Case Report

Amyloid spell – A close mimic of transient ischemic attack!

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ABSTRACT

Transient focal neurological episodes, also called amyloid spells occur as recurrent, transient episodes of spreading paresthesia seen in 14% of cerebral amyloid angiopathy (CAA) patients. An 81-year-old gentleman with coronary artery disease and a left ventricular clot was on anticoagulant treatment. He presented with three episodes of tingling in the left fingers spreading to the left arm and left leg, each lasting for 10 min. Magnetic resonance imaging of the brain with susceptibility imaging showed convexity hemorrhage, and curvilinear blooming in sulcal spaces of the right cerebral convexity and left precuneus. Warfarin was stopped. He was treated with clobazam, aspirin, and atorvastatin. He improved, so was discharged after 2 days. Amyloid spells can be confused with transient ischemic attack (TIA) or its mimics and the treatment given for TIA can lead to intracranial hemorrhage in CAA patients. Radiological features aid in the diagnosis of CAA and antiplatelets need to be administered cautiously in patients with suspected TIA.

Key words: Amyloid spells, Cerebral amyloid angiopathy, Convexity subarachnoid hemorrhage, Cortical superficial siderosis, Transient focal neurological episodes

INTRODUCTION

Amyloid spells are also called Transient focal neurological episodes (TFNEs) and occur as a consequence of cerebral amyloid angiopathy (CAA) in elderly patients. They are observed in 14% of CAA patients [1]. They are recurrent, stereotypical, and transient episodes of positive seizure-like or negative transient ischemic attack (TIA) like phenomena spreading and resolving over a few minutes. These symptoms are considered to be secondary to cortical spreading depression, focal seizures, or transient cortical vasospasm due to amyloid deposition in the wall of blood vessels secondary to CAA [2]. The spread of paresthesia is because of cortical superficial siderosis (CSS) involving the respective areas. Since CAA is often associated with spontaneous intracranial hemorrhage (ICH) in the elderly, mistaking an amyloid spell for a TIA can be a potential pitfall [3].

Amyloid spells due to CAA being a rare and frequently under-diagnosed condition requires a high degree of suspicion and blood-sensitive susceptibility-weighted imaging (SWI) for its diagnosis. We aim to familiarize the treating physicians with the condition and its radiological features through this case.

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CASE REPORT

An 81-year-old man, status post-coronary bypass graft and with a history of the left ventricular clot was on warfarin 5 mg daily for 3 years. He presented to our Neurology outpatient department (OPD) with three recurrent attacks of tingling sensation in the left-hand fingers spreading to the left arm and left leg. These symptoms started a few hours ago after waking up from sleep in the morning. Each episode lasted for around 10 min. He also felt stiffness in his left arm and leg at the time of the attacks. No other associated symptoms were noted. He did not have any history of trauma or head injury. He had no prior history of such episodes and no family history of any neurological illness was noted. He did not have any addictions and was independent in all his activities.

When seen in OPD, his blood pressure was 110/70 mm Hg, pulse rate was 80/min, respiratory rate, and oxygen saturation were normal. His clinical and neurological evaluation was normal.

With the suspicion of a minor stroke or TIA, magnetic resonance imaging (MRI) of the brain as per the stroke protocol was advised. Diffusion-weighted imaging did not reveal any acute infarcts and MRI angiography of the brain was normal. However, MRI brain with SWI showed convexity hemorrhage, curvilinear

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areas of blooming in sulcal spaces of the right cerebral convexity, superior frontal, pre-central, and post-central sulci (Fig. 1a). A small nodular focus of blooming was seen in the left frontal periventricular white matter (Fig. 1b). Small chronic infarcts and small vessel ischemic changes were also seen in our patient (Fig. 1c). These imaging findings are suggestive of CAA. Video-electroencephalograph did not show epileptiform discharges and was normal. Prothrombin time with an international normalized ratio was 1.12. His metabolic and stroke workup including carotid Doppler was normal. Electrocardiogram did not reveal any new changes and showed sinus rhythm.

After a cardiologist consultation, warfarin was stopped as 2D ECHO did not show any clot, and aspirin 75 mg with atorvastatin 20 mg was continued for his coronary artery disease. He was treated with valsartan, spironolactone, clobazam, and other supportive measures. The patient and his son were reassured but were explained about being at risk of developing ICH in the future. The patient did not have any further TFNE. He was asymptomatic at the follow-up visit after 3 months.

DISCUSSION

CAA is due to the amyloid deposition in walls of small-medium-sized arteries and capillaries of the brain parenchyma and leptomeninges [4]. CAA is diagnosed based on modified Boston criteria with supporting radiological evidence on brain imaging [5].

Our patient was an elderly man who presented with multiple short-duration TFNEs in the form of stereotypical, transient, and recurrent episodes of spreading paresthesia in his left-sided upper and lower limbs which were self-resolving in nature with each episode lasting for around 10 min. In the study by Charidimou *et al*., TFNEs were seen in 14.5% of cases [1]. TFNEs can be predominantly positive or predominantly negative symptoms and both of them were equally common (52% vs. 48%, respectively), with 25% having both positive and negative symptoms [1]. The commonest positive symptom was paresthesia in the mouth or hand (32%) usually with a gradual spread to contiguous body parts. The negative symptoms were focal weakness and dysphasia. A few of them (<20%) presented as limb-jerking episodes or transient visual disturbances involving blurred vision or visual loss, flashing lights, and transient zig-zags (teichopsia). Most participants (68%) had multiple episodes (≥2) which were usually stereotyped. TFNEs lasted <6 min in 44% of patients, <30 min in 70%, and ≤3 h in 96% [1]. Another systematic review showed a high frequency of positive spreading sensory symptoms (about 80%) than predominantly negative symptoms (such as hemiparesis or non-fluent dysphasia) [6]. Roch *et al*. proposed that the positive symptoms occur because of the irritant effect of hemosiderin causing cortical spreading depression (CSD) or focal seizure activity [7]. The negative symptoms could be due to cerebral vessel occlusion and spasms resulting from amyloid deposition in the blood vessels [2]. The spread of paresthesia is because of CSS involving the respective cortical areas.

Usual radiological markers of small vessel disease of CAA are lobar cerebral microbleeds, white matter hyperintensities, and enlarged perivascular spaces in centrum semiovale. The radiological spectrum of CAA also includes CSS, acute convexity subarachnoid hemorrhage (cSAH), and lobar intracranial bleeds [1]. MRI brain with SWI in our patient showed sulcal/cortical subarachnoid hemorrhage (SAH) overlying the right cerebral convexity with punctate microhemorrhages, suggestive of CAA, but fortunately, there was no lobar ICH. Warfarin was stopped due to the high risk of intracranial bleeding.

As observed in our patient, TFNEs are common in patients with cSAH who also show disseminated CSS and a lesser number of lobar cerebral microbleeds implicating superficial bleeding due to the pathology [8]. Two cohort studies showed that the majority of patients with CAA-related TFNEs have 1 or both of cSAH or CSS (58% [1] and 61% [9]. respectively). Disseminated CSS is much more common in patients with CAA presenting with TFNEs [6].

The slow spreading pattern of signs and symptoms congruent with cortical somatotopy, the preponderance of mixed positive and negative symptoms, and the transient and often stereotypical nature are the most conspicuous features of CAA-related

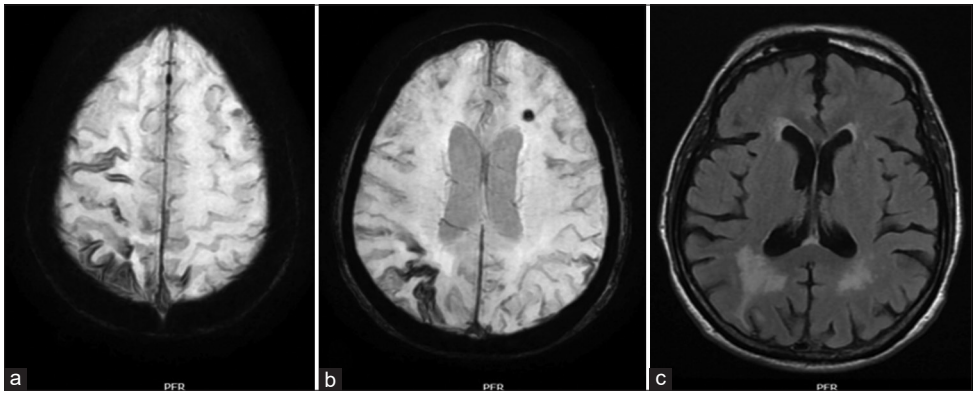

Figure 1: Minimum intensity projection images of the susceptibility-weighted imaging sequence shows (a) Sulcal subarachnoid hemorrhage in right superior frontal, pre-central and post-central sulci; (b) Sulcal subarachnoid hemorrhage in the right intraparietal sulcus and punctate microhemorrhage in the left frontal lobe. (c) T2 FLAIR images of the brain show multiple patchy and punctate foci of T2 hyperintensities involving bilateral periventricular white matter and subcortical white matter of bilateral frontoparietal lobes

TFNEs [6]. CSD is an electrophysiologic phenomenon associated with near-complete depolarization of all cell types in the brain tissue [10]. CSS and acute cSAH are considered as the imaging signatures of CAA which can be best seen in SWI of the brain. Acute cSAH in eloquent areas like central or pre-central sulci usually triggers TFNE's [1]. According to a previous study, warfarin use was seen in 3% of the patients with CAA and associated cSAH [8]. Aspirin and statin usage was seen in 30% and 52% of the patients with CAA and cSAH [8]. TFNEs were present in 76% of CAA patients with cSAH and in 33% of patients with focal CSS [8]. Our patient had TFNE's associated with cSAH, CSS, and fewer cortical microbleeds on the SWI sequence of MRI.

Diagnosing amyloid spells are a huge challenge to physicians because these symptoms usually occur in elderly persons with comorbidities who are also at a high risk of developing TIA and ischemic stroke. These patients are treated with antiplatelets and high-dose statins for presumed TIAs or due to their underlying comorbidities and are susceptible to lobar hemorrhages due to CAA. CSS and acute convexity SAH and the imaging signatures of CAA can be best seen in SWI of the brain. A high index of suspicion is required to diagnose these patients and the treating physicians need to familiarize themselves with the radiological features of CAA for the correct management of such patients.

CONCLUSION

The rare presentation of TFNEs (amyloid spells) due to CAA can be easily confused with TIA or its mimics and the treatment given for TIA can precipitate and lead to frank ICH in patients with CAA. Hence, knowledge about amyloid spells and their radiological signatures is essential. Caution should be exercised in administering antiplatelets to all patients with suspected TIA. An elderly patient who presents with TFNEs should undergo brain imaging studies that are sensitive to detect blood like SWI/Gradient Echo to rule out CAA-related bleed before receiving antiplatelets or anticoagulants for their presumed TIA. SWI has greater sensitivity over T2* GRE for the detection of microhemorrhages and should be included in routine imaging of TFNE.

AUTHORS CONTRIBUTIONS

Sri Sai Srujana Puppala: Case report compilation, acquisition of data, and management of the case. Subhash Kaul: Revision of the case report and management of the case. Ananta Ram Gudipati: Provision of radiological images, reporting, and diagnosing the disease. Rajesh Natuva: Cardiological evaluation and management of the patient.

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