Tetany Due to Hypomagnesaemia with Secondary Hypocalcaemia

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Vaincel, M., Vandeveld, G., Smulders, J., Vosters, M., Hubain, P., and Loeb, H. (1970). *Archives of Disease in Childhood*, 45, 254. **Tetany due to hypomagnesaemia with secondary hypocalcaemia.** The case is described of a 5-month-old boy who had convulsions and persistent tetany, associated with hypomagnesaemia and hypocalcaemia. Vitamin D treatment corrected the hypocalcaemia without modifying the clinical status; parenteral magnesium was given, but the child died shortly thereafter. The pathological examination showed calcinosis of the myocardium, kidneys and in one of the cerebral arteries.

In 1965, Paunier *et al.* described a child of 6 weeks who had generalized convulsions and tetany, associated with low serum magnesium and calcium levels. Magnesium therapy stopped the tetany and established a normal serum calcium level. Similar cases were later reported by Salet *et al.* (1966), Friedman, Hatcher, and Watson (1967), and Skyberg *et al.* (1967).

Most of these authors suggested that the magnesium deficiency was a result of a defect in intestinal transport.

We here report the case of a child with similar clinical and biochemical features, where the disease pursued a rapidly downhill course. The histological findings were those of diffuse calcinosis.

Case Report

II.9 was the ninth child of a mentally retarded mother who had been treated for tuberculosis. He was delivered at term as a breech. Weight, length, and head circumference were normal (3.750 kg., 47 cm., and 36 cm.). The child was fed a dried milk preparation, receiving 400 units vitamin D daily, from the age of 4 weeks. At 3 months, he was admitted to a country hospital because of a series of convulsions. The fontanelle was bulging and the feet were oedematous. The EEG was normal. In spite of treatment with barbiturates and hydantoin, convulsions continued. One month after admission, a low serum calcium was noted for the first time, 7.7 mg./100 ml.

The family history showed that 4 out of 6 sons had had convulsive attacks, and the first and fourth had

died (Fig. 1). The first son had generalized seizures at the age of 3 weeks (in 1948) and died three weeks later. The third had had only one convulsion when aged 6 years: no EEG was recorded.

The fourth son was admitted to a country hospital at 1 month, with generalized convulsive seizures: despite barbiturate treatment the seizures persisted. He died at 3 months (in 1954), and a histological study of the brain was reported by Henneaux, Gambetti, and Tome (1965). There was a chronic meningoencephalitis, the meninges being infiltrated with large epithelioid cells, calcified plaques were observed in the intima and media of the cerebral arteries.

FIG. 1.—Family tree of the patient, showing high incidence of convulsions among male sibs. All three deaths were associated with repeated convulsions.

The sixth son had a seizure at 13 months, but no further details are available.

The disease thus seemed to be familial, and the patient was referred to the Paediatric Centre of the University Hospital for further investigation. He was now 5 months old. Weight and head circumference were normal (6.800 kg., 43 cm.), length was less than the 10th centile (57 cm.). He showed constant tetany

with bilateral Trousseau's sign and carpopedal spasm (Fig. 2 and 3). There was a general increase in muscular tone. He took no notice of his surroundings, nor responded to stimuli, except that noise aggravated the tetany. The eyelids jerked intermittently. Cleft palate, umbilical hernia, and hypospadias were present.

FIG. 2.—General aspect of the child with carpopedal spasm and Trousseau's sign. The feet are oedematous.

The main chemical features were a low level of serum calcium (6.15 mg./100 ml.), a normal phosphorus (5.9 mg./100 ml.), and increased alkaline phosphatase (30 Bodansky units). Plasma electrolytes and BUN were normal. The excretion of calcium in the urine was very low, 1 mg./kg. per 24 hours. Bone x-rays were normal, with no signs of rickets or hypoparathyroidism. The EEG now showed slow wave complexes of weak amplitude in both hemispheres.

Intravenous calcium gluconate was given, which raised the serum calcium to 8.5 mg./100 ml., but did not control the tetany. The Ellsworth-Howard test gave a result similar to that in a control infant. Hypoparathyroidism was therefore excluded and investigations turned towards the idea of magnesium deficiency. Blood samples were taken for magnesium content by an

atomic absorption spectrophotometry method (Wacker, Iida, and Fuwa, 1964). Meanwhile, the child was given a high dose of vitamin D (750,000 units per week). Tetany persisted, even though the serum calcium became normal. Vitamin D treatment was withdrawn after a low serum level of magnesium (0.47–0.78 mg./100 ml.) was recorded. The clinical status worsened rapidly, with cyanosis, intermittent laryngeal spasms, and episodes of fever. Magnesium treatment (600 mg./day) was now given intravenously. However, in spite of the serum magnesium level reaching 2.8 mg./100 ml., the tetany persisted and during the third day of this treatment, he died.

Pathological findings. There were no macroscopical lesions, but histological changes were seen in the heart, kidney, and brain. In the myocardium there was focal necrosis of myocardial fibres, calcium deposits being found in these. One area around a branch of a coronary artery was particularly affected by the calcinosis (Fig. 4).

In the kidney, calcium deposits were found in the lumen of proximal tubules and in the ascending limbs of Henle's loops (Fig. 5). In some other nephrons calcium casts were to be seen within the wall of the tubules, surrounded by a layer of epithelial cells (Fig. 6). Mitoses were present in proximal tubules unaffected by the calcinosis process. Some fibrosis, with proliferative

FIG. 3.—Permanent Trousseau's sign.

change of basement membrane, was noted in some glomeruli.

The meninges were thickened and infiltrated with polymorphonuclear cells. A calcified plaque was observed in the intima of a cerebral artery.

FIG. 4.—*Peri-arterial calcinosis of myocardium. (H. and E. $\times$ 220.)*

FIG. 5.—*Calcinosis of the kidney. (H. and E. $\times$ 220.)*

FIG. 6.—Microlith surrounded by a layer of cells. (H. and E. $\times 600$.)

Discussion

From the age of 3 months, the patient had had convulsions with normocalcaemia. One month later, persistent tetany was present and the calcium level had now fallen; at this stage hypomagnesaemia was recognized.

Hypomagnesaemia occurs in many circumstances, such as in malabsorption syndromes (Goldman, Van Fossan, and Baird, 1962; Booth *et al.*, 1963), hypoparathyroidism (Jones and Fourman, 1966), and vitamin D intoxication (George *et al.*, 1962). A few studies have dealt with the association of low serum calcium and magnesium (Salet *et al.*, 1966; Friedman *et al.*, 1967; Skyberg *et al.*, 1967; Paunier *et al.*, 1968). In every case, the patient has been a male child, in whom tetany, hypomagnesaemia, and hypocalcaemia have occurred during the first weeks of life. Calcium therapy has proved ineffective, and it is only magnesium therapy that stops the convulsions and leads to correction of the low serum calcium. The similarity between these observations and ours is evident, though in our case magnesium therapy was not effective. This may be because treatment with magnesium was of short duration, and was only started when the child was severely ill, and after he had had a low serum

calcium for six weeks with continuous tetany for a month. Vitamin D therapy had already corrected the hypocalcaemia so that the effect of magnesium therapy on this could not be tested.

In 'idiopathic hypomagnesaemia', the cause of the low serum calcium concentration remains obscure. To correct the hypocalcaemia high doses of vitamin D are required, but a prompt response can equally well be obtained by giving magnesium intramuscularly. Salet *et al.* (1966) suggest that the exchangeable calcium pool is reduced by magnesium deficit. The intestinal resorption of calcium is normal (Paunier *et al.*, 1968).

Some authors (Friedman *et al.*, 1967; Skyberg *et al.*, 1967; Paunier *et al.*, 1968) suggest that the low serum magnesium is the result of impaired intestinal absorption of magnesium, though Salet *et al.* (1966) did not find this. Should such a defect in intestinal absorption exist, it could be part of a familial metabolic disorder, as suggested by the family history in our case.

Our case showed lesions of calcinosis in the kidneys and myocardium. Similar lesions have been reported in animals depleted of magnesium (MacIntyre and Davidsson, 1958; Heggteit, Herman,

and Mishra, 1964). Magnesium-depleted rats develop nephrocalcinosis with hypercalcaemia, whereas in 'idiopathic hypomagnesaemia' calcinosis of kidneys and myocardium takes place when the serum calcium level is low.

We have no explanation for the minor changes observed in renal glomeruli. Renal function was normal. Similar alterations were found in a single kidney biopsy by Paunier *et al.* (1968). Hypomagnesaemia might be responsible for this damage.

Calcification of one cerebral artery was found in the brain of our case and also in the fourth son of the family, reported by Henneaux *et al.* (1965). The latter authors observed large epithelioid cells in the meninges which they ascribed to a chronic meningoencephalitic process; in our patient, a polymorphonuclear cellular infiltration was found in the meninges. Unfortunately, no histology other than that of the brain was available for the fourth son, so that it is only the similar clinical course in the brothers that points to a common disease with an inherited metabolic defect.

The disease seems to affect only boys (Skyberg *et al.*, 1969; and our observation), suggesting a recessive sex-linked transmission.

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