

Stroke Note

Recurrent Stereotyped Episodes in Cerebral Amyloid Angiopathy: Response to Migraine Prophylaxis in Two Patients

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Key Words

Recurrent stereotyped episodes · Cerebral amyloid angiopathy · Migraine prophylaxis

Abstract

Background: Cerebral amyloid angiopathy (CAA) typically presents with cognitive decline or symptomatic intracerebral hemorrhage, but episodes of recurrent stereotyped limb attacks have also been reported. **Methods:** Retrospective review of the medical records of 4 patients referred to the general neurology services and a specialist stroke center with clinically probable CAA. **Results:** Four subjects, all Caucasian, mean age 74 years, were followed up over a mean duration of 20 months. They all experienced recurrent prolonged stereotyped attacks of sensory symptoms, lasting 5–30 min, that resolved completely between attacks. Three subjects developed intracerebral hemorrhage, and 2 had an irreversible rapid cognitive decline. Two patients experienced symptomatic improvement with migraine prophylaxis (verapamil or topiramate). **Conclusions:** Recurrent stereotyped prolonged attacks with sensory and motor elements can predate the development of intracerebral hemorrhage in individuals with clinically probable CAA. When evaluating patients with such attacks, neurologists need to consider CAA as a possible mimic of transient ischemic attacks. We suggest a trial of migraine prophylaxis for symptomatic management.

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Introduction

Cerebral amyloid angiopathy (CAA) typically presents with cognitive decline or symptomatic intracerebral hemorrhage, but episodes of recurrent stereotyped limb attacks have also been reported [1, 2]. We describe 4 patients with probable CAA on MRI, with recurrent frequent migraine-like episodes over a period of weeks to months, 2 of whom responded to migraine prophylaxis and a third who responded to antiplatelet withdrawal.

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Case 1

A 74-year-old woman presented with 3 weeks of stereotyped episodes of tingling and numbness, starting in her right arm and spreading within minutes to contiguous body parts until the face, arm and leg were involved. She had had 5–7 events per day for 3 years. Exam was normal. EEG was normal. MRI showed subcortical hemosiderin deposits on gradient echo sequences (GRE) typical of CAA. Topiramate 25 mg twice daily terminated the attacks.

Case 2

A 72-year-old woman had an 8-week history of colorful flashes of different jagged shapes including pinwheels throughout both visual fields lasting up to 30 min between 5 and 10 times per day. Exam was normal. The episodes completely resolved on verapamil 240 mg a day. Four months later, she blacked out while driving and 3 days later 'lost her color vision'. CT showed an acute right occipital hemorrhage. Color vision returned 4 days later. The visual phenomena recurred but were reduced in frequency on verapamil 120 mg. MRI GRE showed multiple focal areas of subcortical hemosiderin typical for CAA.

Case 3

An 81-year-old woman presented with a 2-month history of recurrent 5-min episodes of left hand and arm numbness and leg weakness, later evolving to attacks including speech. Exam was normal. MRI showed areas of subcortical hemosiderin on GRE. One month later, she developed sudden cognitive impairment. MRI showed a right temporal lobe intraparenchymal hemorrhage and edematous T2 lesions in both occipital lobes. Transient left-sided sensory symptoms continued, less frequently, for 2 months and then stopped completely. They have not recurred for 24 months.

Case 4

A 70-year-old woman presented with 18 months of stereotyped episodes of altered sensation in the right or left side. Paresthesia spread slowly within minutes to involve contiguous body parts. Attacks involved the face, arm, leg and tongue, lasted 30 min and occurred up to 3 times per week. EEG demonstrated bilateral frequent irregular slow wave activity with sharp components. MRI performed 18 months after symptom onset showed a small (1.3 cm) intraparenchymal hemorrhage in the right parietal lobe. GRE showed decreased superficial cortical signals probably due to hemosiderin deposition, and numerous dark foci suggestive of microhemorrhages predominantly in cortico-subcortical distribution. The attacks increased in frequency and severity after aspirin and dipyridamole were commenced as a treatment for presumed transient ischemic attack (TIA). When antiplatelets were discontinued, the attacks terminated within weeks. This case has previously been published [3].

Clinical summaries of all 4 cases are given in table 1.

Table 1. Summary of the clinical and radiological features

	Patient 1	Patient 2	Patient 3	Patient 4
Age at onset, years	74	71	81	70
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian
Event type	Face and limb numbness	Visual disturbance (bright lights and pinwheeling)	Upper limb numbness and dysphasia	Face, tongue, arm and leg paresthesia and dysphasia
Headache	No	No	No	No
Lateralization	Unilateral	Bilateral	Bilateral	Unilateral, affecting either side
Event frequency	5–7 attacks/day For 3 years	5–10 attacks/day For 1 year	10 attacks/month For 2 months	12 attacks/month For 18 months
Event duration	20–30 min	30 min	5 min	30 min
Vascular status	Hypercholesterolemia on statin Hypertension, non-insulin-dependent diabetes mellitus Never smoked	Never smoked No vascular risk factors	Hypercholesterolemia on statin Never smoked No other vascular risk factors	Never smoked No other vascular risk factors
History of migraine	No	No	No	No
Clinical sequelae	Progressive cognitive decline over 1 year	Symptomatic intracerebral hemorrhage (right occipital lobe) after 9 months	Symptomatic intracerebral hemorrhage (right temporal lobe) after 1 month with rapid cognitive decline over hours	Asymptomatic intracerebral hemorrhage (right parietal lobe)
Response to treatment	Completely terminated with topiramate 25 mg b.d. Followed up for 9 months	Frequency reduced on verapamil 120 mg/day Completely terminated with verapamil 240 mg/day	Spontaneous resolution of focal neurological spells following symptomatic hemorrhage	Completely terminated weeks after withdrawing aspirin and clopidogrel Followed up for 2 years
MRI (GRE)	Microhemorrhages in subcortical regions	Microhemorrhages in subcortical regions	Microhemorrhages in cortical and subcortical regions Right temporal hematoma	Microhemorrhages in cortical and subcortical regions

Discussion

All 4 of our patients have probable CAA according to the Boston criteria [4]. All 4 patients had frequent stereotyped attacks over a prolonged period of time (mean 4 weeks, range 3–74 weeks). These attacks occurred over a much longer period and were more frequent and stereotyped than attacks previously reported with CAA without or with associated subarachnoid hemorrhage [1, 2]. The attacks had a time course similar to a migraine aura with symptoms spread over several minutes. The frequent and stereotypic nature of the attacks led to a diagnosis of TIA in 1 patient with initiation of antiplatelet treatment.

The development of these attacks may be a predictor of future symptomatic intracerebral hemorrhage, as it occurred in 2 of our 4 patients at 1 and 9 months after the onset of symptoms. Patient 2 who had recurrent positive visual phenomena had subsequent symptomatic occipital hemorrhage. Patient 3 with numbness starting in her left hand subsequently developed right temporal hemorrhage. She also developed concurrent edematous lesions consistent with the ‘inflammatory’ form of amyloid angiopathy, also known as reversible leukoencephalopathy [5]. Patient 4 had an asymptomatic intracerebral hemorrhage.

The duration of the attacks was similar to a migraine aura, and the response to migraine prophylactics supports a ‘spreading depression’ pathogenesis rather than transient ischemia;

we therefore propose the name ‘transient aura attacks’. We hypothesize that these attacks may be initiated by cortical irritation or inflammation caused by blood products or edema from prior cortical hemorrhage, as the disruption of pial arterial walls in CAA is known to cause small focal hemorrhages. These attacks may also herald cerebral hemorrhage. The clinical distinction of these attacks from TIAs is important, as antiplatelet agents [6] and anticoagulation [7, 8] are likely to increase the risk of hemorrhage.

Disclosure Statement

Dr. Pullicino received honoraria as a consultant for Merck and Boehringer Ingelheim. Dr. Paterson, Dr. Uchino and Dr. Emsley have no declarations to make.

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