Bilateral Striatopallidodentate Calcinosis and Severe White Matter Lesions in Hypoparathyroidism

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INTRODUCTION

Hypoparathyroidism is an endocrine gland disorder characterized by hypocalcemia, hyperphosphatemia, and parathyroid hormone deficiency1). The most common cause for hypoparathyroidism is surgery, and this condition mostly appears temporarily or permanently after thyroidectomy and neck dissection surgery2). A recent study reported that 73.8% of patients with hypoparathyroidism had basal ganglia calcification, and calcification was also found in other areas including grey matter, cerebellum, thalamus, and dentate nucleus3). Although white matter lesions (WML) has not been reported in patients with hypoparathyroidism, a pathological examination in patients with bilateral striato-pallido-dentate calcinosis (BSPDC) found extensive mineral deposition and vascular stenosis in cerebral small vessels. Calcification in coronary arteries, aorta and carotid arteries has been reported to be indirectly related to cerebrovascular diseases such as stroke and WML4,5). Here, we report a case of hypoparathyroidism with extensive WML along with BSPDC.

CASE REPORT

An 80-year-old female patient visited the Emergency Department for generalized weakness. The patient found it difficult to walk and relied on a walker for the last 5 years. Cognitive impairment also developed around that time. In the last 6 months, walking and cognitive impairment worsened. The patient had a partial thyroidectomy 30 years ago, and used methimazole for hyperthyroidism for the last few years. She showed severe cognitive impairment, evaluated by the Korean Mini-Mental State Examination, scoring 2 points. Muscle strength of lower and upper extremities was extremely weak and measured at grade 4. Bradykinesia and postural and intentional tremors of 6-8 Hz were observed in both hands. The cerebellar function test revealed a lack of coordination.

Calcification was observed in bilateral basal ganglia, cerebellum, thalamus, and utricle in the patient’s brain computed tomography (CT), and a small amount of acute subdural hematoma was found in the right side of the parietal lobe (Fig. 1). On brain magnetic resonance imaging (MRI), calcification was observed with low signal intensity in T2 and fluid-attenuated inversion-recovery (FLAIR) images, and with high signal intensity in T1 images, in the same area where the CT showed severe WML around the cerebral ventricles (Fig. 2). In addition, high density calcified lesions that looked like radial threads were found in the white matter around the cerebral ventricles in the aforementioned CT. These lesions were also observed with low signal intensity on susceptibility weighted image (SWI) of MRI (Fig. 2). The blood test results showed that parathyroid hormone level was 5.91 pg/mL (15-65 reference level), ionized calcium level was 0.65 mmol/L (0.92-1.25 reference level), calcium level was 4.6 mg/dL (8.5-10.5 reference level), and phosphorus level was 5.0 mg/dL (2.5-4.5 reference level).
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Fig. 2. Severe white matter lesions are seen as high signal intensity lesions on fluid-attenuated inversion-recovery (FLAIR) (A) and T2 magnetic resonance imaging (MRI) (B), which are shown as low signal intensity lesions on T1 MRI (C). (D) Susceptibility weighted image (SWI) shows spreading vessels with low signal intensity in periventricular white matter. Calcified lesions in bilateral basal ganglia and thalamus are seen as low signal intensity lesions on axial FLAIR (E) and T2 (F), and high signal intensity lesions on axial T1 MRI (G). (H) SWI image shows low signal intensity lesions on bilateral basal ganglia.

Fig. 1. Noncontrast axial computed tomography shows calcification in bilateral corona radiate, basal ganglia, thalamus, and cerebellum. In periventricular white matter, numerous spreading high-attenuation lesions are seen.

Along with symptomatic treatment for subdural hematoma, the patient was administered 3-g calcium per day and 0.5-µg calcitriol per day, after we diagnosed that severe WML and BSPDC occurred due to hypoparathyroidism. A month later, the patient’s calcium level rose up to 8.4 mg/dL. She showed improvement in generalized weakness, and could answer questions and show more movement during her daily activities. However, there was no clear improvement in cognitive function or motor function, so she was placed under observation in the outpatient ward.

DISCUSSION

BSPDC that shows calcium deposition in the brain has been reported to show spasm, ataxia, bradykinesia, affective disorder, neurological symptoms, and cognitive impairment. Calcium, iron, zinc, manganese, aluminum, and magnesium deposits are seen in capillaries, arterioles, veins, and small
blood vessels and neuronal degeneration and gliosis have been reported to occur around these deposit areas\(^9\). It is believed that these pathological changes lead to damage to the corticospinal tract, and cause motor and cognitive symptoms.

A previous study on a group of 97 patients with hypoparathyroidism reported that 59% of the patients showed intracranial calcification on brain imaging tests while 70% showed carpopedal spasm, 54% seizures, 11% gait instability, and 11% memory loss\(^8\). In the case of this current patient, hypoparathyroidism might have caused BSPDC observed on the brain MRI.

Furthermore, severe WML that accompanied BSPDC might have contributed to the patient’s symptoms. In this case, WML could have been age-associated since the patient was 80 years old. However, there was no diagnosis about severe stenosis in large cerebral arteries, observed in the brain MRI. Therefore, the patient’s WML might have been caused by small vessel disease. Since she had no risk factors such as hypertension, diabetes, hyperlipidemia, and a history of smoking, the calcium deposition in cerebral small vessels and subsequent vascular stenosis might be one of the major contributing factors\(^9\). The patient’s calcification in cerebral small vessels arising from calcium deposition were identified as thin radial threads in white matter on the brain CT scan and corresponding SWI at low signal intensity (Figs. 1, 2).

Pathological studies in BSPDC patients reported the presence of extensive mineral deposition in the parenchyma of the brain and small vessel walls, and the diagnosis that the lumen of the affected blood vessels was clogged or narrowed\(^4\). A study that conducted MRI on 312 subjects for a medical check-up reported a significant correlation between the level of calcification in coronary arteries and WML in the brain, while a retrospective cross-sectional study on 198 subjects found a significant correlation between calcification of vertebrobasilar arteries and the occurrence of stroke in areas supplied by these arteries\(^10,11\). Taken together, these studies indicate that calcification might be closely related to ischemic changes in the brain.

Although the patient had surgery to remove thyroid tumor 30 years ago, she had not actively been on treatment since then. Recombinant human parathyroid hormone was recently developed and approved by the Food and Drug Administration. Hence, more fundamental treatment could be provided to patients with hypoparathyroidism\(^12\). Multiple factors must be taken into consideration when treating patients with noticeable calcification in the brain. These factors include the symptoms arising from calcification as well as those arising from parathyroid disorders, which could be a underlying disease, or small vessel disease and WML, which are secondary diseases caused by calcification.

**Conflict of Interest Disclosures:** The researchers claim no conflicts of interest.

**REFERENCES**