Bilateral basal ganglia calcifications visualised on CT scan

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SUMMARY Thirty-eight cases of basal ganglia calcification imaged on computed axial tomography were reviewed. Most cases were felt to represent senescent calcification. The possibility of a vascular aetiology in this group is discussed. A less common group of patients was identified with calcification secondary to abnormalities in calcium metabolism or radiation therapy. Three cases of basal ganglia calcifications were detected in juvenile epileptic patients receiving chronic anticonvulsants. These cases may be related to abnormalities in calcium metabolism and alkaline phosphatase activity. Clinical evidence of basal ganglia abnormality was generally absent demonstrating the preservation of neuronal pathways in most cases.

Bilateral basal ganglia calcification is not an unusual finding both on plain skull x-rays (SXR), and in necropsy specimens.^{1–3} It has been said that when visible on SXR, basal ganglia calcification is associated with hypoparathyroidism in 70–80% of cases.¹ A sporadic idiopathic form and a familial form can occur. Familial disease has been associated with progressive mental deterioration and growth retardation;⁴ chorea, dementia, and palilalia,⁵ or dystonia.⁶ A levodopa-resistant Parkinsonian syndrome also has been described.⁷

With the advent of computerised tomography (CT) it has become possible to detect calcifications which are not visible on SXR. Fourteen cases of basal ganglia calcification recently shown by CT had normal SXR.⁸ None showed evidence of calcium abnormality, or evidence of neurological disease referable to the calcification.

In an effort to define further the CAT appearance and clinical features of basal ganglia calcification we reviewed the reports of all cranial CAT scans performed at Mount Sinai Hospital since the inception of the scanning unit in 1975.

Methods

Included in the initial study were all cases showing bilateral calcific densities in the basal ganglia or

cerebellum. In no case did the presence of oedema, compression, cavitation, or lucency arouse the suspicion of tumour, old calcified haemorrhage, or other pathological conditions known to produce calcification. Cases demonstrating unilateral basal ganglia calcification were included when other processes could be excluded. In fact, we found bilateral basal ganglia calcification invariably to be symmetrical.

After the cases were identified, their clinical records were examined, but no necropsy studies were available.

Results

Forty-two cases of basal ganglia calcification (24 females and 18 males) were identified. As 12 000 patients were scanned, this gives an incidence of 3.6 per 1000. Four cases were deleted due to absence of sufficient clinical information. The ages ranged from 10 to 86 years. Two-thirds of the cases occurred after age 60 years.

The globus pallidus was affected solely and bilaterally in 23 of the 38 cases (61%). In four cases (11%) there was unilateral globus pallidus calcification. One case had selective involvement of the caudate nucleus. The remaining cases showed bilateral involvement of the globus pallidus and caudate nucleus which at times included the vermis or dentate nucleus of the cerebellum.

All available laboratory data were reviewed. Detailed laboratory testing was available in 26

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Accepted 10 February 1980

patients. Calcium and phosphorous measurements were normal in 23 of these 26 cases. Two of these patients had known idiopathic hypoparathyroidism and one surgical patient had prolonged sepsis with multiple metabolic abnormalities including hypocalcaemia. Alkaline phosphatase measurements were elevated in seven patients. Four of these elevations were explained by bone fractures, sepsis, or youth. There were no distinguishing abnormalities in blood count, multichannel lab screen, or urinalysis in the 26 patients. Four patients in the study were receiving anticonvulsants for a chronic seizure disorder.

The table summarises the clinical findings. The cases generally fitted into either a senescent group, or into a secondarily acquired group. The senescent (or "physiological") group was characterised by the absence of basal ganglia dysfunction, absence of metabolic abnormalities predisposing to calcification, and an age over 60 years. This included all cases in the cerebrovascular disease and dementia groups. The 81-year-old lady with Parkinson's disease had a normal response to levodopa and probably fits into this senescent group as do most of the miscellaneous cases.

The secondary group includes those cases which acquired basal ganglia calcification either secondary to, or enhanced by, a primary disease process. In this group are two following irradiation for tumours, two with hypoparathyroidism, and three with seizure disorders receiving anticonvulsants. Clinical signs of basal ganglia dysfunction were also absent in this group. The post-irradiation cases include a 59-year-old man who received directed radiation for a parasellar tumor ten years prior to

this scan and a 10 year old boy who received 4500 rads directed radiation for an optic glioma three years prior to his first scan. This second patient had two scans over a three year period showing marked progression of basal ganglia calcification. One of the patients with hypoparathyroidism had the unusual simultaneous occurrence of myasthenia gravis associated with antiacetylcholine receptor and antithyroid antibodies, suggesting an auto-immunity directed against several systems.

The remaining three patients in the symptomatic group are notable for their youth (ages 13, 13, and 24 yr), and the fact that all were receiving anticonvulsant medication for epilepsy. They include a 13-year-old girl with major motor convulsions since age six years receiving phenytoin, a 24-year-old male with psychomotor and major motor convulsions since age five years receiving multiple medications including phenytoin, phenobarbital, primidone, and carbamazepam; and a 13-year-old boy who had received phenobarbital for six months for recently acquired generalised convulsions.

Discussion

Some degree of calcification can be detected in the globus pallidus and dentate nucleus of the cerebellum in 40–72% of routine autopsy specimens.² The calcification consists of hydroxyapatite of a nature similar to that found in bones, teeth and renal calculi enmeshed in a protein rich stroma.^{9 10} Other elements including zinc, iron and magnesium are present in concentrations paralleling those found in hydroxyapatite, but manganese is elevated.¹⁰ Neuronal cell loss and gliosis are usually absent at the site of basal ganglia calcification, but when present may accompany symptomatic basal ganglia dysfunction.¹¹ In this series of patients the absence of clinical symptoms of basal ganglia disease suggests that no significant destruction of neuronal pathways need occur as a result of the deposition of a calcified matrix.

The specific pathophysiology leading to the development of basal ganglia calcification is unknown. Three interrelated factors are suggested (1) a vascular component (2) a disturbance in calcium metabolism and (3) a disturbance in alkaline phosphatase activity. Theoretically a vascular component is suggested by the early proximity of calcification to arteriolar and capillary walls.^{1 12} In this series atherosclerosis and hyaline necrosis is postulated as playing a role in the development of senescent basal ganglia calcification. Thirty-four per cent of our patients had clearly defined cere-

Table Clinical diagnosis in cases of BBGC

	No of cases	Percent of total	Age (yr)
Cerebrovascular disease (stroke or transient ischaemic attack)	13	(34%)	59–86
Senile and presenile dementia	10	(26%)	60–78
Idiopathic epilepsy	3	(8%)	13, 13, 24
Hypoparathyroidism	2	(5%)	68, 75
Post-irradiation	2	(5%)	10, 59
Parkinson's disease*	1	(3%)	81
Miscellaneous†	7	(18%)	31, 47, 71, 71, 72, 72, 73

*Not included is one case S after P bilateral thalamotomy as this may represent traumatic calcification.

†Includes: 2 cases of systemic neoplasia with encephalopathy.

1 case of multiple cranial nerve palsies of unknown aetiology.

1 case head trauma and alcoholism (aged 31 yr).

1 case of acute ataxia of unknown aetiology (a 47 year old male with possible vertebrobasilar insufficiency).

2 cases of metabolic encephalopathy.

bral vascular disease and a vascular component may have been involved in many of the patients in the senile dementia group. In addition to these patients the two cases of post irradiation basal ganglia calcification are also felt to be related in part to vascular changes. The predilection of the basal ganglia for calcification may be dependent on the preferential perfusion of grey matter and the high rate of blood flow to the basal ganglia.¹³

The well-known occurrence of basal ganglia calcification with hypoparathyroidism identifies a disturbance in calcium metabolism as another important factor. The deposition of calcium may be related in part to a change in vascular permeability related to local calcium concentrations. Experimentally thyroparathyroidectomised rats have significantly increased brain tissue calcium concentrations.¹ Recent studies have shown a mild but detectable decrease in serum ionised calcium levels in the elderly.¹⁴ Alkaline phosphatase activity has been previously reported to be regionally elevated in one case of basal ganglia calcification.⁹ This enzyme is located in endothelia and is active in the capillary system of grey matter structures.^{15 16} It is involved in membrane transport systems and is important in calcification.¹⁷ Its activity *in vitro* is manganese-dependent.¹ Local concentrations of these elements would then be expected to influence regional activity, even in the absence of measurable changes in serum enzyme activity.

In contrast to previous estimates of a 70–80% concurrence of hypoparathyroidism and in patients with basal ganglia calcification, this was evident in only 5% of our series. This may represent the increased sensitivity of computed axial tomography. Routine SXR would not detect most of the cases of “senescent” basal ganglia calcification.

Three juvenile patients receiving chronic anticonvulsant therapy for a seizure disorder had calcification of the basal ganglia. The history and physical examination as well as the symmetrical nature of the calcifications excluded other known causes of calcification such as tuberous sclerosis and perinatal infection. The presence of calcification in these patients might have been related to the disturbance of calcium metabolism and alkaline phosphatase activity known to be induced by anticonvulsant medication. Anticonvulsants including phenytoin and phenobarbital are known to influence calcium metabolism and can induce osteomalacia in the young.^{18 19} Abnormalities in calcium, alkaline phosphatase, and bone mineral content occur early, and are present within three months of therapy.²⁰ Parathyroid hormone levels are normal, but vitamin D metabolism is altered,

possibly by induction of hepatic microsomal enzyme activity.²¹ These abnormalities in calcium and alkaline phosphatase activity form a theoretical basis linking anticonvulsants to basal ganglia calcification.

Although the aetiology of calcification of the basal ganglia is rarely defined, abnormalities in vascular supply, calcium metabolism, and alkaline phosphatase activity appear to be associated. It is suggested that chronic anticonvulsant use be considered, along with hypoparathyroidism and post-irradiation changes, as possible causes for basal ganglia calcification. Senescent basal ganglia calcification may be secondary to abnormalities in vascular supply and changes in calcium metabolism.

This study was partially funded by a research grant from the Peggy Engl Trust of the Parkinson's Disease Foundation (TSB). Special thanks are given to Dr Melvin Yahr for his review and comments.

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