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CEREBRAL AMYLOID ANGIOPATHY: CASE REPORT

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Cerebral amyloid angiopathy (CAA) is a disease of the small cerebral vessels and it mostly affects older people. CAA is characterized by progressive deposition of amyloid-beta in small arteries and arteries of medium caliber, as well as in the capillaries. Sporadic amyloid angiopathy is a cause of recurrent cerebral hemorrhage and cognitive impairment in the elderly. The latest scientific researches and a case report of a patient who suffered from cerebral amyloid angiopathy were used in order to prepare this article. The diagnosis and treatment of CAA are considered.

Keywords: cerebral amyloid angiopathy, spontaneous recurrent cerebral hemorrhages, cognitive impairment.

Introduction. Cerebral amyloid angiopathy (CAA) is characterized by the accumulation of amyloid-beta within cerebral blood vessels and commonly affects the elderly. CAA is associated with the intracerebral hemorrhages (ICH), cognitive disorders (CD) and increases the potential risk of hemorrhage complications for antithrombotic and thrombolytic therapy. CAA combines cerebrovascular and neurodegenerative pathways of brain aging [9]. Pathogenetically, amyloid-beta causes an endothelial dysfunction, disrupts the cerebral blood flow autoregulation and the blood-brain barrier. It leads to the cortical atrophy regardless of the Alzheimer's disease [9].

Autopsy researches show that CAA is associated with aging. There are 21% identified as CAA caused in 61-70 years old group over the 69% in 91 and older group [5]. In Alzheimer's disease brains, CAA is identified in an estimated 85–95% of the cases [11]. It is important to note that only few of them were diagnosed with CAA in life.

The purpose of the research is to explore the significance of CAA as a reason of hemorrhagic stroke and the risk factor of Alzheimer's disease.

Clinical presentation. CAA is characterized by spontaneous lobar ICHs, CD and dementia. It also includes transient focal neurological episodes (TFNEs) caused by subarachnoid hemorrhages (SAHs) [9]. It is also difficult to distinguish a specific CAA's cognitive disorders from Alzheimer's disease because of their comorbidity [7].

The Modified Boston criteria are used in order to incorporate cortical superficial siderosis into the radiological diagnosis of probable CAA (Table 1) [10].

Nowadays, the researchers aimed to explore non-hemorrhagical biomarkers in

order to modernize the Criteria. There are some of them: 1) hyperintensity of the white matter in T2 images with a tendency to rearward or a spotted pattern; 2) diffusion-tensor parameter changes, such as global mean diffusion and DTI-global efficiency; 3) vascular reactivity to functional stimulation; 4) cortical thickness; 5) point hyperintensity on DWI, indicating microinfarction; 6) increased perivascular space in the centrum semiovale; 7) PET data with PiB; 8) a decrease in the level of A β in cerebro-spinal fluid (CSF). Patients with CAA have a reduced concentration of A β 42-, A β 40 proteins and an increased concentration of t-tau protein. Patients with CAA differ from patients with AD with a lower level of A β 40 protein and a higher t-tau / p-tau ratio [8].

A Case Report. Chief Complaint and Past History. 77-year-old man who complained about weakness in the right extremities, periodic headaches, memory impairment and slurred speech. The patient had been suffered from arterial hypertension for a long time, the maximum blood pressure reached 180/100 mm Hg. At the age of 65, he had suffered a hemorrhagic stroke in the left hemisphere with the development of deep right-sided hemiparesis. Conservative treatment was positive as a muscle strength increased in the limbs, but hemiparesis remained. The patient denies having a stroke or transient neurological disorders after the case. At the age of 75, the patient had noticed a gait abnormality and a memory impairment, which slowly progressed. He had been regularly taking amlodipine 5 mg per day and bisoprolol 5 mg per day, atorvastatin 20 mg per day. Previously, he worked as a doctor. He also denied bad habits, head injuries, faintings.

Neurological Examination: cranial nerves – convergence insufficiency,

The Modified Boston criteria (2018)

Definite CAA

- full post-mortem examination reveals lobar, cortical, or cortical/subcortical hemorrhage and pathological evidence of severe cerebral amyloid angiopathy
- no other diagnostic focuses

Probable CAA with supporting pathological evidence

clinical data and pathological tissue (evacuated hematoma or cortical biopsy specimen) demonstrate:

- lobar, cortical, or cortical/subcortical hemorrhage
- mild CAA pathological evidence
- no other diagnostic focuses

Probable CAA

Clinical data and MRI/CT demonstrate:

- multiple hemorrhages restricted to lobar, cortical, or corticosubcortical regions (cerebellar hemorrhages allowed) of varying sizes/ages without another cause, or a single lobar, cortical, or corticosubcortical hemorrhage and focal (three or less sulci) or disseminated (more than three sulci) cortical superficial siderosis without another cause*
- age ≥ 55 y.o.

Possible CAA

Clinical data and MRI/CT demonstrate:

- a single lobar, cortical, or corticosubcortical hemorrhage without another cause*, or a focal or disseminated cortical superficial siderosis without another cause;
- age ≥ 55 y.o.

* – traumatic brain injury, hemorrhagic transformation of ischemic stroke, arteriovenous malformation, tumor, taking warfarin with an international normalized ratio > 3 , vasculitis.

smoothness of the right nasolabial folds. Dysarthria. The right-sided pyramidal tract disorder in the form of hyperreflexion and moderate spasticity. The strength in the limbs is sufficient. The upper Rossolimo's sign on the right is caused. Coordination tests are performed with moderate ataxia. The Romberg test is positive. The patient has a wide-based gait there is no microbasia. Kinetic tremor of the right hand (Fig. 1).

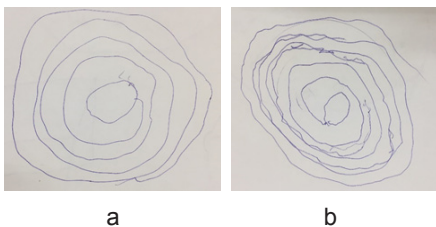


Fig. 1. Archimedes spiral drawing by: a – left hand; b – right hand.

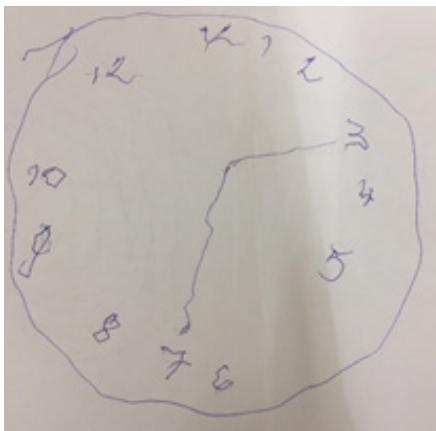


Fig. 2. The "clock drawing" test

The patient was evaluated on a cognitive profile on a 3-CT scale, which includes the "clock drawing" test, assessment of speech activity and visual memory [1]. The "clock drawing" test revealed the incorrect arrangement of numbers on the dial and unequal distance between them (5 points) (Fig. 2).

Assessment of speech activity: phonetic speech (naming "L" words) - 2 words per 1 min, semantic speech (naming "animals") - 3 words per 1 min.

Visual memory: delayed playback - 2 out of 12, true recognition - 7 out of 12, false - no.

The patient had no spatial orientation or time perspective's disorder. A memory impairment is determined as the inability to detail recent events. Memory for remote events is saved. As a result, an amnesic cognitive impairment was revealed.

Diagnostic Assessment. The detailed laboratory investigations revealed a normal

hemogram. Coagulation workup: prothrombin index 103%, international normalized ratio 1.04. Autoimmune workup (antistreptolysin-O, RF, LE cells, C-reactive protein) are negative.

Urine test: normal. Biochemical blood test: dyslipidemia (cholesterol 6.02 mmol / L, triglycerides 0.58 mmol / L, LDL 3.97

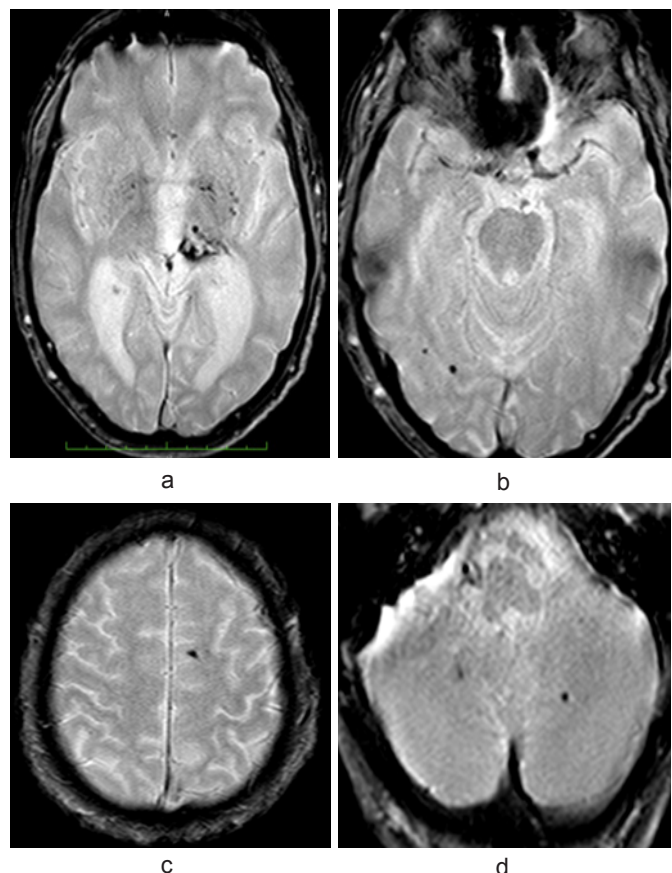


Fig. 3. The foci of cerebral hemorrhages in the SWI mode (description above)

mmol / L, HDL 1.97 mmol / L, atherogenic index 2.06). Other parameters (total and direct bilirubin, hepatic transaminases, creatinine, urea, total protein, albumin, glucose) are normal.

ECG: sinus tachycardia with a heart rate of 110 per min. Violation of intraventricular conduction. Hypertrophy of the left atrium, left ventricle.

Ultrasound of the carotid and vertebral arteries: the initial manifestations of atherosclerosis, stenotic lesions were not detected.

An MRI scan of the brain in the SWI mode reveals a site of cystic-gliosis transformation with deposition of hemosiderin on the periphery in the left thalamus with distribution to putamen and internal capsule on the left (Fig. 3, a). In addition, foci of microhemorrhage in the cerebral hemispheres and in the cerebellum are detected (Fig. 3, b-d).

MRI also determines the atrophy of the hippocampal areas of the temporal lobes, more to the left (Fig. 4, a), mesencephalon atrophy (a 'hummingbird' sign) and moderate atrophy of the cerebellar worm (Fig. 4, b), signs of leukoaraiosis and moderate replacement hydrocephalus due to convexital atrophy of the cerebral hemispheres (Fig. 4, c).

According to the presence of hemorrhagic stroke, the foci of hemorrhages in the cerebral hemispheres and cerebellum, amnesic type of cognitive impairments and atactic syndrome, which are explained by hippocampi and cerebellar atrophy and the absence of other causes for cerebral hemorrhages, it's most likely CAA-induced secondary neurodegeneration, as well as Alzheimer's disease.

Conclusion. According to modern data, CAA is not only a histopathological phenomenon, but also a heterogeneous clinical syndrome. The development of clinical and neuroimaging diagnostic Boston criteria has significantly improved the diagnosis of the disease [3]. Further improvement in the diagnosis of CAA becomes possible in view of the introduction of a new MRI mode - SWI (Susceptibility Weighted - images weighted by magnetic susceptibility). In this mode, microhemorrhages are defined as small foci (from 2–3 to 10 mm) of an MR signal with a "flowering effect" [12].

Patients with signs of the CAA have not only an increased risk of dementia,

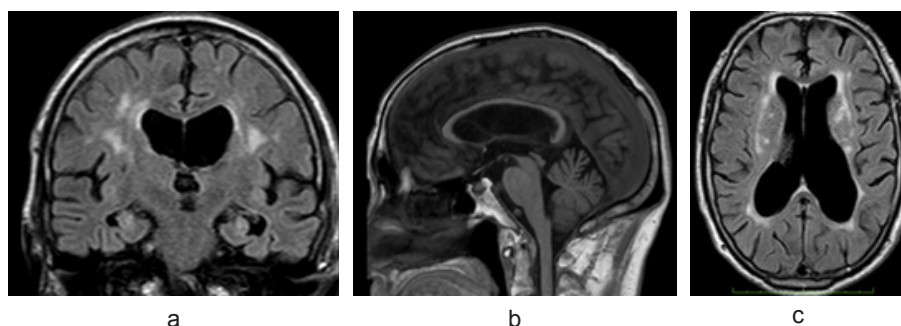


Fig 4. The patient's MRI (description above)

but also a high rate of cognitive decline [7]. Moreover, cognitive impairment in CAA differs from that in AD with relatively preserved episodic memory. Possibly, CAA induced cognitive disorders is due to the combined influence of microinfarctions and disturbance of neuronal connections [9]. In according to the existing pathogenetic classifications, CAA-associated cognitive disorders are more appropriately attributed to vascular ones, although secondary neurodegeneration inevitably joins during the disease [4]. However, amnesic syndrome prevails in the patient's case, which does not allow us to attribute the existing cognitive impairment to the presence of CAA.

Meanwhile, the presence of cognitive disorders of the amnesic type, which is progressive, affects two cognitive spheres (memory, speech) with the absence of dominant behavioral disorders indicate Alzheimer's disease [2].

Further patient's management includes the appointment of anti-dementia medications due to the high risk of cognitive impairment progression and to control the vascular risk factors.

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