MULTIPLE SPONTANÉOUS "PSEUDO-FRACTURES" OF BONE (MILKMAN'S SYNDROME)

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Parkes, in 1882 (quoted by Camp and McCullough, 1941), found at necropsy a fracture in the rib of a 1-year-old child who had rickets. There was no ecchymosis or other evidence of injury or repair. This may well be the first record of a "pseudo-fracture."

Looser (1920a, 1920b) first described the radiological and pathological appearances. He showed that the radiolucent portion was due to osteoid tissue and that sometimes this projected out beyond the cortex. Milkman (1930, 1934) described in detail the case of a 40-year-old woman with multiple "pseudo-fractures" and recorded her progress until death following the onset of diabetes. Three independent pathologists were asked to report on the bones. Two of them made a diagnosis of osteomalacia, while the third considered the lesion to be a congenital bone dystrophy.

Fairbank (1935) reported similar changes in osteomalacia of dietetic origin which healed under calcium and vitamin-D therapy. He also mentions similar changes in the bones in osteomalacia due to idiopathic steatorrhoea.

Since the appearance of Milkman's paper numerous cases have appeared in the literature, especially on the Continent (Debray *et al.*, 1933; Hunter, 1935; Garcin *et al.*, 1937; Leedham-Green and Campbell Golding, 1937-8; Monier-Vinard, 1940; Edeiken and Schneeburg, 1943; Mackay and May, 1944); and it was assumed that multiple spontaneous "pseudo-fractures" of bone might occur in a variety of disease processes.

Albright *et al.* (1946), in a comprehensive study, came to the conclusion that the syndrome is a manifestation of osteomalacia (or its juvenile equivalent, rickets). They point out that the biochemical findings are similar to those of osteomalacia, that the histopathology is that of osteomalacia, and that improvement or cure follows vitamin-D therapy. They reassert that the fundamental mechanism in the causation of osteomalacia is the failure of prompt deposition of calcium salts in newly formed osteoid tissue, due to imbalance in the calcium-phosphorus level in the body. They further stress that "pseudo-fractures" are, in fact, true fractures precipitated by minimal stresses and strains in osteomalacic bone.

In view of the fact that the initial diagnosis of this condition usually rests on the radiological discovery of the "pseudo-fractures," it is important to emphasize the necessity to look carefully for them in the bones of any patient who presents with a history of pain and weakness for months, or even years, in the extremities, pelvis, or chest wall. In those cases in which the pelvis and lower limbs are involved the gait will change to a duck-

like waddle. A graphic description of the disability is given by a patient of Debray *et al.* (1933): "J'avais peur de me casser en faisant un mouvement."

The "pseudo-fractures" show typically as transverse zones of rarefaction, varying in width from 1 mm. to 1 cm. They are multiple and, in general, symmetrical in distribution, and often occur in apparently normal bone. According to Mondor and Leger (1947) their distribution is mainly as follows: ischio-pubis, ilio-pubis, femur, tibia, radius, fibula, iliac bone. Other common sites are the lower ribs and the infraglenoid region of the scapula.

The commonest age is from 40 to 70 years, mainly in women. In a typical case the lesions are seen in varying stages of development: (1) The earliest stage is a small triangular or semicircular infraction in the bony cortex. (2) This extends slowly across the bone, wiping out the normal osseous pattern. This transparent band may be straight or wavy in outline and sometimes gives an "S" or figure-of-8 appearance. (3) When the band has extended nearly across the bone there is usually a well-defined condensation of bone closely above and below it, and also a thin crescent of calcification just external to the cortex on one or both sides. (4) Healing occurs slowly, sometimes taking one or two years under treatment. When it is complete there is seen at the site a faint sclerosis with a small projection external to the cortex. (5) In any given case it is probable that at least one "pseudo-fracture" will have the typical fully developed appearance. (See Figs 1-5.)

It will be clear from these observations that, whenever such a lesion is found in the routine examination of films for any cause, further radiological examinations should be made of the long bones, ribs, and pelvis, preferably with corresponding normal controls.

Radiologically, these "pseudo-fractures" have to be differentiated from fatigue fracture, the increment fracture of Paget's disease and other bone diseases, and cough fractures of the ribs.

Fatigue fractures are not multiple nor usually symmetrical, though one may occur in each tibia. They produce normal callus within a few weeks, and this increases quickly (Hartley, 1942), while the only appearance resembling callus in the "pseudo-fracture" is the thin extracortical crescent of calcification. The radiolucent zone in the developed "pseudo-fracture" is wider than the zone of porosis seen in a fatigue fracture. The zone of condensation above and below a "pseudo-fracture" is denser, narrower, and better defined than that of the fatigue fracture.

The increment fracture of Paget's disease and of other more localized pathological conditions of bone is usually on the convex surface, is of a finely angled triangular shape with slightly irregular surfaces, and always occurs in areas of bone where the disease process shows definite pathological appearances on radiological examination.

Cough fractures have all the appearances of ordinary fractures, with fairly sharp irregular edges, and on healing there is more callus than in "pseudo-fractures."

If multiple "pseudo-fractures" are seen radiologically the presence of osteomalacia can be presumed; no more can be inferred, and it remains for clinical and biochemical examinations to discover the cause of the osteomalacia.

Albright *et al.* (1946) have classified the aetiology of osteomalacia as seen in the U.S.A. They quote the work

FIG. 1.—"Pseudo-fractures" seen in right lower ribs on film taken at cholecystogram examination. Type: well advanced.

FIG. 2.—"Pseudo-fractures" present in upper third right femur, right pubic bone, and right ischium. Film taken when patient first attended out-patient clinic. Type: moderately well advanced.

FIG. 3.—Early "pseudo-fracture" in right fibula. It extends nearly half-way across the bone and shows the slight cortical elevation and semicircular infarction just deep to the cortical elevation.

FIG. 4.—Fairly well advanced "pseudo-fractures" in upper part of radius and ulna with commencing condensation.

FIG. 5.—Almost healed "pseudo-fracture" in ulna. Faint condensation at site with very slight cortical thickening of shallow convex type at borders.

of Albright and Ellsworth (1929), who found that the primary action of the parathyroid hormone is to cause increased urinary phosphorus excretion. This in turn causes a lowering of the serum-phosphorus level leading to increased bone resorption with a rising serum-calcium level followed by increased calcium excretion in the urine. They also found that the serum-calcium level controls parathyroid activity.

Albright *et al.* (1946) proved that vitamin D increases calcium absorption from the gut and decreases phosphorus excretion in the urine. They further found that the rise in serum phosphorus after vitamin-D administration is mainly due to decreased parathyroid activity secondary to raised serum calcium level.

Two cases presented within a twelvemonth at the same hospital and a third case was seen by one of us (S. N.) at another hospital during that time.

Case 1

A smallholder's wife, aged 35, was first seen in March, 1946. She gave a three-year history of weakness in the right thigh, with pain on standing. This had become worse in the preceding year and interfered with walking. During the previous three months pain and weakness affected the left calf and both forearms, so that she was unable to lift moderately heavy weights. It seemed that the symptoms improved spontaneously during the summer months.

Her past history showed her to be a non-smoker and teetotaler who had never worked with chemicals and had never been abroad. She is emphatic that she has always eaten a normal mixed diet, though her appetite has never been large. She had lived on a smallholding or farm since 1926 and had had no serious illness. There were two pregnancies, in 1935 and 1937, and after the latter she was treated for anaemia with liver and iron for a short time. Careful inquiry and investigation failed to elicit any evidence of steatorrhoea. Her family history was devoid of any relevant facts.

When seen in 1946 she was pale, there was tenderness of some of the long bones, and her gait was duck-like. No other physical abnormalities were found. She was admitted to hospital for six weeks.

Radiological examinations show "pseudo-fractures" in the right femur, right and left pubis close to the sacrum, right ulna and fibula, right fifth to twelfth ribs, and left seventh to twelfth ribs. The long bones showed some slight calcium loss and cortical thinning.

She was treated by a full diet and physiotherapy together with 30 gr. (2 g.) of calcium lactate and two capsules of "adexolin" (2,000 i.u. of vitamin D) three times a day. At the time of her discharge she looked, felt, and walked better. She continued on this regime at home. By July, 1946, radiographs showed healing of the lesions. Her anaemia was still present, so she was given iron. By September, 1946, she was working normally, free from symptoms, and her anaemia had responded to treatment. When last seen in November, 1950, she was perfectly fit and symptom-free, though radiographs showed an unhealed "pseudo-fracture" in the os pubis. She has been taking iron and adexolin intermittently since 1946.

Case 2

A collier's wife, aged 42, was a patient in a surgical ward in May, 1945, and she complained that for the previous seven years, since the birth of her second child, her left leg had been weak. During the previous two years the leg had been letting her down, and for 12 months the right leg had become weak and painful and she could walk only short distances with the aid of a stick. A week before admission she was noticed, for the first time in her life, to be jaundiced. While reporting on her Graham's test one of us (S.N.) noticed "pseudo-fractures" in the right lower ribs. The patient, however, discharged herself before investigations were completed.

She was admitted again in August, 1946, suffering from severe jaundice. This had been present ever since her attack in 1945. On examination she was icteric, her liver was slightly enlarged, and the power in her right leg was diminished because of pain. Her gait was very unsteady.

Radiological examination showed "pseudo-fractures" in both fibulae, both tibiae, both ulnae, and the right and left lower ribs. There was a little generalized osteoporosis. Laboratory findings showed hypochromic anaemia and confirmed the diagnosis of parenchymatous liver disease. The glucose-tolerance test showed a normal curve; the Wassermann reaction was negative.

She was given 30 gr. of calcium lactate and high-potency "ostelin" tablets (50,000 i.u. of vitamin D) four times a day. Iron and physiotherapy were also given.

After a month in hospital she went home and continued with this treatment. When seen in January, 1947, she was symptom-free except for her jaundice and was doing her own housework. Extra milk was prescribed and the ostelin reduced to one tablet weekly.

In June, 1947, she stopped all treatment apart from extra milk. In October, 1947, she still had some hypochromic anaemia and was still jaundiced. Her alkaline phosphatase was 42 King-Armstrong units. The patient then defaulted, and was next seen when admitted in January, 1949, complaining of the gradual onset, in the previous two months, of weakness and pain in her arms and legs. On this occasion her family and personal history were again carefully investigated, but no relevant facts were discovered. On examination she was icteric and pale. The liver edge was palpable 2 in. (5 cm.) below the costal margin with a hard non-tender surface. There was tenderness of the subcutaneous border of the left ulna and the outer part of the left clavicle. Her gait was duck-like.

Radiological examination showed healing of some of the "pseudo-fractures" noted previously and fresh ones in both fibulae and in the left ulna. Laboratory investigations showed hypochromic anaemia, low serum phosphorus, and normal serum calcium, and the results of liver-function tests were consistent with cirrhosis of the liver. To exclude the possibility of the de Toni-Fanconi syndrome (de Toni,

1933; Fanconi, 1936) urinary amino-acid and mineral excretion were estimated, with normal results. Investigations excluded the presence of steatorrhoea.

Treatment was instituted on similar lines as before, including 100,000 i.u. of vitamin D daily. After a stay of two weeks she was sent home and continued treatment there. Six weeks later she was free from bone pain and her gait was more normal. In May, 1949, vitamin-D therapy was discontinued for the time being, and she felt well in spite of her jaundice.

She was readmitted in October, 1949, with a history of the onset of ascites and sacral and lower-limb oedema two weeks previously. Laboratory investigations failed to show any new features. In spite of treatment she gradually sank into cholaemic coma and died on October 31, 1949.

At necropsy, 10 hours after death, the significant findings were the bile-stained cirrhotic liver and the bones which showed fusiform swellings at the sites of the by now completely healed "pseudo-fractures." Histological examination of many blocks from all organs of the body failed to show any significant changes except where naked-eye lesions had been seen at necropsy. The liver showed post-necrotic scarring (Himsworth, 1947). The bones showed no histological evidence of any active osteomalacia.

Case 3

A woman aged 62 was referred to the radiological department of the Crewe Memorial Hospital in November, 1946, by her own practitioner for a radiological examination of the ribs and vertebrae. She was complaining of a fairly localized pain in the region of the right ninth to twelfth ribs of some months' duration, and the presence of a neurofibroma was suspected.

The examination showed that "pseudo-fractures," fairly well established, were present in the right ninth, tenth, and eleventh ribs, and earlier ones were found in the left lower ribs. The dorsal vertebrae were normal. Films of various long bones failed to disclose any further "pseudo-fractures" and no appreciable bone porosis or calcium absorption was seen. The patient was never admitted to hospital, but was treated at home by her own practitioner with vitamin D and calcium, and there was much improvement in the symptoms. A year later it was reported that she was keeping well.

In June, 1948, the pain again recurred, and she was referred for further radiological examination. On this occasion no "pseudo-fractures" were seen, but there was a slight thickening at the sites of the previous "pseudo-fractures." This bout of pain subsided rapidly.

The patient ceased visiting the hospital in September, 1948, but a letter from her practitioner states that she is keeping in good general health "but has, to avoid exertion involving her back muscles," as this causes lumbago-like pain. No further radiological examinations have been carried out, and her doctor is of the opinion that the present pains are unrelated to any vitamin deficiency.

Owing to the limited facilities available at the time and the patient's age and rapid relief from pain, no extensive biochemical examinations were carried out. However, serum Ca and P examinations were within normal limits in 1946 and 1948 and no sugar or other abnormality was present in the urine. So far as could be ascertained there was no deficiency in her diet, and the cause of her condition was presumably a mild degree of raised resistance to vitamin D.

We are indebted to Dr. Francis Blacklay, of Nantwich, for the information he has supplied to us.

Discussion

Although at first these three cases appeared to be very dissimilar, closer comparison of the findings make us believe that we have examples of Albright's group A 2 (raised resistance to vitamin D: R. R. D.). A fully investigated case of this type was reported in this country by

McCance (1947). Our first case is a mild one, but in view of the still unhealed "pseudo-fracture" in her os pubis we think that only continued small supplementary doses of vitamin D will keep her symptom-free.

The second case was for a long time a very great problem. In many respects this patient resembled the case of the de Toni-Fanconi syndrome reported by Stowers and Dent (1947). This syndrome, which, however, usually occurs in children, consists of "pseudo-fractures" associated with rickets or osteomalacia, albuminuria, renal glycosuria, amino-aciduria, hypophosphataemia, and, frequently, cirrhosis of the liver. There is sometimes cystinosis with, or without, cystinuria. There is often consanguinity of the parents, and other blood relatives may show one or more features of the disease. Our patient, however, showed no albuminuria, renal glycosuria, or amino-aciduria. Extensive investigations failed to bring to light any relatives with features of the syndrome.

We feel, however, that on the basis of her history and the other findings we have a case of Milkman's syndrome of R.R.D. type complicated by massive fibrosis of the liver following infective hepatitis.

Another condition, atresia of the bile ducts in infancy, may be associated with rickets and "pseudo-fractures" (Gerstenberger, 1933).

Summary

The history and differential diagnosis of multiple "pseudo-fractures" are discussed and three cases are described.

Our thanks are due to Mr. John Young for the photographs of the x-ray plates.

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In terms of man days India loses about a thousand million days per year on the basis of an estimate of loss of one year per sufferer from tuberculosis (Chairman's Report, Tuberculosis Association of India, 1951). During the last three years there was an increase of about 3,000 beds for tuberculous patients in India. Tuberculosis training centres are being established at Delhi, Trivandrum, and Patna, and it is hoped that in the future every State will have at least one of these centres. The Indian Government is encouraging the association to train social workers, and every year there is a conference of tuberculosis workers. The last one was held at Hyderabad in February, and papers on domiciliary treatment, B.C.G., and so on were read and discussed.

Medical Memoranda

Aspiration Pneumonia Due to "Lethane" Hair-oil

Lethane hair-oil is a mixture of equal parts of β -butoxy- β' -thiocyano diethyl ether and white mineral oil, and is commonly used in the treatment of pediculosis capitis. No reference to its toxic effects can be found in the current literature and standard textbooks other than one fatal case reported by Harrison (1947). He described the case of a woman who died before admission to hospital, but the case was complicated by an appendix abscess found at necropsy.

In view of this it has been thought of interest to report the following case.

Case Report

A boy aged 20 months swallowed 1 to 2 dr. (3.5 to 7 ml.) of lethane hair-oil. He immediately coughed and spluttered, and was then given salt and water and two teaspoonfuls of syrup of figs by his mother, but did not immediately vomit. He then became drowsy and dyspnoeic, and was coughing. About 18 hours later, on three occasions, he vomited previously ingested food, then fell asleep, during which time he was seen occasionally to "twitch."

On admission to hospital on May 21, 1950, 24 hours after swallowing the lethane, he was drowsy, pale, and dyspnoeic, and was crying; he also had a hard dry cough. His temperature was 100.8° F. (38.2° C.), pulse rate 168, of good volume and regular, and B.P. 105/55. There was no meningism. Signs of bronchopneumonia were present at both lung bases. The spleen was just palpable. Tendon reflexes were present and equal, and the plantar responses were flexor. A stomach wash-out was attempted, but was abandoned when the child vomited blood-stained mucus.

He remained drowsy and miserable for about two weeks. There was slight neck rigidity only on the day after admission. The pneumonic signs, especially on the right side, increased for three or four days, then gradually diminished. An intermittent pyrexia up to 103° F. (39.4° C.) was present for five days, and the temperature did not become normal for a further seven days.

When discharged on June 10 the child was active, alert, and more cheerful. The only abnormal physical signs were harsh breath sounds in the right mid-zone.

Treatment, which included sulphamerazine, 1 g., followed by 0.5 g. eight-hourly, from May 21 to 29, and aqueous procaine penicillin, 300,000 units twice daily, from May 27 to 29, had no noticeable immediate effect on the temperature.

Investigations.—A blood count on June 24 showed: Hb, 64%; red cells, 3,300,000 per c.mm.; white cells, 9,000 per c.mm. (differential count normal). Radiographs of the chest showed consolidation of the right mid-zone on May 22, increased consolidation of the right mid-zone on May 25, and a little residual shadowing of the right upper zone on June 6. The cerebrospinal fluid was clear, colourless, and under normal pressure; the chemistry and cytology were normal. Examination of the sputum on May 22 and 26 showed the presence of fat globules, with normal pharyngeal flora on culture. The blood urea was 32 mg. per 100 ml. Liver-function tests were normal: serum colloidal gold, 0; thymol turbidity, 1.5; thymol flocculation, negative; serum bilirubin, 0.4 mg. per 100 ml.; alkaline phosphatase, 12 units (King-Armstrong).

Comment

Lethane hair-oil is an unpleasant substance, and it is probable that when it was initially swallowed the child choked and some was inhaled. This gave rise to an