CASE REPORT: EXTENSIVE BRAIN CALCIFICATION IN POSTSURGICAL HYPOPARATHYROIDISM

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ABSTRACT

Basal ganglia calcification is common in hypoparathyroid states. However, extensive brain calcifications from vascular and perivascular deposits in postsurgical hypoparathyroidism are rarely described radiologically. A case of 54-year-old woman with secondary hypoparathyroidism after long standing subtotal thyroidectomy is presented. CT-scan showed extensive bilateral symmetrical calcifications in the region of the basal ganglia, cerebellum, thalamus,cerebral white matter and cortex. The mechanism of metabolic disturbance leading to vascular deposits are reviewed.

INTRODUCTION

Calcification of the basal ganglia has been visualized by skull radiography for more than 40 years.In two-thirds of cases it has been associated with metabolic abnormalities. Twenty percent of the cases had been an incidental findings. Computed tomography (CT) is 5 to 15 times as sensitive as plain skull radiography in detecting intracerebral calcification. Calcification confined to the globus pallidus,of basal ganglia, of a patient older than 40 should be considered physiological and does not warrant further investigation.

Extensive bilateral intracerebral symmetrical calcification is known to occur in idiopathic hypoparathyroidism (IHP), in pseudohypoparathyroidism (PHP), in postoperative hypoparathyroidism and without any detectable cause (Fahr's syndrome). However, the condition is believed to be relatively rare in postsurgical hypoparathyroidism, presumably because patient with this order are treated more expeditiously than patients with other form of hypoparathyroidism.

This is a case with a far more extensive brain calcification in a patient of postsurgical hypoparathyroidism after subtotal thyroidectomy for 24 years.

CASE REPORT

A 54-year-old woman was admitted after recent episode of syncope without any aura. She had previously 5-times attacks of syncope during the past one year. The duration of each syncope is about an hour. She had previously subtotal thyroidectomy for treatment of toxic goiter twenty-four years ago. She developed tetany in the immediate postoperative period and spontaneous recovered. She was treated with antithyroid drug for one year. No further bouts of tetany occurred and no medication was given for 23 years.

Physical examination showed a thyroidectomy scar. The patient had hoarseness, but no neurological deficit, dementia or symptom of basal ganglia dysfunction. Serum calcium level was 8.0 mg/dL (norm: 8-11 mg/dL) and serum inorganic phosphate was 6.4 mg/dL (norm: 2.5-5.0 mg/dL). Other biochemical tests were normal, including

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thyroid function test. The electrocardiography showed sinus tachycardia. The electroencephalography revealed no epileptic discharge or abnormal slow activity.

Computerized tomography of the brain without contrast medium demonstrated a symmetrical pattern of intracerebral calcifications without mass effect. There were widespread calcifications involving both caudate nuclei, globus pallidus, putamen, thalami, dentate nuclei and cerebellar hemispheres. Calcifications of subcortical white matter were presented at frontal lobe, and cortical calcification of occipital lobe was revealed. The caudate body calcification extended laterally into the corona radiata (white matter radiation). The wispy configuration of this lateral extension indicated the vascular nature of calcification.

She was treated with short course of oral calcium and had complete recovery.

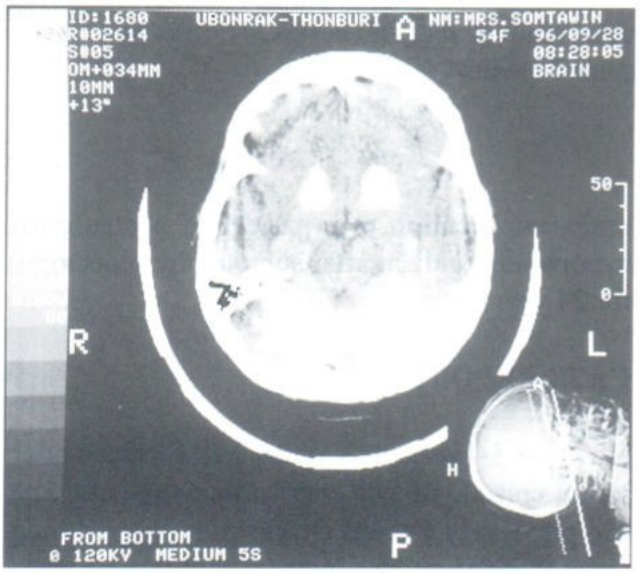

Fig. 1 Noncontrast computed tomography of brain. A slice through the posterior fossa demonstrates calcifications of dentate nuclei and cerebellar white matter.

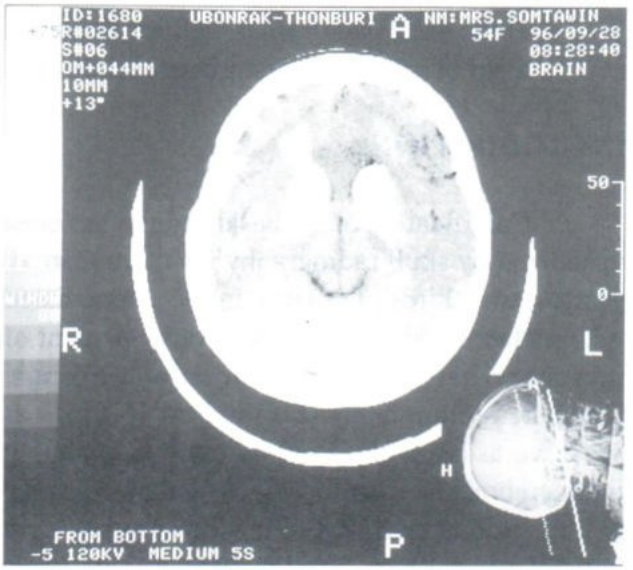

Fig. 2 A central slice through the frontal horns and third ventricle reveals thick calcifications of the basal ganglia (caudate and lenticular nucleus). Subcortical white matter calcifications are present in the frontal lobe.

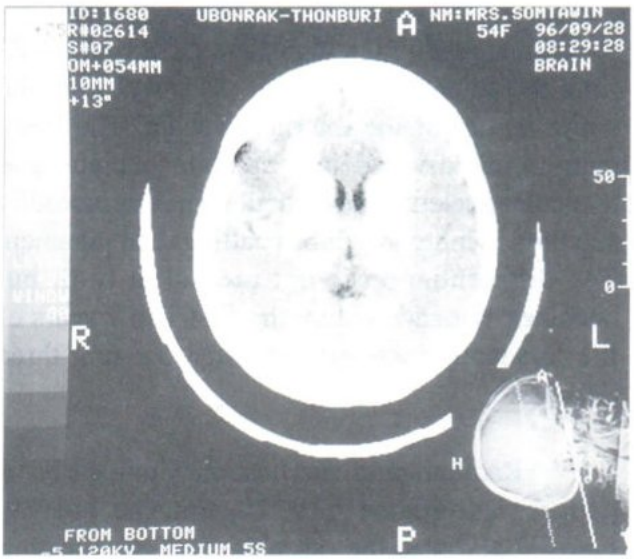

Fig. 3 A slice at higher level shows bilateral, symmetrical basal ganglia and thalamic calcifications.

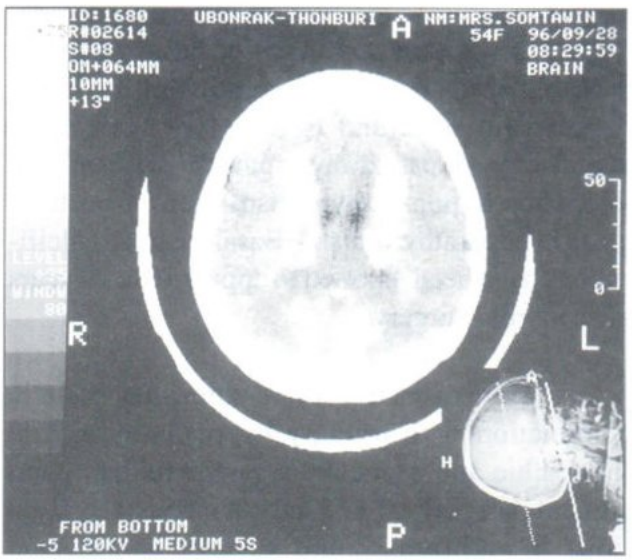

Fig. 4 A slice through the top of lateral ventricles demonstrates caudate body calcifications extending laterally into the corona radiata. Cortical calcifications of occipital lobe are present.

DISCUSSION

Hypoparathyroidism is a clinical disorder characterized by hypocalcemia and hyperphosphatemia in the absence of renal failure and hypomagnesemia. The causes of hypoparathyroidism can be classified as two groups : (1) insufficient parathyroid hormone secretion (hypoparathyroidism) :and (2) impaired parathyroid hormone action (pseudohypoparathyroidism). The hypopara -thyroidism may be idiopathic, but is more often a complication of thyroid surgery. Postsurgical hypoparathyroidism was first described in 1879. The incidence of temporary hypoparathyroidism (lasting six months or longer) following thyroidectomy varies widely in surgical series (a range of 0.2-33% has been reported). As far as thyroid disorders that require bilateral thyroidectomy, a tendency to have persistent hypoparathyroidism is more frequent in patients operated on for Graves' disease and thyroid cancer than in other thyroid disorders. Hypoparathyroidism in patients after radioactive iodine therapy of Graves' disease is extremely uncommon.

Diminution of parathyroid hormone action on kidney and bone leads to hypocalcemia and hyperphosphatemia. Decreased serum ionized calcium concentration increased neuromuscular excitability and the symptom may range in severity from mild paresthesia to severe tetany with muscle cramps, carpopedal spasms, laryngeal stridor and convulsions. Sometimes choreoathetosis is also induced and the symptom is presumably due to calcification of the basal ganglia. Also in some instance there are signs of a cerebellar lesion. Occasionally there may be a long latent period before symptoms will develop and before hypocalcemia is diagnosed. The occurrence of intracerebral calcification in patients with hypoparathyroidism is well known. This calcification occurs not only in the basal ganglia, but also in the dentate nuclei of the cerebellum and/or other areas of the brain, particulary the frontal lobes.

Development of calcified basal ganglia is probably a function of the duration of the hypoparathyroid state and is therefore seen more commonly in pseudohypoparathyroidism and idiopathic hypoparathyroidism than in postsurgical hypoparathyroidism. Basal ganglia calcifications have been reported to appear 10 to 20 years after thyroid surgery.

More extensive calcification may occur in conjunction with primary hypoparathyroidism (idiopathic and pseudohypoparathyroidism) and cortical, subcortical and subcutaneous calcifications in addition should suggest parathyroid diseases. In one serie, 93% of the cases of primary hypoparathyroidism had basal ganglia calcifications. Of the cases with calcifications, 47% had calcification in the cerebral cortex and 21% had calcification in the cerebellum.

The basal ganglia are cental gray matter structures, readily distinguished on CT and MRI from the adjacent lateral ventricles and from the white matter of the internal capsule. The basal ganglia are divided into caudate nucleus and lenticular nucleus. The lenticular nucleus is readily subdivided innto the globus pallidus and putamen. The differentiation is not present at birth but becomes evidence within the first 1 to 2 years of life, gradually increasing through the first three decades.

Radiographic calcification within the basal ganglia was reported in 1935 by Fritzche. In 1939, Eaton et al. noted the association of calcification of the basal ganglia with hypoparathyroidism, and in 1945, Sprague et al. reported its occurrence with pseudohypoparathyroidism. It has since been described in association with many pathological conditions, the most common of which are listed in TABLE 1. [1]

TABLE 1: Conditions Associated with calcification of the basal ganglia

Endocrine	Congenital/ Developmental	Inflammatory	Toxic/Anoxic
Hypoparathyroidism	Familial cerebral vascular	Cytomegalic inclusion disease	Carbon monoxide
Pseudohypoparathyroidism	ferrocalcinosis(Fahr's disease)	Encephalitis(measles,	intoxication
Pseudo-pseudohypoparathyroidism	Cockayne syndrome	chicken pox)	Lead intoxication
	Tuberous sclerosis	Toxoplasmosis	Birth anoxia
	Oculocraniosomatic disease	Cysticercosis	Therapeutic radiation
			Methotrexate therapy

Basal ganglia calcifications are usually small in extent and bilateral, symmetrically confined to the globus pallidus, and are rarely associated with calcification of the other areas of brain. Symmetrical calcifications of the basal ganglia occur in upto 1.5 % of individuals examined by CT-scan. It is most commonly found in patients older than 40 years, who only rarely have symptoms associated with it. The manifestation may be dismissed as an aging phenomenon of no clinical significance and perhaps classified as "physiologic calcification". When calcification occurs early in life (under the age of 40) and is of such degree as to be visible in plain film of the skull, it must always be regarded as abnormal. Patients of any age with calcification in the lenticular nucleus and elsewhere in the basal ganglia, dentate nucleus, or multiple areas of the cerebral cortex should be evaluated for pathological disorders. Thus, the "physiologic calcification" differs from pathological calcification in their density, volume and distribution.

The exact etiologic factor(s) responsible for calcification deposits in the basal ganglia, dentate nuclei and other areas of the cerebral and cerebellar hemispheres are still obscure. Because of generally accepted that 70-80% of cases of basal ganglia calcifications are associate with hypoparathyroidism, a generalized disturbance of calcium metabolism has been suggested. Cerebral anoxia has also been considered solely because the basal ganglia, particulary the globus pallidus, are known to be susceptible to various anoxic and metabolic injuries. It has been postulated that this sensitivity may be a result of the high metabolic activity of the central nuclei, their vascular anatomy, and their autoregulatory physiology. One suggestion has been that basal ganglia calcification may be secondary to an elevated" calcium-phosphorus product" (Ca. x P. value). But, Illum and Dupont found no significant difference in serum Ca. x P. among their 10 idiopathic hypoparathyroidism patients with brain calcinosis compared to their 5 patients without calcinosis. Therefore, the factors governing calcification remain to be elucidated.

The sequence of events in this calcification process apparently begins with the deposition of a colloid protein material in and about the walls of the small cerebral vessels. The substrate is subsequently impregnated first with iron and later with calcium that can coalesce into large masses which obliterate completely the usual microscopic structures and become visible a large calcareous mass. Twenty percent of patients with calcification showed extrapyramidal syndrome, possibly due to calcium salt deposits in the metasynaptic dopamine receptors. Parkinsonism associated with basal ganglia calcification differs from idiopathic parkinsonism in being resistant to levodopa therapy.

CONCLUSION

Basal ganglia calcification which confined to the globus pallidus of patient older than 40 should be considered physiologic, with a prevalence of 0.6-1.5% of the CT-studies. Calcification elsewhere in the basal ganglia, dentate nucleus or multiple areas of the cortex in a patient of any age should also be considered pathological. The extensive calcification of brain have been found in patient with hypoparathyroidism and Fahr's d isease. The mechanism of cerebral calcification remain unknown. There are two main possible factors which alone or in combination may cause cerebral calcification, first : perivascular deposits of an albuminoid matrix attracting calcium ions, second : an imbalance of electrolyte yielding low calcium and high phosphorus levels.

This report describe a case of extensive cerebral calcifications in postsurgical hypoparathyroidism, in which the calcifications not only located in basal ganglia but also in dentate nuclei, central cerebellar white matter zones, corona radiata, thalamus, cortical layer of occipital lobe and subcortical white matter of frontal lobe. The finding is not yet frequently found and has some differences from the previous reports.

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