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【 CASE REPORT 】

A Unique Case with Oral Dyskinesia, Chorea, Ataxia, and Mild Cognitive Impairment with Caudate Atrophy and Characteristic Brain Calcifications

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Abstract:
The authors report a man who developed oral dyskinesia at 46 years of age, followed by slowly progressive choreic movement and mild cognitive impairment over 20 years. He showed caudate atrophy and four types of intracranial calcification in the hippocampus (dot-like), cerebellar white matter (vague-mass), occipital cortices (laminar), and cerebral white matter (linear). Linear-calcification in the corona radiata seems to be deposition along small veins, which may be related to the white matter changes and to the decreased regional cerebral blood flow in the frontal and parietal lobes. The present case shows a slowly progressive disease with caudate atrophy and characteristic brain calcifications.

Key words: choreic movement, cognitive impairment, intracranial calcification, oral dyskinesia, truncal ataxia

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Introduction

Pathological intracranial calcification is usually associated with infections disease, tumors, metabolic disorder, collagen diseases, and Sturge-Weber syndrome, among other afflictions. Idiopathic basal ganglia calcification (IBGC), also known as Fahr disease, is one such disease with parkinsonism, cognitive decline, ataxia, depression, personal changes, and hallucinations (1) associated with gene mutations, such as SLC20A2, PDGFRB, and PDGFB in familial cases. IBGC shows three patterns of mineral deposition mainly in the basal ganglia: (a) lying along capillaries, (b) diffuse deposition within the media of small and medium-sized arteries and veins, and (c) large spherical or lobulated concretions (2). We herein report a patient with four types of brain calcification outside the basal ganglia who developed slowly progressive oral dyskinesia, choreic movement, ataxia, and mild cognitive impairment.

Case Report

A 46-year-old man began to develop oral dyskinesia. The oral dyskinesia became less severe, but choreic movement gradually became noticeable in his ankles, fingers, and shoulders from 49 years of age. He was diagnosed with ulcerative colitis by colonoscopy at 61 years of age and received medical treatment for 5 years. There were no complications with the ulcerative colitis, including opportunistic infections, and no history of encephalitis, meningitis, epilepsy, or head injury. During these five years, his oral dyskinesia and choreic movements of extremities became evident when he was watching TV, talking, or thinking. When he was 66 years of age, he suffered from acute vertigo and visited a nearby clinic. Although the vertigo disappeared on the following day, brain computed tomography (CT) revealed for the first time multiple calcifications in the brain. He was therefore introduced and admitted to our hospital for further investigation. He had no remarkable family history and had graduated from university and worked until his regular retirement at 64 years of age without affective trouble or sub-

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jective cognitive decline.

His general medical examination findings were largely normal on admission: 167.1 cm tall, weighing 65.0 kg without baldness, body temperature of 36.6℃, blood pressure of 122/77 mmHg, and regular pulse rate of 75/min. His cognitive functional test results were slightly decreased, with an mini-mental state examination (MMSE) score of 27/30, revised Hasegawa's dementia scale (HDS-R) of 23/30, and frontal assessment battery (FAB) of 14/18; reduced scores were particularly noticeable for calculation, digit span, letter fluency, conflict, and inhibitory control. He presented with oral dyskinesia and choreic movement on the distal limbs. His cranial nerves were unremarkably normal. The deep tendon reflexes were normal on both sides, and Babinski's signs were negative. There was no significant objective sensory disturbance. He showed slight truncal ataxia but without evident dysmetria or dyssynergia. Romberg's sign was negative. His muscle tone was normal, but his walking was unsteady due to the slight truncal ataxia and choreic movement on the hands and fingers.

The laboratory data showed a moderate inflammatory profile [erythrocyte sedimentation rate (ESR), 61/102 mm; WBC, 8,100/μL; CRP, 11.2 mg/dL]. The data of hematograms, biochemistry, and urinalysis were normal, including serum Ca, P, Cu, ferritin, and caeruloplasmin findings. Biological tests did not support the presence of active inflammation; anti-Epstein Barr virus, anti-cytomegalovirus, anti-varicella zoster virus, and anti-herpes simplex virus IgM and IgG antibodies. Autoimmune tests (such as anti-nuclear, anti-RNP, anti-SS-A/Ro, anti SS-B/Ro, anti-ds-DNA IgG, anti-cardiolipin antibody, proteinase-anti-neutrophil cytoplasmic antibody (PR3-ANCA), myeloperoxidase (MPO)-ANCA, and IgG4), interleukin-2 receptor (IL-2R), a thyroid and parathyroid hormone test, pyruvic acid, lactic acid, and serologic tests for syphilis and HIV as well as tumor markers (CEA and CA19-9) were also normal. A cerebrospinal fluid study revealed a normal initial pressure, but slight lymphocytosis (6/μL, lymphocyte 100%) and mild elevations in protein (82 mg/dl), pyruvic acid (1.0 mg/dL, normal 0.56± 0.19 mg/dL), and lactic acid (15.9 mg/dL, normal 11.1±2.4 mg/dL). A genetic test for Huntington's disease (HD) was negative. Screening tests for mitochondrial DNA point mutations of peripheral blood cells were all negative (m.1555A> G, m.3271T>C, m.8344A>G, m.8356T>C, m.8363G>A, m.8993T>G/C, m.9176T>C, m.11778G>A, m.13513 G>A, m.3243 A>G).

Brain CT showed four types of calcification: (a) the dot-like type in the bilateral hippocampus, (b) vague mass-like type in the cerebellar white matter, (c) laminar type along the occipital cortex, and (d) linear type in the corona radiata (Fig. 1A-E). The frontal horn width-to-intercaudate distance ratio (FH/CC) was low at 1.7 (normal 2.2-2.6), and intercaudate distance to inner table width ratio (CC/IT) was high at 0.19 (normal 0.09-0.12) (Fig. 1F) (3). Chest and abdominal CT studies were normal, with little calcification in the aortic vessels.

Brain magnetic resonance imaging (MRI) demonstrated mild atrophy in the bilateral frontal and temporal lobes with hyper-intensities in the cerebral white matter on T2- and FLAIR-weighted imaging (WI) without gadolinium enhancement (Fig. 1G and H). T2*-WI showed the above calcification on CT with hypo-intense lesions in the hippocampus, occipital cortex, corona radiata, and centrum seminvale (Fig. 1J-L, arrows) with iso-intense lesions in the cerebellar white matter and hypo-intense lesions in the bilateral basal ganglia (caudate nuclei and putamens) (Fig. 1I). A decreased regional cerebral blood flow (rCBF) was detected in the bilateral frontal and parietal lobes on ^{99m}Tc-ECD-SPECT imaging (Fig. 2A), but the rCBF of the caudate heads was preserved (Fig. 2B). Cerebral MR angiography (MRA, Fig. 2C) and venography (MRV, Fig. 2D and E), ultrasonic echo imaging for the carotid arteries, electroencephalography, DAT Scan, and ^{123}I-MIBG scintigraphy showed normal findings.

Discussion

We herein report a case of sporadic idiopathic brain calcification accompanied by four clinical features of oral dyskinesia, choreic movement, truncal ataxia, and mild cognitive impairment. Cognitive declines were found in the tasks of calculation, digit span, letter fluency, conflict, and inhibitory control. These symptoms progressed very slowly in 20 years, and brain images showed bilateral mild caudate atrophy with brain calcification (dot-like, vague mass, laminar, and linear types) and leukoencephalopathy. The choreic movement was a persistent and prominent clinical abnormality in this patient and may be related to the atrophy of the caudate nuclei. Several differential diagnoses were considered, such as HD, chorea-acanthocytosis, McLeod syndrome, spinocerebellar ataxia type 17, and GM1 gangliosidosis (4). However, none of these candidate diseases fit the present case because of the negative genetic test results for HD, absence of acanthocytes, and no cerebellar or brainstem atrophy.

The striking feature of our patient was the distribution of four types of brain parenchymal calcifications, without other ectopic or significant calcification in the visceral organs and blood vessels. The hypo-intensity T2* signal suggests the accumulation of metal elements of mainly calcium but also iron, phosphorus, and copper. However, the serum levels of Ca, P, Cu, ferritin, and ceruloplasmin were normal, and the thyroid and parathyroid hormone test results were also normal. Other data also did not support idiopathic hypoparathyroidism, hyperparathyroidism, collagen disease, angiitis, infection, or mitochondrial encephalomyopathy. However, we cannot deny the possibility that these calcifications occurred as sequelae after inflammation (5), and genetic abnormalities, including mitochondrial mutations, may also be involved, as the cerebrospinal fluid cell number was slightly high, as were the protein, pyruvate, and lactate levels. IBGC and diffuse neurofibrillary tangle with calcification (DNTC) are known as intracranial calcification diseases. These dis-

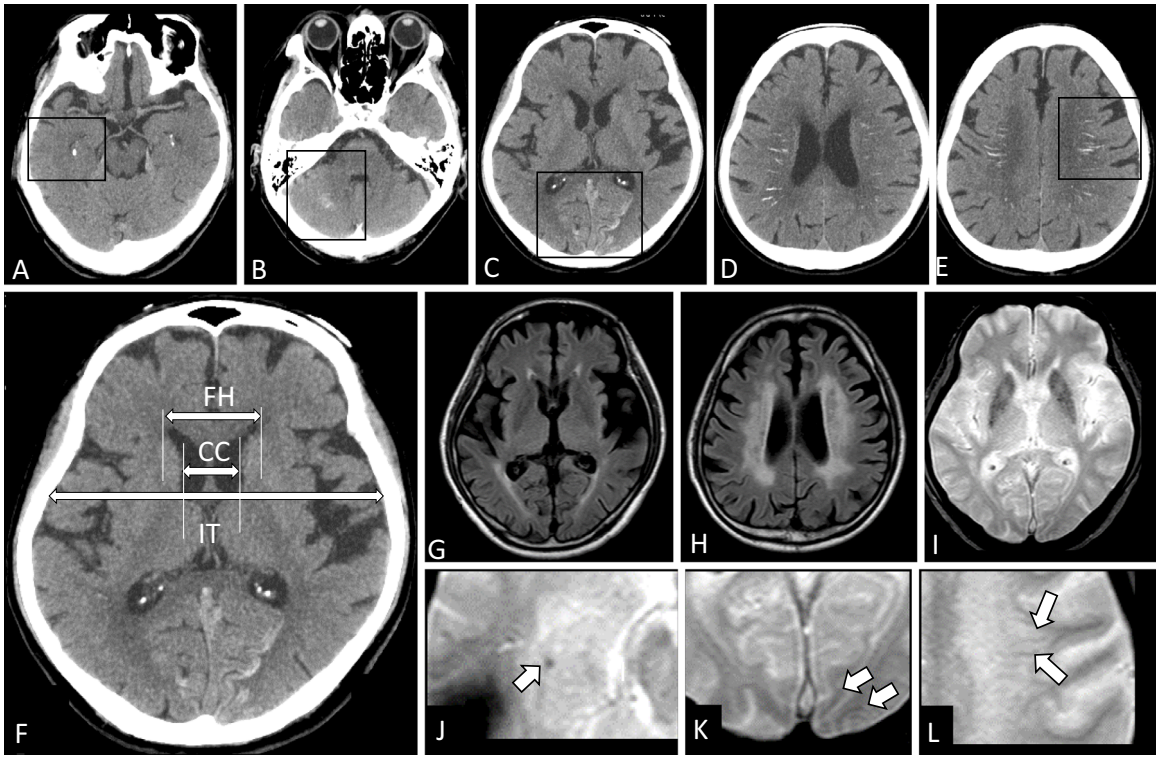

Figure 1. **(A-E) Brain CT on admission, showing four types of calcification: dot-like (bilateral hippocampus), vague mass (right cerebellar white matter), laminar (occipital lobe), and linear types (corona radiata) from right to left (squares). (F) The frontal horn width-to-intercaudate distance ratio (FH/CC) was low at 1.7, and intercaudate distance to inner table width ratio (CC/IT) was high at 0.19. (G, H) FLAIR-WI on brain MRI showing mild brain atrophy in the bilateral frontal and temporal lobes with diffuse pathological signal hyperintensities in the corona radiata and centrum semivale. Horizontal sections of T2*-WI of brain MRI (I-L) corresponding to the CT sections (C, and squares of A, C, and E). Note the high CT signals (J-L, arrows) corresponding to MRI low T2*-WI with magnification.**

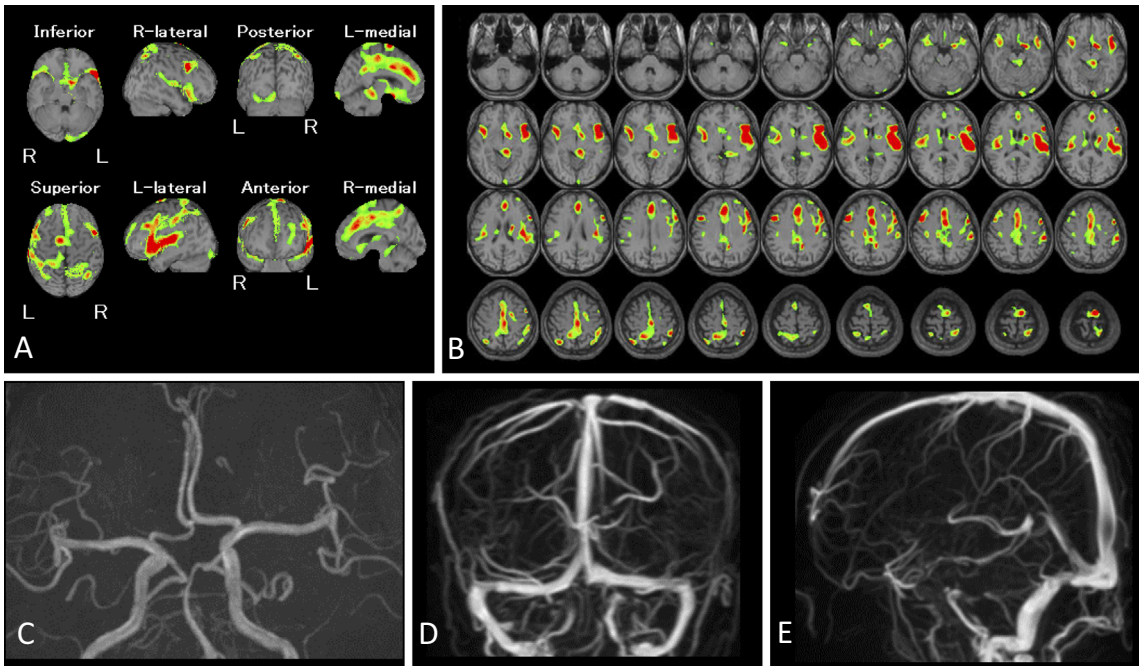

Figure 2. **^{99m}Tc-ethylcysteinate dimer (ECD)-SPECT imaging showing a decreased regional cerebral blood flow in the bilateral frontal and parietal lobes (A, B). Cerebral MR angiography (C: frontal view,) and venography (D: frontal view, E: lateral view).**

eases are characterized by the bilateral symmetrical calcification of the basal ganglia and dentate nucleus of the cerebellum, but not linear type in the centrum seminvale. Although parkinsonism and psychotic symptoms were not noted in this case, IBGC and DNTC could not be excluded, given that T2*-weighted images showed hypointense spots in the bilateral basal ganglia, suggesting mineral deposition in the basal ganglia (6).

In the present case, linear projection in the corona radiate was strongly related to the white matter high intensities along the deep white matter veins, although the patient's MRA and MRV studies were normal. In general, the major risk factor of leukoencephalopathy is arterial small vessel disease due to hypertension and metabolic syndrome, but this patient did not have any such vascular risk factors (VRFs). Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and cerebral autosomal recessive arteriopathy with subcortical infarctions and leukoencephalopathy (CARASIL) also show diffuse leukoencephalopathy without VRFs, but these two diseases do not accompany vascular calcification in their white matter lesions, and the present case did not show any evident family history or typical clinical symptoms of these two diseases (7).

Conclusion

This is the first case report of four unique intracranial types of calcification, clinically characterized by oral dyskinesia, choreic movement, truncal ataxia, and mild cognitive impairment.

The authors state that they have no Conflict of Interest (COI).

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