

# Cerebral Amyloid Angiopathy ---“A rare cause of Primary Intracranial Hemorrhage in Indian Elderly patients”.

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## Citation

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## Abstract

Cerebral amyloid angiopathy (CAA) is one of the important causes of primary intracerebral haemorrhage (PICH) in older people. Lobar, recurrent or multiple simultaneous hemorrhages in older patients should raise suspicion of its diagnosis. A definitive diagnosis of CAA requires pathological examination of the affected tissue. However, with modern imaging techniques, it is possible to make a diagnosis of 'probable CAA' in patients presenting with PICH.

## INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a disease of older people. It occurs as a result of extra cellular deposition of a fibrillar protein, amyloid in the walls of small- and medium-sized arteries<sub>1</sub>. CAA can manifest in several ways, and the most serious manifestation of CAA in older people is the rupture of cerebral vessels, leading to primary intracerebral haemorrhage. The following case is a patient who was diagnosed with this entity.

## CASE REPORT

A 56 year old male, non hypertensive, non addict used to stay alone in his house was found unconscious at home in morning by relatives. He was taken to the hospital immediately. A CT Scan of the brain was done at this hospital which showed right temporo-parietal bleed with generalized cerebral edema with no mass effect or midline shift. Later with these investigation patient was referred to our hospital which being a tertiary referral center admitted the patient for further management.

On examination the patient had a Glasgow Coma Scale (GCS) of 8/15 (E3M4V2) and his Blood Pressure was 130/90 mmHg. On examination of Central nervous system he was moving his left side less as compared to his right side. All his reflexes were 2+ and both the planters were extensors. He had no cerebellar signs or signs of meningeal irritation. His hematological and biochemical tests were normal.

Thus a diagnosis of right temporoparietal hematoma was

reached. But the cause of this bleed was yet to be investigated.

The patient was treated with I.V. mannitol, Injection Phenytoin, steroids and IV Fluids. The patient continued to deteriorate in sensorium and had 1 episode of seizure, which was left focal seizure with secondary generalization. His electrolytes and sugar levels were rechecked at this moment which again came to be normal.

At this stage the patient's MRI and MRV of brain was done to find out the cause for his intracranial hemorrhage.

The MRI of the patient showed multiple small hemorrhages in whole brain besides the temporoparietal hematoma on right side, this was pathognomic of Cerebral

Amyloid Angiopathy. (Picture No 1)

{image:1}

The patient was managed conservatively Neurosurgeons did not operate the patient for evacuation of hematoma in view of his poor GCS, He deteriorated further and finally died.

His postmortem examination was done and a histopathology report of brain showed that there were amyloid deposits in the cerebral blood vessels which were confirmed by Congo red stain and visualization under polarized light of A.O microscope.

This was thus a case of temporoparietal hematoma secondary to Cerebral Amyloid Angiopathy. (CAA)

## DISCUSSION

CAA is one of the rarest causes of non hypertensive intracranial hemorrhage in India, there are very few reported cases of this entity. This case reported was a patient below the age group of 60 years. CAA has been reported in persons of >60 years of age.

CAA usually manifests as repeated hemorrhages in the brain and the patient improves.

This case presented for the first time with a large hematoma which was ultimately fatal for him.

Very few cases have been finally proven as CAA after the histopathological confirmation; this case confirmed the diagnosis by the postmortem examination of brain, with visualization of amyloid on Congo red stain.

Cerebral amyloid angiopathy (CAA) is a very rare entity. This is an age related disease and is not a manifestation of systemic amyloidosis. This condition should be considered when a spontaneous non hypertensive intracerebral haemorrhage with lobar pattern or one situated very superficial location in the cortical region is present.

It can occur as a sporadic disorder, in association with Alzheimer's disease (AD), or with certain familial syndromes <sup>2</sup>. CAA is characterized by the deposition of congophilic material in small to medium-sized blood vessels of the brain and leptomeninges. In its most severe stages, the amyloid deposits cause breakdown of the blood vessel wall with resultant hemorrhage.

**EPIDEMIOLOGY:** The incidence of cerebral amyloid angiopathy (CAA), like Alzheimer's disease (AD), is strongly age-dependent. Based upon a series of autopsy cases from various studies from UK,USA and Japan the prevalence of moderate to severe CAA has been found as 2.3 percent for patients between the ages of 65 and 74, 8.0 percent between the ages of 75 and 84, and 12.1 percent over the age of 85 <sup>3</sup>. CAA-related symptoms are uncommon at ages younger than 60 to 65.

There are very few Indian studies on this entity but one such autopsy study from Mumbai showed that the incidence of CAA observed was 14% <sup>4</sup>. The incidence in general population has never been documented. This entity thus could be a rarity in Indian population.

**PATHOGENESIS:** In CAA, there is a localized deposition

of amyloid in the media and adventitia of the small arteries, arterioles, veins and capillaries of the cortex and leptomeninges.

The primary constituent of each is amyloid beta-peptide, a 39 to 43 amino acid fragment of the amyloid precursor protein. There is essentially no clinical overlap between CAA and the non-CNS systemic amyloidoses, such as primary (amyloid AL) and secondary (amyloid AA) amyloidoses. It is proposed that the combination of a greater amount of amyloid and vasculopathic changes (cracking and fibrinoid necrosis) in the amyloid-laden vessel walls leads to high risk of haemorrhages in CAA <sup>2</sup>.

## DIAGNOSIS

The Boston's criteria which were proposed in the 90's are still useful in diagnosis of CAA. The Boston criteria were developed in the mid-1990s as a tool to both improve and standardize the diagnosis of CAA. The criteria specify four diagnostic categories: definite CAA, probable CAA with supporting pathologic evidence, probable CAA, and possible CAA, depending on a combination of clinical, imaging, and histologic data <sup>5,6</sup>.

A “definite” diagnosis of CAA is made with a full postmortem examination providing confirmation of lobar, cortical, or corticosubcortical ICH and severe CAA.

{image:2}

As histologic analysis is often not practical, recognition of the imaging findings of CAA is important for correct diagnosis.

A patient presenting with an acute neurological deficit or TIA-like symptoms

should undergo non enhanced computed tomography (CT) of the head. CT allows rapid establishment of the presence or absence of an ICH and exclusion of the main clinical differential diagnostic consideration of an acute cerebral infarction.

If an ICH is present in a cortical-subcortical location and the patient does not give any history of other causes for ICH like hypertension, drug abuse, trauma etc. CAA should be suspected and the patient should undergo additional evaluation with MR imaging including a gradient-echo (GRE) sequence. GRE is currently the most sensitive MR imaging sequence for detection of the chronic cortical-

subcortical micro hemorrhage.

These chronic micro hemorrhages can be associated with acute CAA-related ICH, and detection of these chronic micro hemorrhages with GRE imaging increases the probability for CAA.

## MANAGEMENT

Currently, there is no treatment to halt or reverse-amyloid deposition. Acute ICH caused by CAA should be treated in the same way as ICH due to any other aetiology.

It is important to avoid anticoagulation therapy after CAA-related ICH unless absolutely indicated, and survivors of lobar ICH with atrial fibrillation should not be offered long-term anticoagulation.

## PROGNOSIS

Like with ICH due to any cause, outcome depends on the size and site of bleeding, patient's age and the level of consciousness. Major concern in the survivors of CAA-related ICH is the recurrent bleeding. A recurrence rate of 10% per year has been reported.

There are very few Indian reports of CAA, further studies are required on general population and in elderly patients of primary intracranial hemorrhages to conclude on the definitive incidence of this disease in Indian patients. Till then it would not be wrong to state that it is a rare entity in Indian adults with symptoms of cerebrovascular accidents.

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