INFANTILE CORTICAL HYPEROSTOSIS

S. LEVIN, M.B. (RAND), M.R.C.P. (EDIN.), D.C.H.; and J. FRIEDMAN, M.B. (RAND), D.M.R.D. (LOND.), *Johannesburg*

'O Lord, heal me; for my bones are vexed.'

Psalm 6 : 2.

It is some 15 years since Caffey and Silverman[1] gave the first lucid description of this disorder — so-called because of the age incidence and the characteristic hyperplasia of cortical bone.

Since then considerably more than 100 cases have been reported in the medical literature, though this total is certainly but a small fraction of all cases diagnosed. 'Caffey's disease' is especially well recognized in the USA, where it has also been noted in Negroes and indigenous Indians. The disorder is probably not too rare; in mild or atypical forms it is easily overlooked or misdiagnosed. In this country it has also been recognized — individual radiologists approached have indicated that they have seen rare cases locally, but we have been unable to find any case report in South African literature.

CASE REPORT

In March 1960 an 8-week-old girl was presented for examination because her legs were swollen.

A full-term infant, she appeared well after birth. Nursing failed when the mother and baby returned home on the 10th day, and a milk-water-sugar-cereal mixture was substituted. At 14 days a polyvitamin supplement was added in conventional dosage, and a day or two later the mother observed that the infant's shins were slightly swollen. During the next 6 weeks the shins became markedly convex and tender to the touch, but otherwise she was well, gaining weight, eating satisfactorily, not unduly irritable and not feverish.

Pregnancy was uneventful, but from about the 4th month the father, a representative of a pharmaceutical house, insisted that his wife take daily doses of vitamin capsules ('prenalac'). This she did, more or less faithfully, until term.

The first child, a healthy girl of 2½ years, was born after a normal full-term pregnancy during which vitamin supplements were not taken by the mother.

There was no history of bony disorders in either parent or their relations.

Physical examination of the patient revealed an unhappy 9 lb. infant with astonishingly well-marked sabre tibiae. The subcutaneous tissue overlying the thickened bones was also brawny, but there were none of the usual signs of inflammation. On the dorsum of the right foot there was a solitary *café-au-lait* spot. There was some doubt whether the right ramus of the mandible was swollen. Blood pressure was 90 mm.Hg systolic. There was no fever.

The diagnosis was considered to be either infantile cortical hyperostosis or periosteal neurofibromatosis, and radiology was suggested with these possibilities in view.

Radiological Findings

Radiographs of the lower limbs demonstrated marked periosteal new-bone formation surrounding both tibiae, affecting the diaphyses and stopping at the level of the metaphyses. The periosteal margins were fairly smooth and no spiculation was observed. The right fibula was similarly affected, but

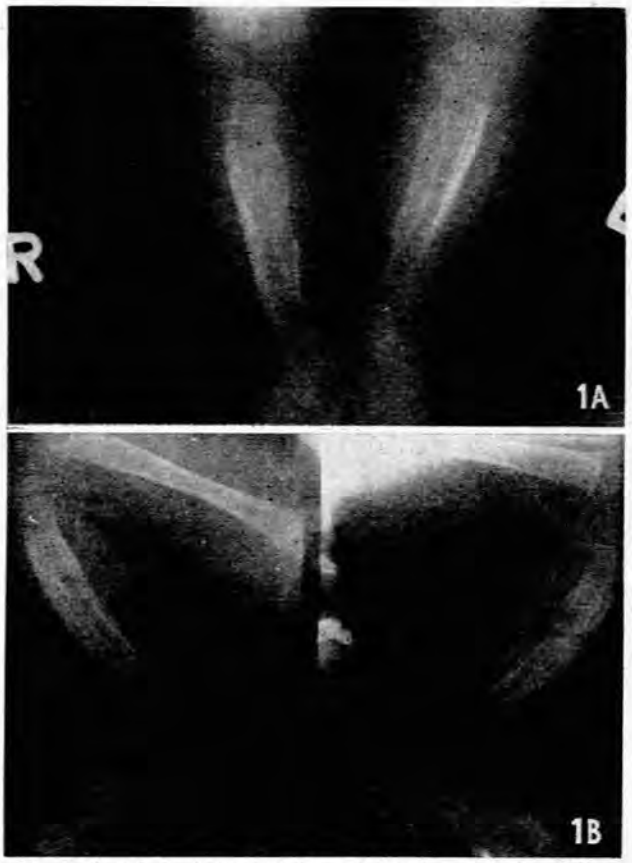

Fig. 1. A and *B*. Antero-posterior and lateral radiographs of legs, demonstrating the extensive periosteal new-bone formation of both tibial shafts and right fibula with a tendency to onion-peel layering.

the left fibula appeared normal (Fig. 1).

A similar periosteal area of new-bone formation with smooth margins was seen in relation to the middle third of the right humerus (Fig. 2). A slight degree of periosteal reaction was also found on the medial side of the middle third of the left

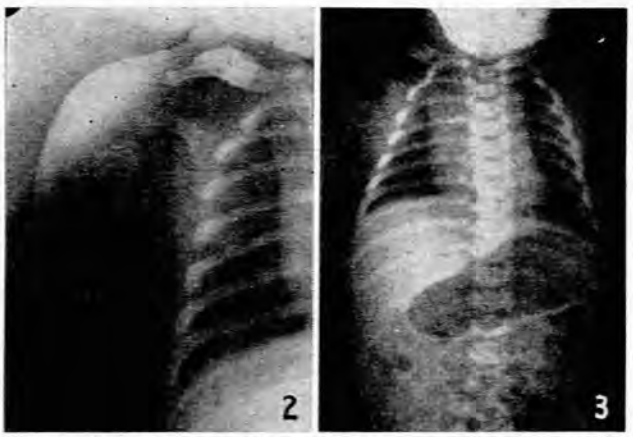

Fig. 2. The periosteal new-bone formation around the right clavicle and humerus is clearly evident.
Fig. 3. The reaction around the right clavicle and the irregular bossing of the mandible, frequently found in infantile cortical hyperostosis, is demonstrated.

humerus. The right clavicle showed marked new-bone formation. The femora, forearms, spinal column and pelvis appeared normal.

The mandible was also seen to be irregular in contour, consistent with patchy zones of periosteal new-bone formation (Fig. 3).

The radiological appearances were typical of an infantile cortical hyperostosis.

Progress

When the diagnosis was established the baby was re-examined. This time there was no doubt that, although the rami of the mandible were not enlarged, small bony knobs projected from the middle of each side. An enlargement of the right clavicle could not be felt clinically; presumably the hyperostosis was limited to the internal surface. No treatment was given.

In early April blood studies revealed the following: Haemoglobin 11·7 G. per 100 ml., WBCs 12,800 per c.mm., neutrophils 32%, lymphocytes 55%, eosinophils 4%, monocytes 7%, basophils 0·5%, platelets numerous, sedimentation rate 25 mm. in the 1st hour, alkaline phosphatase 23·5 King-Armstrong units (normal 10 - 20 units).

A month later the sedimentation rate was 18 mm. in the 1st hour and the alkaline phosphatase was 19 King-Armstrong units.

Over the course of the next few months the tiny knobs on the mandible disappeared, but the patient's shins remained bowed. Teeth erupted at 10 months, and her physical and mental progress was normal. The routine immunizations caused no untoward reactions.

In March 1961 she was re-X-rayed, with findings as follows:

There was complete absence of periosteal new-bone formation. Some residual bowing of both tibiae was present (Fig. 4), but it is confidently expected that this will revert back to

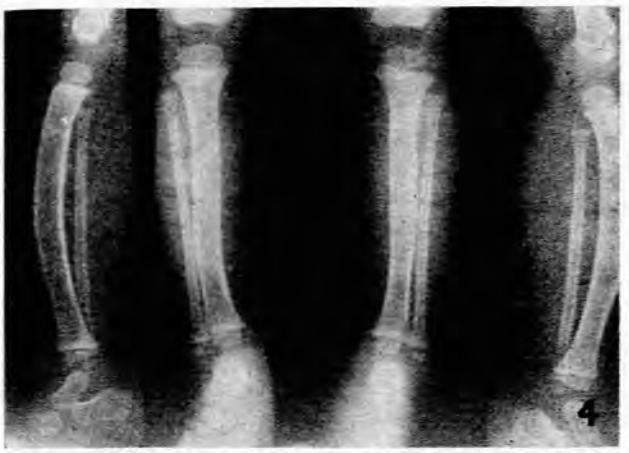

Fig. 4. One year after Fig. 1 was taken. No trace of the periosteal new bone is seen, but some residual bowing is still present. It is confidently expected that, with the passage of time, both tibiae will revert back to normal.

normal. The right clavicle and right humerus appeared perfectly normal (Fig. 5).

DISCUSSION

The disorder occurs equally in both sexes and is usually first manifested at the age of 2 - 3 months, although it has been correctly diagnosed prenatally at 31 weeks' gestation; in that case the foetus was born dead by Caesarean section, and the disease was already well-advanced.[2]

Clearly the aetiology is to be sought within the prenatal period. So far, all studies — bacterial, viral, immunological, nutritional and blood chemical — have been negative.[2] Pathologically the picture is not clear. The bone formation is not secondary to subperiosteal haemorrhage; infective and also benign hyperostotic changes have been suggested.

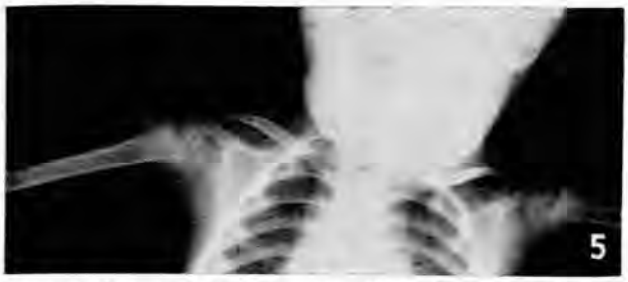

Fig. 5. The normal appearance of the right clavicle and humerus seen one year after Fig. 2 was taken.

Sometimes the picture is virtually indistinguishable from that of osteogenic sarcoma, and there have been instances of the disease affecting a single bone (especially the mandible or scapula) with misleading biopsy reports, resulting in radical surgery with amputation of mandible or limb.[4] In the radiological differentiation it should be noted that, unlike osteogenic sarcoma, there is no spiculation in infantile cortical hyperostosis.

All bones in the body may be subject to the disease, though the spine, carpus, and tarsus appear to be exempt, and the skull is only rarely affected. The mandible is nearly always involved, and the clavicles, tibiae and humeri frequently affected. Also not exempt are the femur, radius, ulna, ribs, fibula and scapula.

In the acute phase of the disease there may be irritability, fever, anorexia and leucocytosis. During resolution the bones may be bowed, but by about 3 years this has nearly always rectified itself. Very rarely, bowing and crippling residua may persist into adulthood and may require orthopaedic correction.

Because the prognosis, though usually benign, may be unpredictable, Caffey[3] suggested that all patients should be treated with cortisone. One death has been reported, apparently from the disease itself, for no other cause could be found at autopsy.[5]

Of late, attention has been directed to the familial incidence of the disease.[6-8] Tampas *et al.*[9] have even noted 11 cases in 2 generations of one family group, though to be sure, half of them had minimal bony involvement and would not have been diagnosed had there been no knowledge of typical instances among relations. Holman and Gerrard[10] observed 13 cases over 3 generations in one family group.

Paradoxically, despite the familial incidence — at least in some cases — the disease appears to be quite new. Sherman and Hellyer[11] reviewed all their X-ray films from 1930 to 1950 and found none that might be relabelled infantile cortical hyperostosis.

The Rôle of Vitamin A

Superficially, infantile cortical hyperostosis is similar to vitamin-A intoxication. Both show hyperostosis, though the distribution differs,[12] and vitamin-A poisoning only appears towards the end of the first year of life, and then only if the preceding months have witnessed the (usually unwitting) intake of astronomical doses of vitamins. It is impossible to induce infantile cortical hyperostosis during the first few months by administering large doses of vitamin A, and affected infants do not have high blood levels of vitamin A.[13]

On the other hand, the disorder known as idiopathic hypercalcaemia is not only considered to follow on excessive vitamin-D administration, but may also be a consequence of abnormal sensitivity to normal intakes of vitamin D or provitamin D.[14]

It was decided to evaluate the rôle of vitamin A in our patient on the basis of the above supposition. Clearly, the disorder is a legacy of the womb, and about the only widespread change in prenatal care during the past 15 years has been the extensive use of (? necessary) vitamins for perfectly well-fed pregnant women.

It was theorized that infants might be sensitized to extraneous vitamin A during foetal life and that, when exposed to vitamin supplements after birth, the disease would become manifest. Our patient's illness began promptly after getting a vitamin preparation.

When the diagnosis was made, the vitamin supplements were stopped, and some 3 weeks later blood was taken and showed the results indicated earlier. Thereafter the patient was encouraged to eat carrots, and was also given a vitamin-A concentrate equivalent to a daily dose of about 1,500 units; a month later blood was again taken. Far from showing an expected exacerbation, there was an improvement, though clinically the bony swellings were unchanged.

SUMMARY

Infantile cortical hyperostosis is a bony disorder of unknown aetiology occurring during the first few months of life. It is a 'new' disease, and probably not too uncommon, even though this is the first case to be recorded locally. Our patient showed the classical features of a hyperostosis affecting the mandible, clavicle and tibiae, as well as other bones. The course of the disease is usually benign, the bony swellings disappearing after some months or years. The lesion may be confined to one bone, and histological features may falsely indicate an osteogenic sarcoma — with tragic consequences. There is no evidence to link the disease with hypervitaminosis A or with an abnormal sensitivity to this vitamin. Present conceptions point to a familial or genetic influence as an aetiological factor.

REFERENCES

1. Caffey, J. and Silverman, W. A. (1945): Amer. J. Roentgenol., **54**, 1.
2. Bennett, H. S. and Nelson, T. R. (1953): Brit. J. Radiol., **26**, 47.
3. Caffey, J. (1957): Proc. Roy. Soc. Med., **50**, 347.
4. Eversole, S. L. jnr. *et al.* (1957): Bull Johns Hopk. Hosp., **101**, 80.
5. Matheson, W. J. and Markham, M. (1952): Brit. Med. J., **1**, 742.
6. Barba, W. P. and Freriks, D. J. (1953): J. Pediat., **42**, 141.
7. Boyes, J. G. and Demy, N. G. (1951): Amer. J. Roentgenol., **65**, 924.
8. Sidbury, J. B. jnr. and Sidbury, J. B. (1954): New Engl. J. Med., **250**, 309.
9. (*a*) Tampas, J. P. *et al.* (1961): J. Amer. Med. Assoc., **175**, 491.
   (*b*) van Buskirk, J. P. *et al.* (1961): Amer. J. Roentgenol., **65**, 613.
10. Holman, G. H. and Gerrard, J. W. (1960): A.M.A. Amer. J. Dis. Child., **100**, 781.
11. Sherman, M. S. and Hellyer, D. T. (1950): Amer. J. Roentgenol., **63**, 212.
12. Rothman, P. E. and Leon, E. (1948): Radiology, **51**, 368.
13. Caffey, J. (1951): Amer. J. Roentgenol., **65**, 12.
14. Forfar, J. O. *et al.* (1959): Arch. Dis. Childh., **34**, 525.