Cerebral amyloid angiopathy

Definition

Cerebral amyloid angiopathy (CAA) AKA congophilic angiopathy. Pathologic deposition of beta amyloid protein (appears as birefringent “apple-green” under polarized light when stained with congo red) within the media of small meningeal and cortical vessels (especially those in white matter) without evidence of systemic amyloidosis.

In a subset of chronic traumatic encephalopathy patients this involves the vessel walls giving rise to cerebral amyloid angiopathy.

Epidemiology

Incidence increases with age: CAA is present in ≈ 50% of those over 70 years of age, but most do not hemorrhage. CAA is probably responsible for ≈ 10% of cases of ICH. May be associated with genetic factors (including the apolipoprotein E ε4 allele), and may be more prevalent in patients with Down syndrome. Although they are distinct diseases, there is some overlap between CAA and Alzheimer’s disease; the amyloid in CAA is identical to that found in senile plaques of Alzheimer’s disease. CAA may increase the risk of ICH by potentiating plasminogen (may be of special relevance to patients receiving tissue plasminogen activator (t-PA) to treat MI or stroke).

Etiology

Iatrogenic cerebral amyloid angiopathy

Several pathological studies using autopsied patients with iatrogenic Creutzfeldt-Jakob disease (CJD) showed that cerebral β-amyloidosis in addition to the CJD pathology could be transmitted among humans via medical procedures, such as human growth hormone derived from cadaver injection and cadaveric dura mater graft. In addition, although cerebral amyloid angiopathy (CAA), which is Aβ deposition in the cerebral vessels, related cerebral hemorrhage rarely develops in young people, several patients with CAA-related cerebral hemorrhage under the age of 55 with histories of neurosurgeries with and without dura mater graft in early childhood have been reported. These patients might show that Aβ pathology is often recognized as Aβ-CAA rather than parenchymal Aβ deposition in the transmission of cerebral β-amyloidosis in humans, and Hamaguchi et al. proposed an emerging concept, “acquired CAA”. Considering that there have been several patients with acquired CAA with an incubation period from neurosurgery and the onset of CAA-related cerebral hemorrhage of longer than 40 years, the number of cases is likely to increase in the future, and detailed epidemiological investigation is required. It is necessary to continue to elucidate the pathomechanisms of acquired CAA and urgently establish a method for preventing the transmission

of cerebral β-amyloidosis among individuals [1)].

Clinical

Patients with CAA may present with a TIA-like prodrome.

A subset of CAA patients treatable with immunosuppressants have CAA-related inflammation (CAA-ri) as a result of an autoimmune response to the amyloid protein. These patients present with H/A, subacute cognitive impairment or seizures, with vasogenic edema on imaging. Anti-β-amyloid antibodies appear in the CSF, but currently no clinical test is available. To avoid resorting to brain biopsy, MRI criteria for probable CAA-ri have been developed: uni- or multi-focal asymmetric white matter hypertintensities that extend to subcortical in addition to the typical CAA findings of lobar- ICH, microbleeds, superficial siderosis...(82% sensitive, 97% specific).

Diagnosis

Cerebral amyloid angiopathy diagnosis.

Complications

Cerebral amyloid angiopathy complications.

Case series

Cerebral amyloid angiopathy case series.

Case reports

An autopsy case of repeated recurrent intracerebral hemorrhage (ICH) diagnosed as having cerebral amyloid angiopathy-related inflammation (CAA-ri) in a 65-year-old woman. She had no history of hypertension or other risk factors for stroke. She had a history of lobar hemorrhage in the right parietal lobe 30 months prior. Follow-up magnetic resonance imaging (MRI) performed 29 months after the initial ICH revealed superficial siderosis in the left frontal lobe. She initially presented with severe headaches and dysarthria. An initial computed tomography (CT) revealed a subarachnoid hemorrhage on the left frontal lobe. One hour later, an epileptic seizure occurred, and another CT performed at the time revealed lobar ICH in the frontal lobe. Emergency surgical hematoma evacuation was performed. The cortical artery was removed from the surgical specimen. Hematoxylin and eosin (HE) staining revealed lymphocytic perivascular cuffs, and immunohistochemical staining revealed abundant amyloid-β (Aβ) deposits. The patient was diagnosed as having CAA-ri. On the next day, and 19, 46, 55, 78, 79, and 85 days after admission, ICH recurred. We did not administer immunosuppressive drugs, such as high-dose corticosteroids or cyclophosphamide, because of the patient's condition. Following the last ICH, the patient died on the 90th day after symptom onset. An

autopsy was performed. Histologically, abundant Aβ deposits were observed within the leptomeningeal and cortical arteries. Further dense-cored amyloid plaques were observed in the cortical samples. Our findings that ICH occurred initially three times in the left hemispheres and later five times in the right hemispheres were considered immune-mediated effects on vascular function. Further, superficial hemosiderosis in the left frontal lobe occurred before the first three ICH events, and hyperintensity of the white matter on MRI was identified in the right parietal lobe, a typical finding of CAA-ri. We hypothesize that the inflammatory process in CAA-ri may be related to recurrent ICH [2].

1)
Hamaguchi T, Ono K, Yamada M. Transmission of Cerebral β-Amyloidosis Among Individuals. Neurochem Res. 2022 Mar 11. doi: 10.1007/s11064-022-03566-4. Epub ahead of print. PMID: 35277809.
2)
Maruyama K, Kashiwazaki D, Shiro T, Hori E, Akioka N, Okuno N, Kuroda S. Repeated recurrent intracerebral hemorrhage may be involved in cerebral amyloid angiopathy-related inflammation: An autopsy case. Neuropathology. 2022 Mar 9. doi: 10.1111/neup.12801. Epub ahead of print. PMID: 35261085.