Int J Clin Exp Med 2017;10(1):1439-1442
www.ijcem.com /ISSN:1940-5901/IJCEM0027925

Case Report

Capsular warning syndrome caused by anterior choroidal artery stenosis: report of a case

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Received March 10, 2016; Accepted August 13, 2016; Epub January 15, 2017; Published January 30, 2017

Abstract: The "capsular warning syndrome" (CWS) is characterized by recurrent stereotypical episodes of motor and/or sensory deficits without cortical symptoms. CWS is associated with a high risk of capsular stroke. The stroke is most likely due to the hemodynamic changes in the diseased single small penetrating vessels. However, till date, the exact pathophysiological mechanism of CWS has not been fully understood. The available treatment options remain controversial and non-effective. The patients with CWS are refractory to classical therapies, including aspirin. We described an unique case of a 63-year-old woman with CWS having 19 episodes of transient ischemic attacks. DSA demonstrated the anterior choroidal artery stenosis. According to the finding of DSA, possible mechanisms of CWS are discussed. Combination therapy including dual antiplatelets, heparin, hydration and statin also proved to be effective in the treatment of CWS.

Keywords: Capsular warning syndrome, anterior choroidal artery, cerebral angiography, antiplatelet therapy

Introduction

Capsular warning syndrome (CWS) is characterized by recurrent stereotypical episodes of motor and/or sensory deficits without signs of cortical dysfunction [1]. CWS is associated with a high risk of developing a completed stroke [1]. Till date, little is known about the pathogenic mechanisms involved in CWS. We report a case of a patient with repetitive CWS in the setting of anterior choroidal artery atherosclerotic disease. This is the first study to date where in the role of combination of dual antiplatelets, heparin, hydration and statin was studied in patients with CWS moreover our study demonstrated a total of 19 episodes within 7 days which was never reported before. The patient had severe stenosis of the right anterior choroidal artery (AchA). We propose that the proximal stenosis causes an intermittent hypofusion of the distal vascular territory of the AchA, thereby causing CWS.

Case report

A 64-year-old woman experienced an episode of left hemiplegia at 9:30 AM on December 14, 2013, while she was walking in a supermarket. She did not have double vision, vertigo, headache, nausea, or dysphagia. The initial episode lasted 10 minutes and disappeared spontaneously. Two subsequent episodes of the stereotype recurred and lasted for 5 minutes and 10 minutes respectively, with complete recovery. There is no prior history of hypertension, migraine, arrhythmia, diabetes mellitus, or cardiac diseases. She was sent to our emergency department at 11:00 AM. On arrival, her blood pressure was 110/70 mmHg and heart rate was 66 beats/min. On admission in hospital, her neurological examination was unremarkable. Cranial CT scan revealed no sign of the actual ischemic changes. Antithrombotic therapy (aspirin 100 mg once daily) and atrovastatin 20 mg once daily was given immediately. At about 9:00 AM on the following day, she experienced an episode similar to her initial presentation. On neurologic examination, the patient was alert, cooperating and oriented. Speech was intact with normal comprehension. There was no gaze preference and right-left confusion. Cranial nerve exam was normal. She had a left-sided arm-leg mild hemiplegia, with left

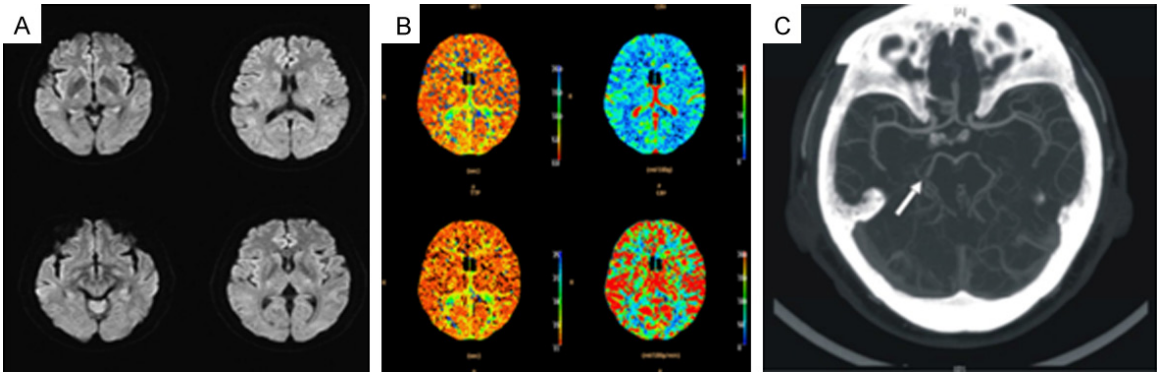

Figure 1. Diffusion weighted imaging (DWI) showed normal features (A). Mean transit time (MTT), time to peak (TTP), cerebral blood volume (CBV), and cerebral blood flow (CBF) showed no abnormalities (B). Computed tomographic angiography showed mild stenosis of posterior cerebral artery (PCA) (arrow in C).

extensor plantar response. Neither sensory nor cortical signs were noted. Her neurologic status was 4 on the National Institutes of Health Stroke Scale (NIHSS). Her condition fulfilled the criteria for tissue-plasminogen activator (tpA) therapy. Despite the informed consent from the family, tpA therapy was not performed because the patient's left hemiplegia improved completely within 30 minutes. However, after 9:30 AM, she had at least 4 recurrent episodes of left hemiplegia and each episode lasted for 10-20 minutes. She did not have any remarkable fluctuation of blood pressure during each episode. At that point in time, her fasting glucose 5.64 mmol/L, serurn total cholesterol 4.91 mmol/L, high-density lipoprotein cholesterol 1.68 mmol/L, low-density lipoprotein cholesterol 2.53 mmol/L, triglyceride 0.94 mmol/L and lipoprotein (a) 29.2 mg/dL were assayed. Urine analysis, levels of glycosylated hemoglobin, protein C activity, protein S activity, partial thromboplastin time (PTT) and prothrombin time (PT) were all within normal limits. Increased levels of serum homocysteine (19 umol/L) and Hs C-reactive protein level (3.13 mg/L) were observed. Plasma fibrinogen level was 310 mg/dL. Interictal electroencephalography (EEG) was normal. Doppler ultrasound showed internal carotid atheromatosis without significant focal stenosis. Electro-cardiography and transthoracic echocardiography were unremarkable. Intravenous fluids and clopidogrel (75 mg once daily) were also administered.

During the next 5 days, she experienced frequent episodes of left hemiplegia lasting 5 to 56 minutes. Most of these episodes began while standing or walking and occurred one to four times daily and were preceded by an aura of a sensation of "it's coming". She was kept flat in bed and treated with plasma expander. Blood pressure remained stable. Due to the intractable recurrent episodes of hemiplegia, an intravenous infusion of low-molecular-weight heparin was prescribed along with the antiplatelet therapy on the 4th day of hospitalization.

After receiving these treatment, the duration of attacks abbreviated, and the severity of attacks weakened. Diffusion-weighted Magnetic Resonance (MR) imaging of the head performed 3 days after admission in hospital was normal (**Figure 1A**). Computed tomographic perfusion revealed no significant abnormalities (**Figure 1B**). Computed tomography angiography showed mild stenosis of posterior cerebral artery (PCA) (**Figure 1C**).

On Day 15, a cerebral angiogram was obtained which showed the presence of high-grade stenosis (>70%) of the right proximal anterior AchA (**Figure 2**). Over all, she had 19 episodes of stereotypical transient ischemic attacks with no lasting deficit. She was discharged with no neurologic deficit after 18 days of hospitalization. The patient did not have attacks during 3 month follow-up.

Discussion

This case describes an unique cause of CWS. Our patient experienced recurrent hemiplegic spells. Neither the carotid Doppler ultrasound nor the CT angiogram of head revealed any large or medium-sized artery stenosis. However, due to the recurrence of CWS and subsequent

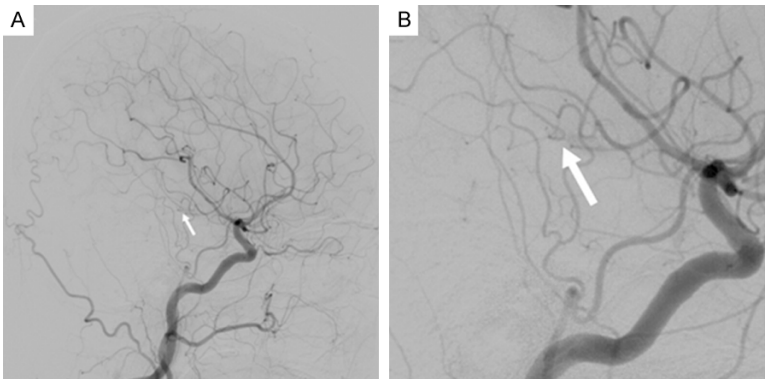

Figure 2. A cerebral angiogram revealed the high-grade stenosis of the right anterior choroidal artery (AchA) (arrow in A) and (B) is enlarged view of (A).

transient ischemic episodes, a cerebral angiogram was performed. Cerebral angiography presented a high-grade stenosis of the right proximal anterior choroidal artery. Although the brain MRI showed no abnormality, a non-stenoic MCA along with the patterns of blood supply and unilateral motor deficit correspond to the involvement of AchA territory. In our patient, the presumed cause of CWS is hemodynamic inadequacy in the penetrating vessels territory due to the AchA stenosis. We observed the onset is not instantaneous. In our study, most of the attacks were preceded by an aura of weakness and a sensation of "it's coming". These symptoms are consistent with the earlier studies [1, 2]. A previous study demonstrated 13 episodes over a period of 4 days in 50 patients with CWS [1], while, our study demonstrated a total of 19 recurrent episodes within a period of 7 days.

The term "capsular warning syndrome" was introduced by Donnon et al. [1] to describe the phenomenon of recurrent stereotyped motor and/or sensory dysfunction that simultaneously involve at least two of the face, arm or leg, without cortical symptoms. The commonest presentation was pure motor hemiparesis involving the face, arm and leg [1], although the onset was usually accompanied by sensory symptoms that often cleared quickly before the motor symptoms resolved. This syndrome is especially important because it has a high early risk of developing capsular infarction with a permanent deficit [1]. In a large population-based study, the CWS is rare (1.5% of TIA presentations) and the prognosis is poor (7-day stroke risk of 60%) [3]. Something like the one we have added the possible pathogenic mechanism of CWS. Although, the exact pathogenic mechanism of CWS is not fully understood, yet an infarction in the AchA territory or the lacunar infarction in the territory of diseased, single, small penetrating vessel has been proposed as the most common cause of CWS [1]. This is in accordance to the findings of our study, as our case also demonstrated the development of CWS due to stenosis in the AchA territory as evident by the cerebral angiogram. Moreover, treatment with the combination of clopidogrel, aspirin, heparin and plasma expander reduced the severity and duration of attacks and resulted in a complete recovery.

The AchA is a thin artery that usually originates from the internal carotid artery, above the origins of the posterior communicating artery and the intracranial carotid bifurcation [4]. The AchA territory reveals large variations amongst individuals. The AchA supplies the posterior limb of the internal capsule, lateral geniculate body, optical tract, medial temporal lobe, and medial part of the pallidum [5, 6]. The triad of AchA syndrome includes [7], hemiparesis, hemianaesthesia, and hemianopia. In the triad of AchA syndrome, the most frequently described triad is the motor deficit, which may be caused by the involvement of the pyramidal tract in the posterior limb of the internal capsule, or the cerebral peduncle [7, 8].

Different treatment modalities have been proposed in patients with CWS, including anticoagulants, antiplatelet agents, thrombotic agent (aspirin), plasma expanders and blood pressure therapy [1, 2, 8-17]. Most patients with CWS are refractory to these traditional therapies [1, 8]. It remains a challenge to develop therapies that prevent the occurrence of irreversible damage in patients with CWS. Moreover, it is uncertain whether these treatments alter the natural feature of the syndrome.

At present, the most important therapeutic goal is to prevent the formation of infarct during the period of clinical fluctuations. Thus, numerous studies have indicated the beneficial effect of thrombolytic treatment in patients with CWS [13, 15, 18, 19]. Interestingly, in our study, a

favorable outcome in terms of reduction in the severity and duration of attacks was noted after the administration of combination of clopidogrel, aspirin, heparin and plasma expander.

In summary, we have reported a case of CWS that had more recurrent hemiplegic episodes than those reported previously. Our report provides a causal link between CWS and AchA atherosclerotic stenosis. Moreover, our study highlights the beneficial effect of combination of clopidogrel, aspirin, heparin and plasma expander in altering the patterns of attacks in CWS and thereby resulting in a favorable outcome. We have tried to mention the limitation of this study in the role of combination of clopidogrel, aspirin, heparin and plasma expander in CWS.

Acknowledgements

The authors thank Dr. Shujuan Li for revising the article.

Disclosure of conflict of interest

None.

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