

Cerebral Amyloid Angiopathy - Novel Imaging Appearance

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Abstract

We describe a novel presentation of cerebral amyloidosis. The strongly enhancing appearance of this deep white matter mass with large 'stippled' hematoma in a young patient has not been previously described. Our case serves to highlight the varied imaging appearance of cerebral amyloidosis, as well as the therapeutic dilemma. CAA should be considered when faced with the presentation of an unusual hematoma or enhancing mass.

CASE REPORT

A 46 year-old otherwise healthy male inmate with a 10 month history of impaired balance, dysarthria, and progressive right-sided pain, initially occurring in the upper arm, and then spreading to involve the right hand and right leg, for which analgesics were ineffective, presented to the emergency department with acute right upper extremity weakness and acute headache. Vital signs were stable. There was no decreased level of consciousness, and cranial nerve exam was normal.

CT scan revealed hemorrhage in the left caudate body and deep left white matter (Figure 1A). A study obtained following intravenous contrast administration demonstrated unusual heterogeneous enhancement adjacent to the hematoma (Figure 1B).

Figure 1

Figure 1A: Initial non-contrast axial CT scan demonstrates acute hemorrhage within the deep left cerebral white matter and caudate body. Surrounding hypodensity in the white matter has the appearance of vasogenic edema.

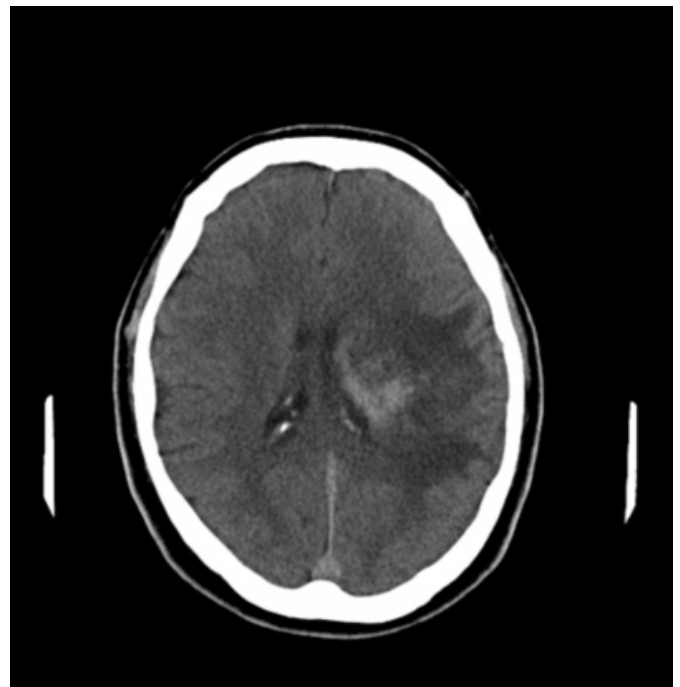


Figure 2

Figure 1B: Following intravenous contrast administration, there is minimal patchy nodular enhancement adjacent to the large hematoma.



An MRI was performed the same day and revealed iso-intense to cortex T1 (Figure 2A) and dark T2 (Figure 2B) and gradient echo (Figure 2C) signal, representing subacute blood products, with surrounding vasogenic edema. With intravenous contrast administration, there was avid enhancement in an unusual 'stippled' pattern in a mass-like lesion within the left hemisphere (Figure 2D).

Figure 3

Figure 2A: T1-W sequence before contrast demonstrates an iso-intense area within the deep left fronto-parietal region.

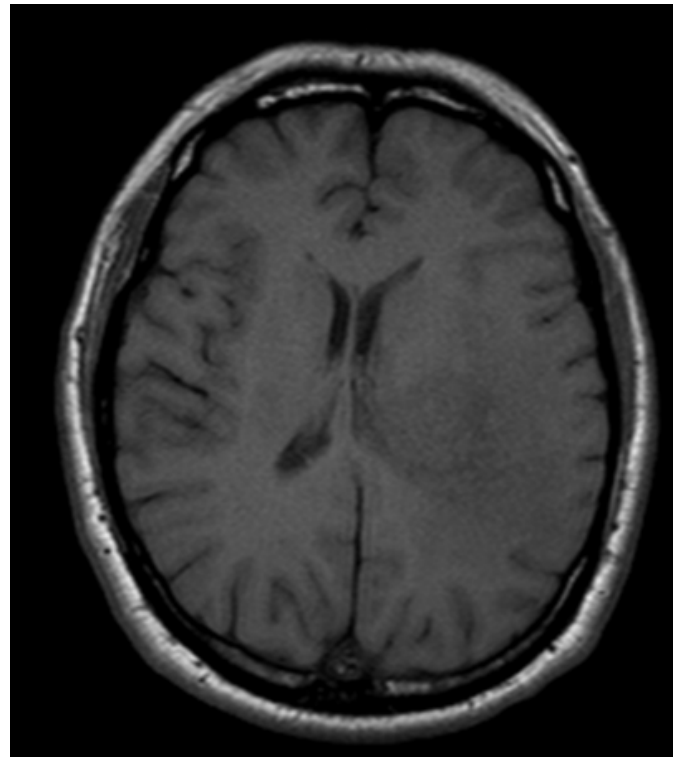


Figure 4

Figure 2B: Unusual 'stippled' pattern of acute blood products, that are dark in signal on T2-W. Note the large amount of surrounding vasogenic edema.

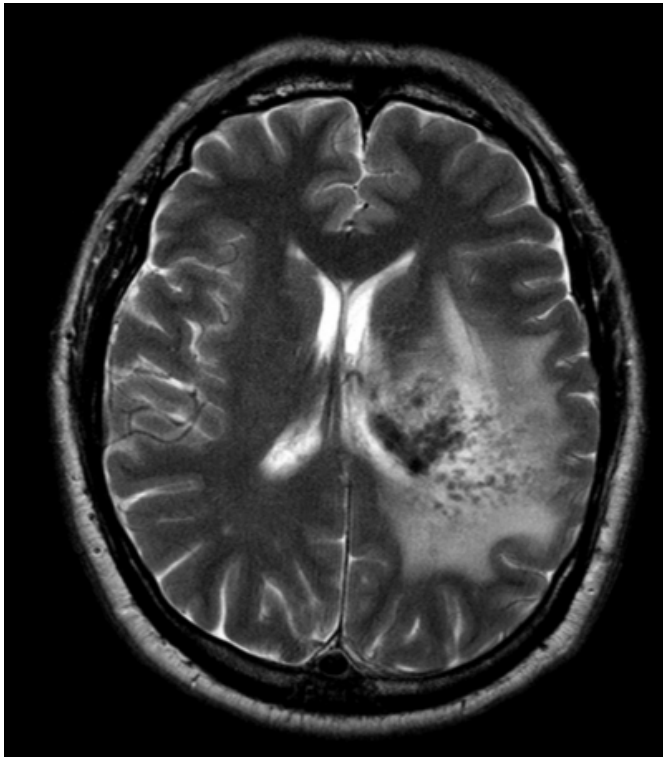


Figure 5

Figure 2C: The gradient echo sequence confirms the presence of dark blood products in the deep left hemisphere.

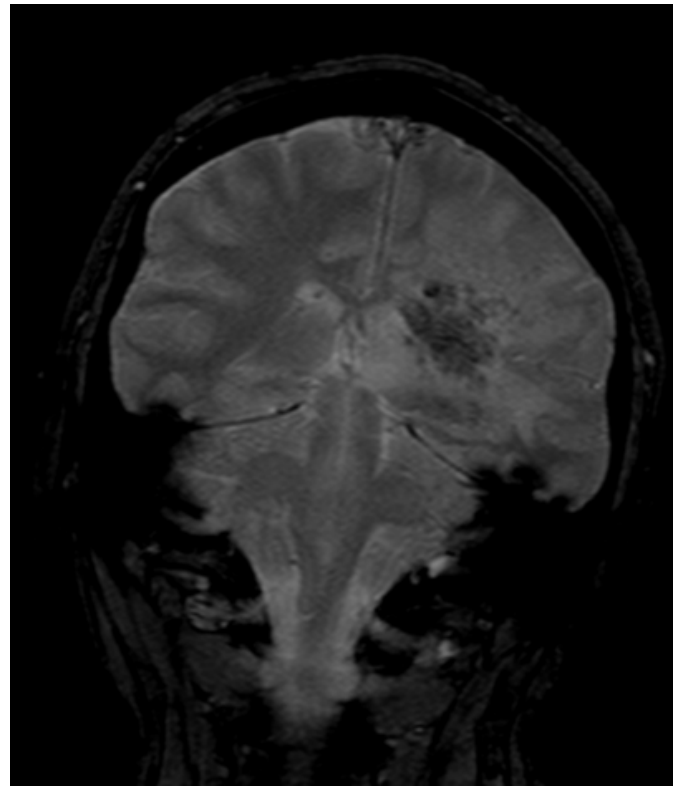
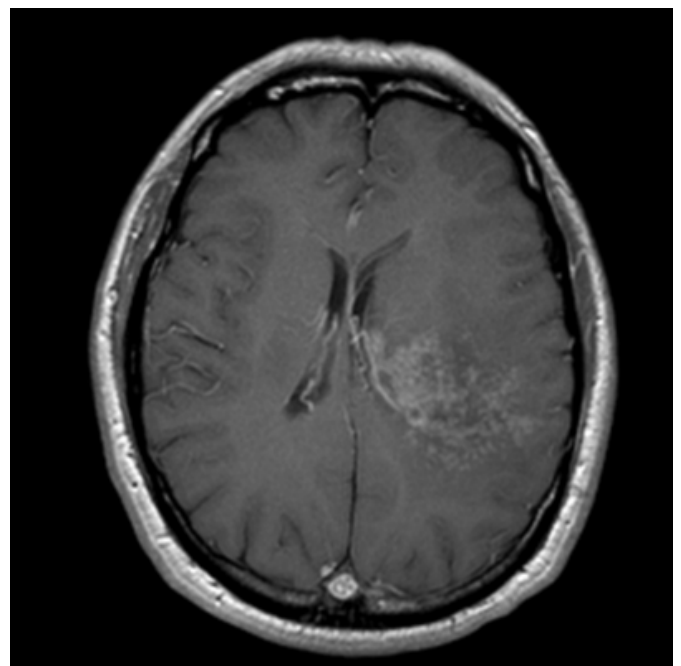


Figure 6

Figure 2D: With intravenous contrast administration, there is an odd pattern of avidly enhancing mass-like lesion with the deep left cerebral hemisphere.



The patient was taken to the OR and via a left parietal burr hole, biopsy of the lesion was performed. Microscopy revealed masses of concentric lamellated concretions, eosinophilic, surrounded by elongated cells and a few giant cells. Staining with Congo red demonstrated classic colour change and birefringence confirming the amyloid nature of these concretions.

Various laboratory tests, including CBC analysis, serum and protein electrophoreses, CT scan of the chest, abdomen, and pelvis, echocardiography, and bone marrow investigation were all negative. Genetic testing for the rare familial form of amyloidosis was also negative.

Surgical removal was not an option for this deep cerebral mass. Low-dose radiation therapy was instituted (50 Gy in 25 fractions), with concurrent Dexamethasone. Subsequent follow-up to 15 months post presentation did not reveal any clinical change, with persistent right-sided hemiparesis and mild headaches. There was no radiographic improvement, with persistent low-T2 signal intensity (Figure 3A) and mass demonstrating avid stippled enhancement following intravenous Gadolinium administration (Figure 3B) within the deep left cerebral hemisphere on an MRI study performed 15 months after the initial examination.

Figure 7

Figure 3A: Axial T2-W sequence reveals persistent dark blood products with a large volume of surrounding vasogenic edema.

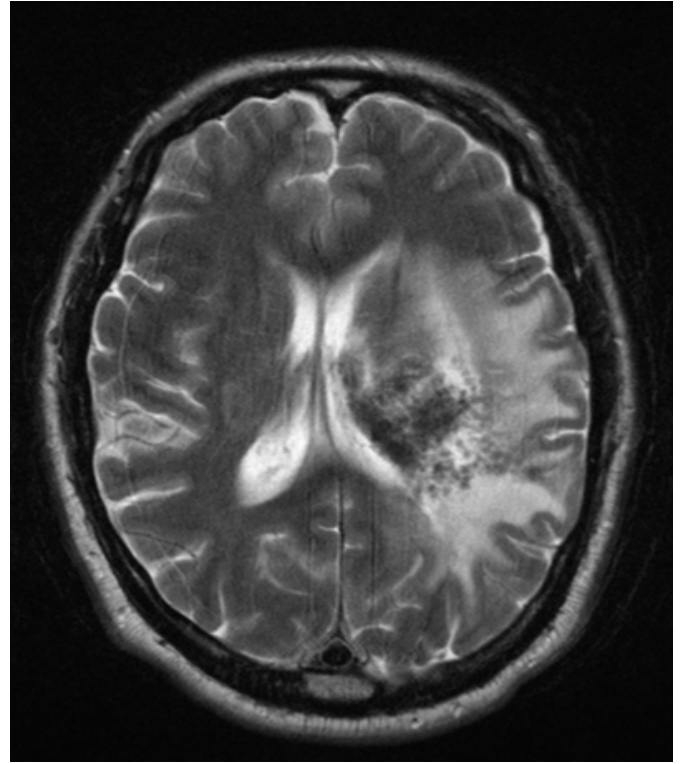
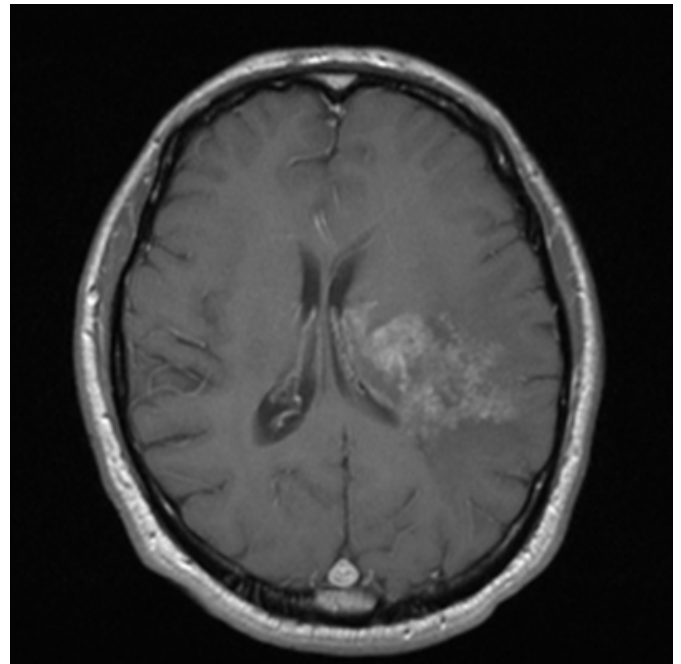


Figure 8

Figure 3B: There is avid enhancement in a 'stippled' pattern on the T1 post contrast sequence.



DISCUSSION

Cerebral amyloid angiopathy (CAA) is a vascular disease, often associated with spontaneous and recurrent hemorrhagic stroke in the normotensive elderly, which can be devastating. Most cases are asymptomatic. In autopsy series, the prevalence of CAA increases to 75% of those older than 90 years.⁹ Despite such high prevalence, CAA is a relatively under recognized cause of cerebrovascular disease both clinically and at imaging.

When symptomatic, cognitive impairment is a common feature; according to Ellis et al, 40% of patients with CAA-related intracranial hemorrhage have dementia, and more than 80% of patients with Alzheimer disease have CAA.⁴ However, there may be a sub clinical course, and detection may not occur until autopsy. There is an age dependant prevalence of 8% for ages 75-84 to 12% for ages >84. Prevalence is highest in patients with Alzheimer's disease, and up to 90% of patients with Alzheimer disease have changes of CAA at autopsy.^{4,8}

CAA is unrelated to systemic amyloidosis. There is an association with increasing age, dementia, Alzheimer's disease, post-radiation necrosis, and spongiform encephalopathies. There are both sporadic and hereditary forms. The hereditary forms demonstrate an autosomal dominant transmission, but are generally quite rare. Hereditary forms may have a different clinical presentation than the sporadic form, and are seen in younger patients, some as early as in the third decade.⁸

Definitive diagnosis is by biopsy or autopsy. Pathologic analysis reveals fibrinoid degeneration of the vessel walls with microaneurysms. There is classic yellow-green birefringence under polarized light of amyloid deposits stained with Congo red. There is accumulation of B-amyloid protein within the media and adventitia of small and medium-sized vessel walls within the cortex, subcortical white matter, and leptomeninges. Similar sized vessels in the deep white matter are typically spared.¹⁰ These structural alterations in the vessel walls lead to loss of elasticity and increased fragility.⁵ Vessel wall fragmentation and microaneurysm formation occur, and tiny hemorrhages (microbleeds) result. Microbleed-induced damage causes further loss of wall elasticity and thinning of the vessel wall. In addition, fibrinoid necrosis results in luminal narrowing, which can lead to ischemic change.¹¹

Early clinical and radiographic recognition is important for

patients on anticoagulation or aspirin therapy, as they are of increased risk for subsequent hemorrhage, reported as high as 38%.⁷ In these patients, the risk of hemorrhage should be weighted against the risk of thromboembolic disease. Strict blood pressure control may be useful in patients with CAA-related hemorrhage.

The recognition of imaging findings in CAA is important in guiding management of patients with CAA. Computed tomography is the imaging study of choice for detection of intracerebral hemorrhage and its complications. MR imaging can be performed for identification of small or microhemorrhages, associated white matter abnormalities, and to assess disease progression.

On imaging, CAA manifests with a variety of findings, including hemorrhages of varying ages within a distinctive cortical-subcortical distribution, atrophy, and leukoencephalopathy.¹⁰ Hemorrhages involving the peripheral cortex or subcortical white matter are most commonly seen in the frontal or parietal lobes. The cerebellum is rarely involved. Multiple hemorrhages may be present, and evidence of subarachnoid extension may be seen, characterized by pial hemosiderin staining. Co-existing white matter disease, due to small vessel involvement is usually present. Symptomatic hemorrhages are commonly large (>5mm), whereas microhemorrhages (5mm or smaller) are typically clinically occult. Regardless of size, CAA-related hemorrhage is distinctive in that the distribution is typically cortical-subcortical with sparing of the deep gray and white matter and brainstem, conforming to the anatomic distribution of B-amyloid containing vessels.¹⁰ Multiplicity of hemorrhages and recurrent hemorrhages are findings that should elevate the suspicion of an underlying vascular disease, such as amyloid angiopathy.

Subarachnoid and subdural hemorrhage may be seen, usually in conjunction with macrohemorrhages, and as a result of direct extension of peripheral parenchymal bleeding.⁸

Leukoencephalopathy, or white matter disease, is characterized by low density on CT and high signal intensity on T2-weighted MR imaging. This is a non-specific finding, and in the context of cortical-subcortical hemorrhages and/or progressive dementia, CAA should be considered in the differential diagnosis.¹²

Atrophy is commonly seen in these patients, especially the elderly. This is most likely the result of chronic small vessel

ischemic disease secondary to B-amyloid deposition and is usually seen in conjunction with leukoencephalopathy.¹⁰

The microhemorrhages of CAA are best detected on gradient echo (GE) sequences, which demonstrate dark foci corresponding to hemosiderin deposition, due to the paramagnetic effects of hemosiderin. The signal intensity loss is proportional to the amount of hemosiderin present. These lesions may be relatively inconspicuous on standard T1 and T2 weighted sequences. In fact, almost 25% of patients with CAA do not show microhemorrhages even on GE imaging.^{3,6} With the advent of susceptibility-weighted imaging, a new imaging method that maximized sensitivity to magnetic susceptibility effects, lesion detection can be increased.³ The white matter disease is best seen on conventional T2 and FLAIR MR sequences. Typically, there is no enhancement of the microhemorrhages or white matter disease with intravenous Gadolinium administration.

A single large cortical/subcortical hematoma is not specific for CAA. Other entities to consider include hypertension, illicit drug use, trauma, vascular malformation, tumor, vasculitis, or bleeding diatheses. Hypertensive hemorrhages, the most common cause of non-traumatic bleeding in adults, in contrast to CAA-related hemorrhage, is typically involves the deep gray matter such as the thalami and basal ganglia.¹³ It can also occur in the cerebellum and pons. Hemorrhagic tumor may be located in the cortical/subcortical location, however, it usually demonstrates enhancement or another enhancing lesion may be seen, leading to the diagnosis of metastatic disease.

Currently, there is no treatment to halt or reverse B-amyloid deposition. Management is therefore aimed at preventing hemorrhage and minimizing the impact of dementing illness. Prognostically, higher numbers of microhemorrhages on baseline gradient echo MR imaging is a predictor of a greater risk of recurrent bleeding, future cognitive impairment, or death.¹⁴ The risk-benefit ratio of anticoagulation and thrombolytic therapy should be carefully considered in patients diagnosed with CAA. Even therapeutic levels of anticoagulation have been shown to be associated with increased frequency of hemorrhage in CAA patients.¹⁵

Our case is unusual for several reasons. While CAA is typically a disease of the elderly, our patient was 46 years of age. The deep white matter location present in this case is uncommon for CAA. Also there were no other lesions and

there was no background white matter disease. It was surprising to find both the presence and degree of enhancement, visible on both CT and MR imaging. The pattern of enhancement was also unusual for most disease entities, including primary CNS tumors and metastatic disease. The appearance was not consistent with infection, although fungal infection or granulomatous disease such as sarcoidosis or tuberculosis may have nodular enhancing foci.

CONCLUSION

We describe a novel presentation of cerebral amyloidosis. The strongly enhancing appearance of this deep white matter mass with large 'stippled' hematoma in a young patient has not been previously described. Our case serves to highlight the varied imaging appearance of cerebral amyloidosis, as well as the therapeutic dilemma. CAA should be considered when faced with the presentation of an unusual hematoma or enhancing mass.

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