A CASE OF CALCIFICATION OF THE BASAL GANGLIA WITH OSTEOPOROSIS AND OTHER ABNORMALITIES

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Introduction

Calcification of the basal ganglia is often found microscopically in normal adult brains. It is no longer believed to represent the end result of inflammation or other disease process (Foley, 1951). Cases where this calcification is gross enough to be visualized radiologically are much more rare. In most instances these have been associated with hypoparathyroidism, either idiopathic or post-operative. It is also found in pseudo-hypoparathyroidism where the target organs are believed to be refractory to parathyroid hormone which is normally produced (Albright, Burnett, Smith and Parson, 1942; MacGregor and Whitehead, 1954). Toxoplasmosis is another cause (Sutton, 1951). The intracranial calcification of the Sturge-Weber syndrome may also involve the basal ganglia.

There remains a group of adult cases with calcification of the basal ganglia visible radiologically, which is often familial and is frequently associated with a progressive neurological disorder. The only child in the literature with this abnormality is one of two brothers described by Neill and Dingwall (1950). In the case to be described, calcification of basal ganglia was associated with other bizarre findings to make a symptom complex not previously reported.

Case Report

J.C., aged 12 years (Figs. 1 and 2) was admitted to University College Hospital on June 17, 1957, for investigations of spinal osteoporosis detected on a lateral radiograph of the chest.

She was born two weeks prematurely after a normal pregnancy and delivery. Her birth weight was 5.0 lb.

There were no neonatal disturbances and apart from being below average weight and stature, she progressed normally.

Her milestones were a little delayed, she sat up unaided at 9 months, stood alone at 15 months, and said a few single words at 2 years.

At the age of 2 years when she weighed 15 lb. 8 oz. (below the third percentile: Stuart, Anthropometric chart), she was seen at another hospital where the presence of dwarfism led to the diagnosis of hypopituitarism. From about 2 years of age she was subject

FIGS. 1 and 2.—J.C., aged 12 years, showing pubic hair and moderate breast enlargement.

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to recurrent attacks of bronchopneumonia. A systolic cardiac murmur was detected at 5 years of age by the school doctor. At the age of 8 years she was admitted to a second hospital with severe enteritis, in a semi-conscious, collapsed state requiring a blood transfusion of two pints. She recovered within a week after chemotherapy. A lateral radiograph of the chest taken at this time already showed a moderate degree of osteoporosis of the spine with biconcave vertebrae.

Following an attack of pneumonia she was admitted to the City General Hospital, Sheffield (under a Dr. Brown) for cardiac investigation, including catheterization and angiography. A diagnosis of ventricular septal defect was made.

At 12 years 8 months regular menstruation started. At this time she still wet her bed about three times a week.

Several records of her height and weight after the age of 8, showed these all to be below the third percentile (Stuart, Anthropometric chart). Her parents and her only sibling, a 14-year-old sister, were well and of average height: father, 5 ft. 11 in.; mother, 5 ft. 6 in.; sister, 5 ft. 6 in.

Physical Examination. She was a cheerful but emotionally immature girl, retarded mentally with an I.Q. of 63 (Dr. K. Soddy). She was small and slender with a dorsal kyphosis and a short neck.

Her measurements at 12 years of age were as follows:

Height	..	..	46 inches
Upper segment	..	..	22½ "
Lower segment	..	..	23½ "
Head circumference	..	..	18 "
Arm span	..	..	49½ "

There was therefore proportional dwarfism with microcephaly. She had pubic and axillary hair with moderate breast enlargement. There was no skin pigmentation, cyanosis or clubbing.

Her heart apex beat was at the fifth left intercostal space in the anterior axillary line. There was a loud blowing systolic murmur, without a thrill, maximal at the third interspace at the left sternal border. The peripheral pulses were normal and the blood pressure was 105/70.

On walking up four flights of stairs slowly, she became pale, slightly cyanosed and breathless. Her chest movements were symmetrical and moderately good, with a prolonged expiratory phase. The percussion note was normal but there were coarse crepitations over both lungs.

No abnormality was found in the nervous system. Her sight and hearing were quite normal. Her fundi appeared normal. There was no evidence of a cerebellar or other motor disorder. Her tendon reflexes were normal and her plantar responses flexor.

The liver, spleen and kidneys were not palpable and a normal sized uterus could be felt rectally. Her external genitalia appeared normal. Her teeth were in good condition and normal for her age and size.

Investigations. BIOCHEMICAL. A calcium balance was performed in the Metabolic Ward with the usual full

FIG. 3.—Calcium balance.

precautions (Fig. 3). The child was given a constant normal diet throughout which approximated to her previous home diet. After six days' equilibration, six-day faecal specimens were collected between carmine markers, and also three-day urines. These, together with the diet, were analysed for total calcium. After the first two six-day control periods pure dihydrotachysterol (DHT) was given orally as indicated in Fig. 3. Professor Dent reports on the results as follows: 'It was unfortunate that a capricious appetite led to slightly inconstant intake as shown. In addition the most important balance period (the fourth) at the height of the vitamin D intoxication had to be scrapped owing to vomiting. The control balance is less positive than it should be for a child of her age. The sudden rise and fall in plasma and urine calcium coinciding with giving and stopping the DHT are clear and unequivocal. They indicate an excessive, sudden vitamin D-like action. The balance changes are more ambiguous but there was no markedly positive balance induced by the DHT. The unusual clinical and biochemical sensitivity to the DHT is fully consistent with the diagnosis of severe osteoporosis and definitely excludes any possibility of there being any form of dietary or metabolic rickets. It also means that she cannot benefit from administration of large doses of vitamin D in any of its forms.'

Vitamin A absorption was normal. Five-day fat balance: absorption 94.5%. Glucose tolerance: blood sugars fasting 105 mg. %, then half-hourly after 23.5 g. glucose, 135, 152, 125, 110 mg. % (normal). Plasma values are shown in Table 1.

Urinary gonadotrophin was 10 units/24 hr. and urinary oestrone 1.9 g./24 hr., oestradiol 1.5 g./24 hr., and oestriol 1.0 g./24 hr.

A urinary amino-acid chromatogram was normal. Serum proteins: total 7.4 g. %; albumin: 4.7 g. %;

TABLE 1
PLASMA VALUES

Date	Plasma Calcium (mg./100 ml.)	Plasma Phosphate (mg./100 ml.)	Plasma Alkaline Phosphatase (K.A. units/100 ml.)	Plasma Urea (mg./100 ml.)
18.6.57 ..	9.3	5.3	16.5	30
25.7.57 ..	9.8	5.0	14.0	54
26.8.57 ..	10.1	4.6		48

globulin: 2.7 g. %, A/G 1.7. Plasma electrophoresis was normal. Plasma cholesterol was 149 mg. % and plasma bicarbonate: 24.2 mEq./l. Plasma chloride: 103 mEq./l., plasma sodium: 139 mEq./l., plasma potassium: 4.3 mEq./l. Renal function tests showed a maximum urea clearance of 34.6%, 43%; a urine concentration test 1,020 (5 specimens after 8-14 hr. dehydration) and a urine dilution test of 1,003.

HAEMATOLOGICAL. Hb 67%, 84%, 82%, 80%. W.B.C., 19.7.57: 27,000/c.mm. (neut. 82.5%, lymph. 11.5%, monos. 6%); 20.8.57: 16,000/c.mm. (neut. 95.0%, lymph. 4.0%, monos. 1%). E.S.R. 35, 40, 30, 40 mm./hr.

OTHER INVESTIGATIONS. Routine urine tests were normal. Chromosomal sex: (buccal smear) chromatin positive. Complement fixation test for toxoplasmosis: negative; dye test for toxoplasmosis: 1:8 (Dr. I. A. B. Cathie). Deciduous teeth: (Professor Prophet) teeth small, structure and histology normal. E.C.G. and E.E.G. were normal. Radio iodine uptake: 40.1%, normal. Sweat electrolytes: not increased (Shwachman palmar plate method).

Radiographs (Dr. C. J. Hodson) showed: bilateral calcification of the basal ganglia of the skull not seen on skull radiographs done in 1951 (Figs. 4 and 5); a moderate osteoporosis of the spine with biconcave vertebrae (Fig. 6); moderate osteoporosis of the long

bones; probably a stone in the right kidney (straight radiograph) I.V.P.: normal. No definite signs of stone seen. Chest: marked cardiac enlargement, probably affecting mainly the right side, with some evidence of increased vascularity. Bone age: 11 years.

Discussion

The unusual finding of radiologically demonstrable symmetrical calcification of the basal ganglia with osteoporosis and the subsequent discovery of a probable renal calculus, suggested the possibility of gross disorder of calcium metabolism. Studies were therefore undertaken by Professor Dent in the Metabolic Ward. They confirmed the radiological diagnosis of osteoporosis as distinct from rickets (or osteomalacia), and at the same time excluded any possibility of the presence of true or pseudo-hypoparathyroidism.

The low levels obtained in the maximum urea clearance test (34.6% and 43%) may indicate a diminished renal functional reserve in spite of a nearly normal blood urea.

Radiologically demonstrable calcification of the basal ganglia was first reported by Fritzsch (1935) in two brothers and a sister examined in the third decade. They had been retarded since childhood.

FIGS. 4 and 5.—Bilateral calcification of basal ganglia.

FIG. 6.—Moderate osteoporosis of spine with biconcave vertebrae.

Two had fits and two had a progressive muscular rigidity without tremor. The parents were consanguineous and inheritance by a recessive gene was suggested by the author. Kasanin and Crank (1935) described a male, aged 32 years, who had a 10-year history of convulsions. He became mentally retarded and developed a progressive spasticity. At necropsy, extensive cerebral calcification was found. The fundamental lesion was degeneration of the finer blood vessels, with the production of an iron-containing albuminoid matrix on which calcium was precipitated. Eaton, Camp and Love (1939) reported six cases of calcification of the basal ganglia. Of these, Cases 1, 2 and 6 were probably due to hypoparathyroidism. Case 3 was a 55-year-old female with syphilis and thyrotoxicosis. Case 4 was a male, aged 31 years, who presented with a hemiplegia. Case 5 was a female of 40 years with 'obvious mental retardation' and a basal metabolic rate of +39%. Rand, Olsen and Courville (1943) described a 24-year-old female who had always been a problem child. She also suffered from epilepsy

and hypertension, but showed no evidence of hypoparathyroidism. Neill and Dingwall (1950) described two brothers, aged 16 years and 11 years, with microcephaly, optic atrophy and retinal degeneration. They were mentally retarded and had an unsteady gait, gross tremor and dysarthria. Radiologically they had calcification of the basal ganglia and osteoporosis. The elder became almost completely deaf. The authors considered that these signs resembled those present in the syndrome of progeria. Retinal changes and ataxia were also present in the cases described by Strobos, De la Torre and Martin (1957). Foley (1951) described a female, aged 60 years, who four years earlier developed a progressive illness characterized by slow movements, failing memory and frequent attacks of vertigo. She was mentally retarded with an I.Q. of 79. Her lower limbs were spastic. Her daughters, aged 28 and 21 years, though symptomless, both showed calcification of the basal ganglia. Sammet and Bucy (1951) described a male, aged 43 years, with calcification of the basal ganglia. He was a dipsomaniac but had no mental or neurological disturbance. Strobos *et al.* (1957) described two brothers, aged 48 and 44 years, with dysarthria, ataxia and heavy pigmentation of both maculae, showing calcification of the basal ganglia. Twenty-eight other members of the family were examined but no other cases of calcification were found. The authors include arteriosclerosis, encephalitis, tuberous sclerosis and toxic adenoma of the thyroid as causes of radiologically visible calcification of the basal ganglia. Matthews (1957) described a family of three sisters, aged 54, 61 and 59 years, who showed a slowly progressive neurological disorder resembling Parkinsonism. The two elder sisters showed calcification of the basal ganglia. The youngest had not been radiographed. The blood chemistry was normal but as no response was obtained to parathyroid hormone administered intravenously, the author suggested that these cases may represent a 'different fraction' of pseudo-hypoparathyroidism.

The presence of dwarfism, congenital heart disease and osteoporosis in a patient with female configuration, suggested the diagnosis of gonadal dysgenesis (Turner's syndrome). The absence of anomalies such as neck webbing or valgus elbow, or the presence of pubertal changes, or even the occurrence of menstruation is compatible with the diagnosis (Hoffenberg and Jackson, 1957). However, the present case was not thought to be an example of this condition. The urinary excretion of gonadotrophic hormone was normal and the chromosomal sex was female (Dr. G. I. M. Swyer). Direct inspection of the gonads at laparotomy was not thought

justified, especially as some authorities believe that both complete gonads must be examined histologically before gonadal dysgenesis can be ruled out.

In conclusion, the metabolic studies failed to reveal a cause for the osteoporosis or calcification of the basal ganglia, or the probable presence of a renal calculus. A genetic aetiology is suggested by the presence of multiple, apparently unconnected abnormalities.

Summary

A 12-year-old girl is described with dwarfism, mental retardation, and a ventricular septal defect. Radiologically she showed calcification of the basal ganglia, generalized osteoporosis and probably a renal calculus. Her blood chemistry was normal. There was no evidence of a hereditary disorder.

The diagnosis of hypoparathyroidism and gonadal dysgenesis were considered, but discarded. No similar case has been found described in the literature on idiopathic symmetrical calcification of the basal ganglia.

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