

Short communication

Callosal warning syndrome[☆]

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ARTICLE INFO

Article history:

Received 16 August 2011

Received in revised form 3 October 2011

Accepted 4 October 2011

Available online 8 November 2011

Keywords:

Disconnection syndrome

Callosal infarction

Stroke warning syndrome

ABSTRACT

Objective: To report the clinical and imaging findings in a patient with an initial fluctuating disconnection syndrome due to corpus callosal ischemia that ultimately culminated in infarction with persistent symptoms.

Case report: A 40-year-old, hypertensive, right-handed man presented with transient, stereotyped symptoms of corpus callosal disconnection (intermanual conflict, apraxia, dysgraphia and construction difficulties in his left hand). Serial magnetic resonance imaging scans demonstrated the ischemic nature of the initial fluctuating symptoms and later showed callosal infarction when the symptoms were persistent. Magnetic resonance angiogram did not reveal significant stenosis or occlusion of the internal carotid or proximal portion of anterior cerebral arteries. Patient received standard treatment for ischemic stroke and at follow-up 1 month later, had mild left hand apraxia, dysgraphia and construction difficulties.

Conclusion: The case highlights the unusual occurrence of crescendo transient ischemic attacks culminating in infarction in the location of corpus callosum. We have termed this novel stroke syndrome as 'callosal warning syndrome' as the temporal profile was quite indistinguishable from that of relatively well-known stroke warning syndromes in the location of internal capsule and pontine tegmentum.

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1. Introduction

Stroke warning syndrome refers to a cerebrovascular syndrome that is characterized by recurrent, stereotyped episodes of transient neurological symptoms and signs leading up to infarction in the corresponding anatomical site [1–4]. Based on the neuro-anatomical location of the final infarction, the syndrome has been given the corresponding name. For instance, when the recurrent episodes of transient hemiparesis are followed by infarction in the internal capsule, it is called capsular warning syndrome [1,2]. On the other hand, when the corresponding infarction heralded by transient events occurs in the region of the pontine tegmentum, it is termed as pontine warning syndrome [3,4]. In this communication we report on a novel stroke syndrome that is characterized by initial fluctuating symptoms of corpus callosal disconnection followed by an ischemic infarction in the same region. In keeping with the naming convention, we have coined the term 'callosal warning syndrome' for this particular stroke syndrome.

2. Case report

A 40-year-old, right-handed man with a history of heavy cigarette smoking, hypertension and occurrence of stroke in his father, presented with recurrent episodes of symptoms dominated by intermanual conflict lasting for a few minutes. During these episodes, he described that his left hand was clumsy and acted at cross-purpose to the action of the right hand as, for instance, his left hand untucked the shirt that was tucked by the right hand or unbuttoned the shirt in conflict with the action of the right hand. He could not account for the actions of his left hand that were 'bizarre and weird'. This symptom was not associated with reflexive grasping, groping, compulsive manipulation of objects, impaired consciousness, staring spell, aura, automatism or tonic-clonic limb movements. However these episodes were accompanied by dysarthria, whole body numbness and mild unsteadiness of walking. He denied history of any other neurological symptoms or stroke in the past. Upon arrival in the emergency room 5 h after the onset of his symptoms, his blood pressure was 154/102 mm Hg. He demonstrated mild left hand apraxia and dysgraphia and construction difficulties, mild dysarthria, slightly broad-based gait and National Institute of Health (NIH) stroke score of 2. He scored 30/30 on mini-mental status examination (MMSE) and on Addenbrooke's cognitive examination (ACE-R), his general/total score was 95 [subscores: attention and orientation – 18/18; memory – 26/26; fluency – 10/14; language – 26/26 and visuospatial function – 15/16]. Initial CT brain showed old

[☆] All the authors have contributed to the study design, analysis and intellectual contents.

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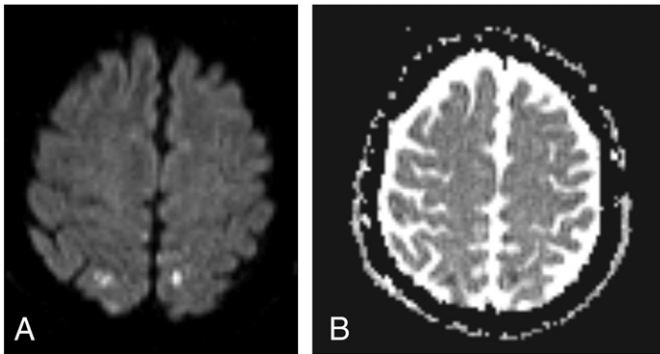


Fig. 1. Diffusion weighted axial MRI (DWI) brain demonstrating small foci of restricted diffusion [hyperintense lesions on DWI, b1000 (panel A) and hypointense lesions on apparent diffusion coefficient (ADC) map (panel B)] suggestive of acute small infarction in bilateral parietal parasagittal areas.

lacunes in bilateral basal ganglia and right thalamus but there were no new infarcts. MRI brain revealed additional few, scattered, small, new infarcts in the parietal parasagittal region bilaterally and right centrum semiovale posteriorly (Fig. 1). There was no lesion in the corpus callosum on fluid attenuated inversion recovery MRI, diffusion weighted sequence and apparent coefficient map (Fig. 2, upper panel). MR angiogram of extracranial carotid arteries, circle of Willis and intracranial arteries did not reveal any significant stenotic/occlusive lesions or vascular malformation. Trans-thoracic echocardiography was normal. His blood tests including peripheral smear, arterial blood gas, urea, creatinine, glucose and lipids were unremarkable. He received treatment with aspirin and amlodipine (his usual antihypertensive medication). During 24 h of observation in the hospital, he had no further occurrence of transient symptoms or persistent signs. He was discharged on antiplatelet, statin and antihypertensive medication with advice to stop smoking and to return for review immediately if there was further recurrence of symptoms. Meanwhile we had arranged an out-patient appointment for appraising the pending results of vasculitis panel and thrombophilia work-up.

Seventy-two hours after the initial hospital visit, he presented with increasing frequency of the same symptoms. On arrival, his blood pressure was 130/78 mm Hg. His MMSE and ACE-R scores and NIH stroke scale score remained the same. He demonstrated persistent apraxic errors in his left hand while pantomiming to verbal commands and left arm dysgraphia and construction difficulties, apart from the other

clinical finding of slightly broad-based gait with mildly impaired tandem walking. There were no primary sensori-motor deficits, unilateral verbal anosmia, tactile anomia, hemi-alexia, double hemianopsia or extinction or neglect on double simultaneous sensory testing and line bisection test. Repeat MRI brain showed acute infarction (Fig. 2, lower panel) in the body of corpus callosum (sparing the rostrum, genu and splenium), in addition to the small, acute infarcts in bilateral parietal parasagittal regions and right centrum semiovale as mentioned above. MR angiogram did not reveal any occlusive lesions of the intracranial arteries including anterior cerebral arteries and extracranial carotid arteries or vascular malformation. Trans-esophageal echocardiography and ECG did not reveal any cardiac source of embolism. There were no epileptiform discharges on EEG. Anti-nuclear antibody, anti-cardiolipin and anti- β 2 glycoprotein antibodies and anti-neutrophil cytoplasmic antibodies, HIV and syphilis serologies were non-reactive/in the normal range. During the eight day stay in the hospital, he had persistent left arm apraxia and dysgraphia and construction difficulties while other symptoms viz. intermanual conflict, dysarthria, numbness and gait problems improved significantly. At neurological follow-up 1 month, 3 months and 6 months later, he had mild left arm apraxia and dysgraphia and construction difficulties. MRI brain obtained 1 month after the ictus showed the same callosal infarction (Fig. 3).

3. Discussion

Our patient had recurrent, transient episodes of callosal disconnection syndrome in the form of alien limb sign (with intermanual conflict), left hand apraxia and dysgraphia and construction difficulties initially. Later, he developed persistent but incomplete syndrome with unilateral hand apraxia, dysgraphia and construction difficulties. The etiological spectrum of callosal lesions in adults includes vascular processes (infarction, arterio-venous malformation, aneurysmal hemorrhage, Susac's syndrome), demyelinating diseases (multiple sclerosis, progressive multifocal leukoencephalopathy, Marchiafava-Bignami disease, acute disseminated encephalomyelitis), tumors (lipoma, glioblastoma multiforme, lymphoma), trauma (diffuse axonal injury), encephalopathy with reversible splenial lesion (viral and parasitic infections, toxic-metabolic disorders, anticonvulsant withdrawal and high altitude cerebral edema) and surgical procedures (shunting for long-standing hydrocephalus, callosotomy for refractory epilepsy) [5,6]. These competing diagnoses, other than ischemic stroke, were ruled out in the present case in the absence of appropriate clinical and imaging evidence. Interestingly the initially fluctuating transient

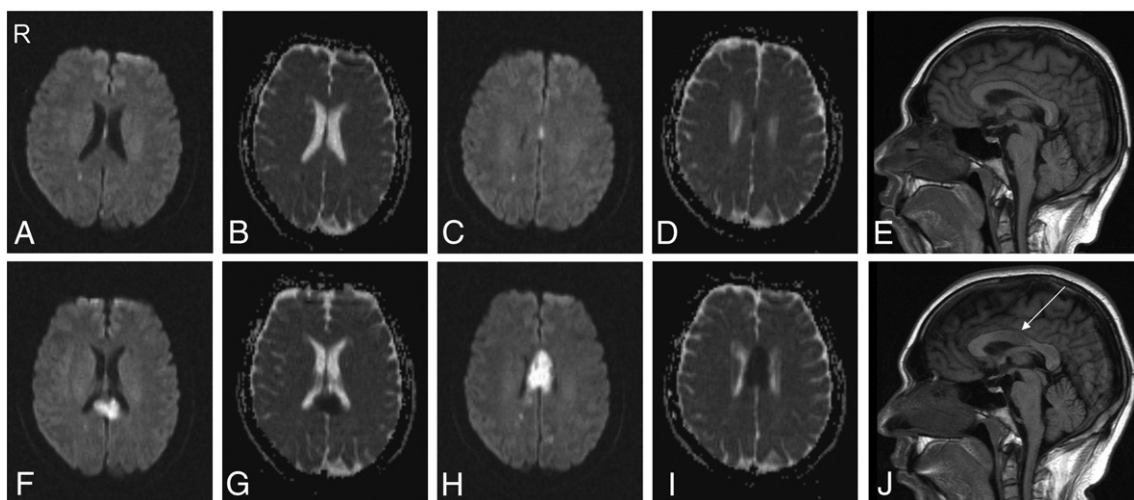


Fig. 2. Upper panel. MRI brain [axial DWI, b1000 (panels A, C), ADC map (panels B, D) and sagittal T1 weighted image (panel E)] performed within 24 h of onset of initial symptoms of callosal disconnection. There is no abnormal signal intensity or infarction in the region of corpus callosum. Lower panel. MRI brain [axial DWI, b1000 (panels F, H), ADC map (panels G, I) and sagittal T1 weighted image (panel J, arrow depicts the hypointensity/infarction)] obtained one week after the initial symptoms shows acute infarction involving the body of corpus callosum.

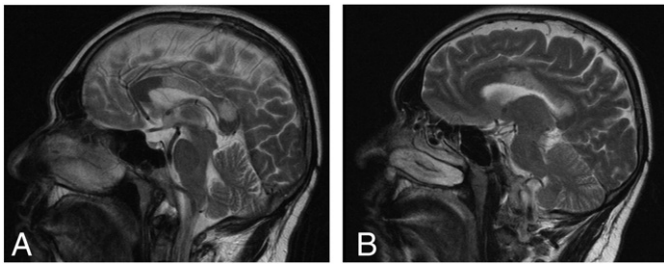


Fig. 3. MRI brain [sagittal T2 weighted image (panels A and B)] obtained 1 month after the ictus demonstrates established infarction involving the body of corpus callosum.

symptoms were not accompanied by corresponding lesion/infarction in the corpus callosum on the diffusion weighted MRI and apparent diffusion coefficient map obtained within 24 h of onset of symptoms (Fig. 2, upper panel), while the subsequent brain MRI (performed one week after the initial symptoms) revealed the characteristic callosal infarction (Fig. 2, lower panel) when the symptoms were persistent. As diffusion-weighted MRI is quite sensitive to depicting infarction within hours of ischemic symptoms [7], the temporal course of clinico-imaging findings suggest that there was initial symptomatic callosal ischemia culminating in infarction in the subsequent days. The accompanying small, scattered, acute extra-callosal lesions in the distribution of anterior cerebral arteries or anterior-middle cerebral border zone area (distal vascular field) also favored ischemic infarction over hyperacute demyelination or tumor as the underlying causative mechanism.

The corpus callosum is supplied by three main arteries viz. anterior communicating artery, distal anterior cerebral artery and distal posterior cerebral artery [8]. The anterior portion of the corpus callosum (rostrum and genu) is usually supplied by the subcallosal and medial callosal branches of the anterior communicating artery. The pericallosal branch of the distal anterior cerebral artery often provides blood supply to the body, whereas the splenium derives its vascular supply, most often, from the splenial or posterior pericallosal branch of the distal posterior cerebral artery. As in our patient, infarction of the callosal body (and or rostrum and genu) could present with the disconnection syndrome as mentioned above [9–13]. In contrast, splenial infarction accompanying occipitotemporal lesion of the dominant hemisphere due to posterior cerebral arterial occlusion usually presents with alexia without agraphia [14]. This form of pure alexia arises from the disconnection of the non-dominant occipital lobe from the language area and was not observed in our patient in whom the splenium was spared (Fig. 3). The crescendo transient ischemic attacks involving the callosal body culminating in ischemic infarction and persistent symptoms were in keeping with the temporal profile of warning syndromes that has been described for capsular and pontine tegmental strokes [1–4]. The predominant pathophysiologic mechanisms underlying these stroke warning syndromes include hemodynamic compromise of penetrating arterial branch and peri-infarct depolarization [1,2]. Consistent with this mechanism of branch vessel occlusion, there were no stenotic or occlusive lesions in the proximal portion of anterior cerebral or extracranial carotid arteries on serial MR angiograms in our patient who had vascular risk factors such as hypertension and heavy cigarette smoking. To the best of our knowledge, callosal warning syndrome presenting with callosal disconnection syndrome has not been reported earlier, although there are case reports of disconnection syndrome due to established infarction or hemorrhage involving part or whole length of the callosum [9–13].

Regarding the symptoms of disconnection syndrome, alien limb phenomenon has been attributed to the failure of supervisory attentional system to inhibit inappropriate motor routines [15]. The transient nature of this symptom in our patient could be due to potentially reversible ischemia of the genu and rostrum as this part of the callosum was spared at the time of ultimate infarction. The callosal apraxia and dysgraphia could result from the disconnection of the right motor association area from the left hemisphere. The stereotyped, transient episodes of stroke warning syndrome could be mistaken for seizures, paroxysmal symptoms of multiple sclerosis, recurrent hypoglycemic spells and migraine aura. Recognizing the ischemic basis of this syndrome has clinical relevance as this would avoid diagnostic uncertainty. From a therapeutic perspective, this syndrome could pose considerable challenges for decisions regarding intravenous thrombolytic therapy in the emergency room, where the patients present with transient symptoms that appear to improve within the therapeutic time window only to be left with persistent symptoms and established infarction later.

In conclusion, we provide the first account of callosal warning syndrome, a rare stroke syndrome that manifests with a flurry of episodes of transient symptoms dominated by the findings of callosal disconnection due to callosal ischemia initially. Later, the symptomatic ischemia culminates in callosal infarction with persistent neurological signs. This novel stroke syndrome adds to the growing list of well-known stroke warning syndromes that have been described in the location of the internal capsule and pontine tegmentum.

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