RICKETS WITH SECONDARY HYPERPARATHYROIDISM IN A SEVERELY SUBNORMAL CHILD

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Classical nutritional vitamin D-lack rickets is practically non-existent in countries where child care and treatment are available, but it is occasionally present especially in mentally subnormal children (C. E. Dent, 1961, personal communication). This could be due to the much more serious feeding problem they present, or there may be a neuro-biochemical defect due to brain damage, or a combination of both.

The role of vitamin D has in recent years been thoroughly investigated and it is now fairly well established that vitamin D influences at least three processes: intestinal absorption of calcium, renal tubular reabsorption of phosphate, and mobilization of calcium from bone (Harrison, 1959). The action of vitamin D is exerted directly or indirectly on the end organs, depending on the starting level and especially on the functional state of the parathyroid glands (Fanconi, 1959).

In view of recent advances in endocrinology, which show a more obvious central nervous control over glands (Jancar, 1961), and case histories which show that secondary hyperparathyroidism occurs frequently with vitamin D deficiency rickets (Illig, Uehlinger and Prader, 1959), we feel that damage to certain regions of the brain may be directly responsible for the malfunctions of parathyroid glands and indirectly for the action of vitamin D.

We present a case history of a severely subnormal brain-damaged child who in spite of being on an adequate diet suffered from rickets and secondary hyperparathyroidism.

Case Report

Female child, born February 9, 1954, after normal birth; weight 9 lb. (4,082 g.), was the first child of mentally and physically normal parents. She gained weight and made satisfactory progress for nine weeks, when she had a subarachnoid haemorrhage with fits of screaming followed by convulsions and was unconscious for half an hour. She was treated in two hospitals, and in November 1954 was transferred to The Hospital for Sick Children, Great Ormond Street, London.

On admission to the hospital the only abnormalities were obvious mental and motor retardation with some overweight, and generalized hypotonia of the limbs. Skull radiographs were normal, apart from some flattening of the left half of the skull vault. A left percutaneous carotid arteriogram was performed and revealed the presence of a large left subdural haematoma. Craniotomy was done with the intention of removing the membrane of this haematoma. At operation, however, although the outer membrane could be removed the inner membrane was thick and tough and merged imperceptibly into the underlying small shrunken brain. It was obvious that this brain would never be able to expand and that the membrane could not be removed.

The baby made an uneventful recovery from this operation and was transferred to her home-town hospital. Because of increasing fits, screaming attacks at night and because she was difficult to feed, she was admitted at 2 years of age to Stoke Park Hospital.

When examined on admission, she was mentally severely subnormal and untestable on any scale. No result was gained on the Griffiths Scale. She lay passively in her cot; her lethargy was interrupted only by myoclonic movements.

She vegetated unchanged mentally and physically in complete dependence on nursing staff, and on drugs for the epilepsy for the next two years and 10 months, when it was noticed that her left wrist suddenly became very dorsiflexed. A radiograph ruled out fracture but also showed ricket-like changes of the wrist joint. This observation led to further radiographs and biochemical investigations. Physical examination, apart from dorsiflexion of the wrist, did not show any of the classical signs of rickets.

Investigations

X-ray Report on Skeletal Joints (December 1958). The changes shown in the wrist joints look like rickets which is probably active. Some changes are also present in the head of the humeri. The films also show some splaying out of the epiphysis of the lower end of the femur and the upper end of the tibia. As there is no bowing of the long bones, this may be renal rickets. As for the scurvy,
there is no evidence of subperiosteal haemorrhage. The examination also shows congenital dislocation of the right hip joint.

**Blood** (January 1959). Blood urea 20 mg./100 ml.; serum calcium 10 mg./100 ml. (phosphate not estimated due to haemolysis of the blood).

**Urine** (January 1959). Slightly hazy yellow urine; alkaline, pH 7·6; specific gravity, insufficient; trace of albumin, no sugar. Microscopy of urine revealed a moderate amount of mucus, 1-3 cells per high-power field; no red cells or casts, many triple phosphate and stellar phosphate crystals. Sulkowich's test revealed that urinary calcium was not increased.

**Faeces** (January 1959). Moist brown stool, weight 23 g.; faecal fat (as fatty acid) 0·61 g./day (normal up to 5 g.).

**Electroencephalogram** (January 1960). The records showed frequent high amplitude delta and slow spike discharges from the left hemisphere, which were often focal in the left temporal region. At times this activity spread to other areas. Photic stimulation failed to have any significant effect. The records are indicative of an epileptogenous lesion of the left temporal region.

**Blood** (April-July 1960). Plasma bicarbonate, 49·4 vol. %, 22·1 mEq/l. (normal 54-70 vol. %, 24-31 mEq/l.); blood urea, 14 mg./100 ml.; plasma protein: total protein 8·19 g./100 ml. serum (normal 6·02-7·42); γ globulin 17·63%, 1·444 g./100 ml.; β globulin 14·43%, 1·183 g./100 ml.; α₂ globulin 11·62%, 0·951 g./100 ml.; α₁ globulin 5·15%, 0·422 g./100 ml.; albumin 51·17%, 4·19 g./100 ml. A/G ratio: 1·05; mild increase in α globulins.

**Urine Chromatography** (April 20, 1960). The routine chemical tests were normal except for a rather low calcium concentration. The amino acid chromatogram is interesting as it shows a slight increase in excretion of the low molecular weight amino acids, glycine, alanine, serine, threonine and glutamine. This is a non-specific aminoaciduria that can arise in acquired nutritional disturbance such as vitamin D or other vitamin deficiencies and sometimes in early renal tubular damage for which, however, there is no definite evidence on chemical tests.

On July 2, 1960 the urine has a little more calcium in it and is otherwise normal on routine chemical tests. The amino acid chromatogram is different from the previous one. It shows a large glycine spot only, within the normal range of variation.

This report fits well into the picture of rickets treated with vitamin D.

**Blood** (December 1960). Plasma urea 18 mg./100 ml. (normal 25-40); plasma sodium 349·5 mg./100 ml., 152 mEq/l. (138 ± 5); plasma potassium 17·0 mg./100 ml., 36 mEq/l. (4·8 ± 0·7); plasma chloride 615
mg./100 ml., 105 mEq/l. (100 ± 6); and plasma bicarbonate 51-9 vol./100 ml., 23-2 mEq/l. (30 ± 5) as CO₂ combining power.

Urine Chromatography (December 1960). This is now quite normal on routine tests and gives a quite normal amino acid chromatogram. This is just what one would expect in a case of treated classical rickets.

Full blood count was performed periodically and on each occasion it was within the normal limits.

The estimations of serum alkaline phosphatase, calcium, inorganic phosphate (as P) and calcium excretion in urine (per 24 hours) and the dates when specimens were collected are shown in the Figure (previous page).

Treatment. In view of the satisfactory general physical condition, gain in weight and the vague differential diagnosis, and the fact that she was very difficult to feed, we decided to persevere with the diet which was given to the other children in the ward, who did not show any signs or symptoms of vitamin or mineral deficiency. It was calculated from the diet sheets that the patient was receiving approximately 70 I.U. of vitamin D daily, plus exposure to sunlight; a quantity which, though low, is usually considered to be sufficient for prevention of rickets (Stearns, Jeans and Vandecar, 1936).

When the patient did not show satisfactory progress on the diet alone, we added, on February 12, 1960, 4 ml. of ‘vi-Daylene’ t.d.s.

4 ml. of ‘vi-Daylene’ contains: vitamin A, 2,400 I.U.; vitamin D, 320 I.U.; aneurine hydrochloride, 1-2 mg.; riboflavin, 0-96 mg.; ascorbic acid, 32 mg.; pyridoxine hydrochloride, 0-8 mg.; nicotinamide, 8 mg.

Further radiographs of the wrists on July 7, 1960, showed increased signs of hyperparathyroidism. However, we continued the same treatment, especially when later biochemical tests showed an improvement which was also confirmed by further radiological reports in December 1960 and September 1961. The patient has gained 14 lb. (6·35 kg.) in weight since the beginning of the treatment.

Her epilepsy is fairly well controlled by phenobarbotone 1 gr. (65 mg.) t.d.s. and metharbital (’gemonil’) 0·1 g. b.d.

Psychological Assessment. She was tested in March 1960 and again in September 1961. The following is a report on her mental condition: ‘Mental development stationary at about 4-month level. Passes and fails same tests at 4-month level as when last seen in March 1960. Fails all 6-month Gesell test. Makes noises and uses her voice more but cannot say words. She is a little more placid.’

Summary
A case of a severely subnormal brain-damaged child with rickets and secondary hyperparathyroidism is recorded. Patient developed rickets on a normal diet which contained about 70 I. U. vitamin D daily. This healed completely, but only very slowly after the supplementation of an additional 320 I. U. of vitamin D and other vitamins t.d.s. Mental condition and investigations are noted. The role of vitamin D, functional state of the parathyroid glands and case histories of rickets with secondary hyperparathyroidism are mentioned.

It is postulated that difficulty in feeding and damage to certain regions of the brain may be directly responsible for the malfunction of the parathyroid glands and for the level and action of vitamin D. This increases the normal requirement of vitamin D and results in hyperparathyroidism. This is cured by only a moderate increase in vitamin D intake.

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