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# A Case of Cerebral Amyloid Angiopathy-Related Inflammation (CAA-RI) Presenting as a Generalized Tonic Clonic Seizure

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**Abstract** Cerebral Amyloid Angiopathy (CAA) is characterized by amyloid beta-peptide deposits within the small to medium-sized vessels of the brain and leptomeninges. CAA is an important cause of intracerebral hemorrhage in older adults. Cerebral Amyloid Angiopathy Related Inflammation (CAA-ri) is, however, a rare variant of CAA that results from an autoimmune response to the deposits and is characterized by acute or subacute encephalopathy, headache, or focal neurological deficits. We present a case of a 62-year-old female who presented with a generalized tonic-clonic seizure witnessed by a family member. The event was preceded by a worsening of her dementia in the past few months. The patient had features suggestive of CAA-ri on Magnetic Resonance Imaging of the brain and was treated with high dose IV steroids. With an improvement in her cognitive symptoms and no further seizure episodes, she was discharged on oral steroids. Although CAA is well studied and well documented, its subset CAA-ri is uncommon with its clinical course and complications mentioned infrequently in medical literature. In conclusion, CAA-ri is underdiagnosed because of its rarity and remains a potentially treatable cause of subacute cognitive decline and seizures demanding further research in this area.

***Keywords:*** *format, microsoft word template, style, insert, template*

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## 1. Introduction

CAA is represented by the by the deposition of amyloid-beta peptides within the small and medium-sized vasculature of the brain and leptomeninges [1,2]. CAA-ri is characterized by inflammation that is postulated to be due to the body's, inflammatory response to the aforementioned amyloid deposits [2,3,4,5]. The incidence of the disease is equal in both men and women with onset of symptoms usually in the 7th Decade of life. The most widely reported symptoms are cognitive and behavioral changes, other less common symptoms include focal neurological signs, headaches, and seizures [4]. We present a case of a patient with CAA-ri presenting with a generalized tonic clinic seizure with a background of subacute cognitive decline and worsening dementia in the preceding months.

## 2. Case

We present a 62-year-old female with a past medical history significant for anxiety, depression, fibromyalgia, hypothyroidism, lupus, and dementia who presented with an event concerning for a seizure-like episode. The patient's last known normal was the night before admission. On the day of the presentation around 7: 30 in the morning the patient had a generalized tonic-clonic seizure. Witnessed by her grandson this episode lasted only a few minutes before spontaneously resolving. There was tongue biting associated with the event but no report of bowel or bladder incontinence. The patient was confused after the event and EMS was contacted and subsequently, the patient was brought to the hospital. The patient did not have any further seizures in her return to her neurological baseline during the rest of her hospital

stay. The patient has a history of dementia over the past several years however in the ensuing months her clinical condition seemed to have rapidly progressed. The patient denied any symptoms of headache and was a nonsmoker. She did routinely see a neuropsychologist but had not seen a neurologist recently.

The patent had a normal general physical examination. On neurological examination, the patient was alert and oriented to person, place, and time, however, she did have difficulty narrating her past medical history resorting to confabulations at times requiring redirection. Overall she displayed poor insight into her condition. Cranial nerves were intact. The speech was clear without dysarthria and language was intact to fluency, comprehension, naming, and repetition.

Routine laboratory testing revealed a WBC of 4.6*103/ul, Hemoglobin of 13.7 gm/dl, Platelets of 200*103/ul, Sodium was 143 mmol/L, Potassium of 3.6 mmol/L, and creatinine of 0.8 mg/dL. Her TSH was 1.16 ulU/ml, free T4 was 0.92 ng/dl and Prolactin of 73.5 ng/ml (ref range 1.2-29.9 ng/ml). The patient underwent a head CT scan as well as a brain MRI. The head CT showed a high cortical attenuation in the posterior medial right occipital lobe, which may represent cortical traumatic hemorrhage versus small hemorrhagic infarct or possible cortical calcifications. MR imaging of the brain was recommended which was subsequently done and showed that the cerebral hemisphere had focal cortical and subcortical T2 hyperintensity of the left lateral temporal lobe without restricted diffusion. There were also countless punctate foci of hemosiderin throughout the subcortical white matter of both hemispheres manifest as block dots on axial gradient imaging. Finally bilateral symmetric punctate and patchy T2 hyperintensities in the subcortical and deep white matter without restricted diffusion or mass effect. The rest of the brain structures including ventricles, brain stem, and cerebellum were normal. The conclusion of the MRI was an inflammatory cerebral amyloid disease with amyloid beta-related angiitis in the right temporal lobe neocortex, diffuse supratentorial white matter, and countless old microbleeds.

Based on the findings of the MRI a Neurology consult was obtained to evaluate the patient. Given the patient's clinical history with the constellation of subacute worsening of dementia, seizure, and MRI findings, Cerebral amyloid angiopathy related inflammation CAA-ri was considered the most likely diagnosis by neurology. After discussing the risks and benefits with the family the patient was started on IV Solu-Medrol 1000mg daily for 5 days. The patient completed 5 days of IV steroids in the hospital and remained seizure-free for the remaining of her hospital stay. She showed improvement in her cognitive function towards the end of her hospital stay and was subsequently discharged on a tapering dose of oral steroids of 80mg prednisone on week 1 and then a reduction of 10mg every week till completion of therapy.

## 3. Discussion

Cerebral Amyloid Angiopathy (CAA) is a fairly common finding associated with the deposition of Amyloid Beta along the walls of small to medium-sized arteries, arterioles, and capillaries in the cerebral cortex, as well as leptomeningeal arteries [2]. This can occur most commonly in patients with Alzheimer's Dementia as well as a sporadic non-pathological finding in older, otherwise healthy individuals. It is a condition both well studied and documented. There is a subset of CAA that is associated with pathologic vascular inflammation and subsequent manifestations in the form of seizures, headaches, and subacute cognitive decline [6]. While there have been some isolated case reports and studies regarding this particular subset of CAA, this is still an area that requires a considerable amount of research. While it is underdiagnosed, because of its rarity, it remains a potentially treatable entity. This subset is further typed into CAA related inflammation (CAA-RI). This is a condition characterized by perivascular nondestructive inflammatory infiltration [4]. Yet another type is a vasculitic transmural, sometimes granulomatous, inflammatory infiltrate, namely Aβ-related angiitis (ABRA) [7]. Though rare, these two conditions can sometimes coexist within the same patient as evidenced in our case. CAA-RI presents predominantly with Subacute cognitive decline and seizures [8]. ABRA has shown to present more with new-onset headaches, neuropsychiatric manifestations, focal neurological deficits, and epileptic seizures [6]. The median age for diagnosis for both CAA-RI, ABRA is > 50 years. In terms of imaging findings, CAA-RI shows MRI findings consistent with shifting multifocal white matter T2 hyperintensities abnormalities colocalized with petechial hemorrhages on SWI [9]. In ABRA, T2-weighted (T2W) or fluid-attenuation inversion recovery (FLAIR) images show hyperintensities with minimal gadolinium enhancement. Most patients also have the presence of scattered cortical and subcortical microbleeds at GRE images [10,11]. There are considerable differences between the two conditions, however. ABRA presents a younger age than CAA-RI. It also has a lower incidence of strokes or focal neurological deficits, a decreased risk of intracerebral hemorrhage, and a low frequency of altered cognition [6]. Both conditions have shown good response to corticosteroids and immunosuppressive therapy [12]. Brain Biopsy has long been considered the gold standard for diagnosis of these conditions however recent literature suggests that diagnosis can be made based on the clinical picture, MRI findings, and response to corticosteroids [13].

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