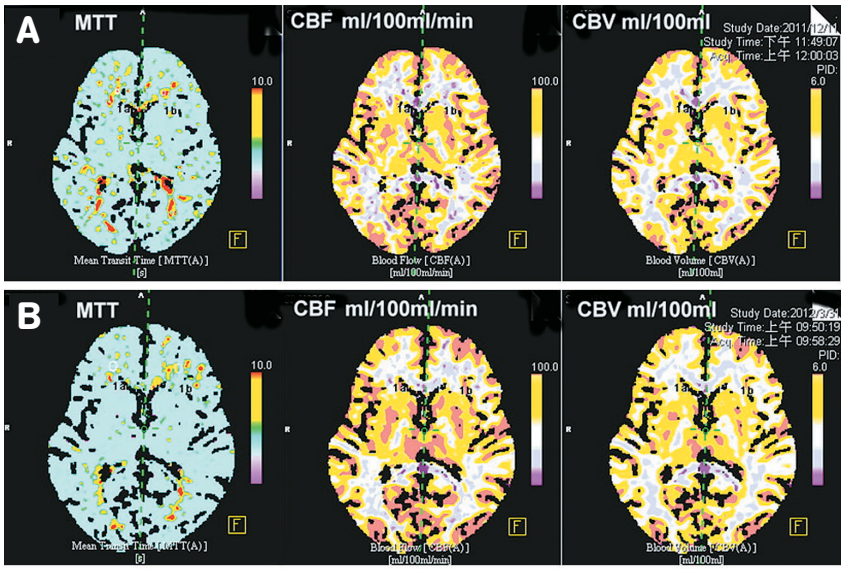

Figure 2. CT perfusion study during acute stage and follow up study at about 3-4 months later. (A) CT perfusion on day 3 shows no significant perfusion difference between the left and right anterior cerebral arteries and middle cerebral arteries by means of cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT) measurement; (B) A follow-up study at 3-4 months later showed similar results.

while taking history from any patient with an acute headache. SAH is the foremost consideration in a patient presenting with thunderclap headaches; therefore, neuroimaging study is an indispensable first step. Given the potential of significant morbidity and mortality from many of these possible etiologies, physicians should be cautious in the recognition and the diagnostic evaluation of a patient with thunderclap headache. Patients present with typical patterns of such headache, with the evidence of vasoconstriction of intracranial arteries that reverse without specific intervention therapy, and with appropriate exclusion of other causes could be diagnosed as having RCVS. This syndrome most often occurs in women between the age of 20 and 50 years and almost presents with abrupt onset headache. It could be idiopathic or associated with specific conditions such as pregnancy and puerperium, or exposure to vasoconstrictive agents (sympathomimetics, serotonergic drugs, cannabinoids)[5]. Neurologic deficits including visual problems, limb weakness, and speech or language deficits may be present if such a vasoconstriction is sufficient enough to cause downstream ischemia. In these cases, angiography usually shows alternating segments of vasoconstriction and dilatation (string of beads) of one or more cerebral arteries[3,5]. Complications of RCVS include posterior reversible encephalopathy syndromes (PRES), brain edema, ischemic stroke, subdural hemorrhage, cortical SAH and intracranial hemorrhage[5-8].

Table 1. Transcranial color-coded sonography measured at acute stage and 3-4 months later.

Intracranial arteries	PSV (cm/s) First evaluation	PSV (cm/s) 3-4 months later
Right		
MCA, M1	154	104
MCA, M2	166	107
ACA	69.7	53.8
PCA, P1	89.9	57.1
PCA, P2	46.9	48.4
Left		
MCA, M1	94.9	102
MCA, M2	155	80
ACA	83.7	60.1
PCA, P1	68.3	48.7
PCA, P2	54.5	57

Abbreviations: MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; PSV, Peak systolic velocity

Conventional angiography remains the gold standard in evaluating the intracranial vessels. The angiographic findings of segmental narrowing and dilatation (string of beads) of one or more cerebral arteries are essential for the diagnosis of RCVS[3]. However, it is invasive and not practical for follow-up. MRA has been confirmed as a valid tool for the evaluation of arterial vasoconstriction [9]. Diffuse segmental arterial constriction is detectable in 85% patients on the first MRA performed at around the first week[5]. The severity and distribution of vasoconstriction revealed by MRA were associated with the complications of RCVS, such as PRES or ischemic strokes[9]. The severity of vasoconstriction on initial MRA provided a significant prognostic value. Clinicians should pay attention to patients who have severe vasoconstriction upon initial presentation.[9]

Table 2. Diagnostic criteria of benign (or reversible) angiopathy of the CNS in the International Classification of Headache Disorders, 2nd Edition.

6.7.3 Headache attributed to benign (or reversible) angiopathy of the CNS
A. Diffuse, severe headache of abrupt or progressive onset, with or without focal neurological deficits and/or seizures and fulfilling criteria C and D
B. 'Strings and beads' appearance on angiography and subarachnoid hemorrhage ruled out by appropriate investigations
C. One or both of the following:
1. headache develops simultaneously with neurological deficits and/or seizures
2. headache leads to angiography and discovery of 'strings and beads' appearance
D. Headache (and neurological deficits, if present) resolves spontaneously within 2 months

In many institutes, CT scan is the first investigation for patients with thunderclap headaches. According to the study by Ducros et al., among 65 patients who had been diagnosed as RCVS, brain CT was the first investigation. CT scan was performed on the mean of 4.1 (ranged 0-20) days after headache onset and was abnormal in 8 patients (12%), including cortical SAH, parenchymal hemorrhages or both[5]. Helical CT has been enabled rapid imaging of the vascular status by means of CTA and CT perfusion scan. CTA can provide cerebral vascular assessment of major arterial disease; while perfusion scan can give information regarding cerebral perfusion and detect the potential ischemic zone before the morphological changes are visible on CT scans[10]. Most important, CTA is usually readily available, fast and can be performed immediately after an initial non-contrast CT. It is not affected by flow-related inhomogeneities, which is commonly seen in MRA and can certainly reveal regions of vasoconstriction[11]. CTA is performed in seconds to minutes, as opposed to MRA, and effectively eliminating MRA-limiting patient motion. In addition, CTA has more complete intracranial coverage than MRA does[11]. However, CTA may lack the sensitivity to visualize smaller distal vessels as compared with digital substraction angiography (DSA). Modern multidetector-row spiral CT angiography produces vascular imaging potentially equivalent to DSA and appears to be a reliable alternative imaging technique to DSA[12,13]. The advantage of dual energy CT scan applied in this patient includes high-resolution image, high scanning speed and low radiation dose[14].

In addition, dual energy CT is able to remove bone structure using only a single CT data acquisition and is a powerful tool to evaluate intracranial aneurysms and arterial stenosis[15]. The limitation of CTA image in accessing vessels in contrast to MRA and DSA may be the delineation of vessels adjacent to bony structures (e.g., the skull base). Dual energy CT provides a new technique approach for bone removal in CTA image. It provides better bone suppression, especially in 7 vessel segments (external carotid artery, superior and inferior part of the common carotid artery , the segments V1-V3 of the vertebral artery, subclavian artery)[16]. In comparison with bone subtraction CTA (BSCTA), both vessel integrity and bone suppression around the skull base are less accurate with dual energy CT[16]. In addition, the additional non-enhanced scan in BSCTA may result in radiation dose increase. In this patient, we chose dual energy CTA as the initial diagnostic test for its readily availability at any time and we used the same tool for follow-up. We demonstrated complete resolution of the arterial vasoconstriction within 3-4 months in this patient.

Radiation exposure is the main shortcoming of CTA as compared with MRA. The radiation dose of the brain CT, CTA and CT perfusion using this dual energy CT scan were 2, 0.74 and 6.6 mSv, respectively. We first chose MRI and MRA as the follow-up tool and found no evidence of cerebral arterial flow disruption in MRA and no hyperintensity lesions in DWI. However, the resolution of the time-of-flight MRA was not as clear as that of CTA. The differential diagnoses other than RCVS are our major concern, and an accurate diagnosis by a clear image outweighs the risk of radiation exposure. Therefore we arranged one follow-up CTA scan after explaining to the patient the benefits and the potential risks.

TCCS has been widely used and validated in studying vasospasm of intracranial vessels and is therefore suitable for evaluating the hemodynamic changes in patients with RCVS[17]. TCCS can reflect the severity of vasoconstriction in RCVS patients and therefore can be used to assess the risks for posterior leukoencephalopathies and ischemic strokes[7]. Hemodynamic aberration in RCVS patients is more obvious than that of healthy individuals but less severe than that seen in SAH patients. According to one study, only 13% of RCVS patients had their vasoconstriction fulfilling the criteria of mild vasospasm for SAH (VMCA>120 cm/sec and Lindegaard Index (LI)>3)[7]. Peak flow velocity and LI are important markers of risk for developing delayed ischemic complications in SAH patients[18] and also predictive of PRES and ischemic strokes in RCVS patients[7]. Even if the headache has been resolved for 10 days, the flow velocities of the MCA could still remain in a high plateau[7]. This finding may explain sometimes

ischemic complications occurred after headache remission [19]. Our patient had increased arterial velocities on bilateral MCA (right M2-MCA,166cm/sec; left M2-MCA, 155 cm/sec) in the first investigation of TCCS and the velocities returned to the normal range in follow-up TCCS performed 3-4 months later (Table 1). The follow-up MRA and DWI at about 1 month after first symptom onset also demonstrated no ischemic or hemorrhagic stroke complications.

An important differential diagnosis of RCVS is primary angiitis of the CNS (PACNS), which also demonstrates segmental cerebral vasoconstriction. This differential diagnosis is important because it is crucial to avoid the unnecessary use of long-term immunosuppressant in patients with RCVS. PACNS is an uncommon vasculitis resulting in inflammation and destruction of the blood vessels which restrict to the brain and the spinal cord. The onset of PACNS can be acute, especially while associated with ruptured aneurysm, but more frequently it is insidious onset and slowly progressive over weeks to months with the potential of step-wise deterioration[20]. Cerebral and meningeal biopsy remains the gold standard for diagnosis of PACNS[21]. High-resolution contrast-enhanced vessel wall MRI may distinguish RCVS from PACNS by demonstrating circumferential arterial wall thickening and enhancement in PACNS. By contrast, vessel wall MRI showed arterial wall thickening and a lack of arterial wall enhancement in patients with RCVS[22]. Our patient did not receive meningeal biopsy. However, several distinguishing features in our patient suggested PACNS is not likely: acute onset followed by a monophasic course, several episodes of thunderclap headaches, normal brain MRI findings, and the constrictions of the intracranial arteries completely resolved within 4 months without any immunosuppressive therapy[21].

Patients with RCVS should avoid the various triggers that could lead to thunderclap headache, such as vigorous physical efforts. Vasoactive medications must be avoided in all patients. For the absence of randomized trials, empirical treatment with nimodipine may be started when the typical angiographic pattern is demonstrated[3,5]. Nimodipine may be given intravenously in the same doses as for aneurysmal SAH (1-2 mg/kg/h with monitoring of blood pressure) for a few days. Nimodipine may also be given by oral administration. The dose varies from 60 mg every 4-8 hours, and the duration of treatment may need 4-12 weeks [3]. Intra-arterial therapy may be considered in severe cases[23]. Our patient was unresponsive to oral administration of nimodipine but had a good response to the another analgesics (diclofenac) and nimodipine treatment was not maintained.

CONCLUSION

RCVS should be kept in a list of differential diagnosis when approaching patients with thunderclap headaches. Early and correct diagnosis is utmost important to make appropriate management and prognostic prediction. MRI with MRA and MR venography is the choice for initial investigation; however, CTA is an alternative diagnostic tool when MRI is not readily available. As compared with standard CTA, dual energy CTA has the great advantage in providing high-resolution imaging and high speed scanning with lower radiation dose. Whether CT perfusion provides a predictive value for the complications of RCVS needs further study.

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