CASE REPORTS

Osteomalacia following vagotomy and pyloroplasty

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Summary
Osteomalacia, due to defective absorption of adequate dietary vitamin D, has been found in a 79-year-old woman, 5 years after an anterior selective vagotomy and pyloroplasty.

The evolution of the recognition of postgastrectomy osteomalacia is reviewed, and reasons are advanced why similar problems are to be expected following vagotomy and pyloroplasty.

Case history
Mrs. J.L., a 79-year-old widowed housewife, had been first seen in 1950, complaining of dyspepsia. A barium meal and cholecystogram revealed no abnormality, and she was treated symptomatically. In 1960 a haematemesis with malaena followed self medication with aspirin for a cold; repeat barium meal was normal. She continued to complain of dyspepsia and, following the radiological demonstration of a lesser curve gastric ulcer, anterior selective vagotomy and pyloroplasty was performed by Mr H. Burge in February, 1964.

Postoperatively, dyspepsia continued and she developed dysphagia. She had transient episodes of diarrhoea and her weight fell to 101 lb, having remained steady around 120 lb for 13 years pre-operatively. A barium enema showed a few diverticulae, and a barium meal revealed gastro-oesophageal reflux with a hiatus hernia. Review of the previous barium meals found this to have been present before the operation. A Nissen repair was performed by Mr Burge in August 1965. The dyspepsia was relieved and has not recurred. Diarrhoea became more frequent postoperatively and was controlled with diphenoxylate (Lomotil). Her weight has remained 15–20 lb below her pre-operative weight, while her haemoglobin concentration remains between 14·0 and 15·6 g/100 ml.

In October 1968 she developed a constant ache in the left side of the sacrum with local bony tenderness; in December 1968 she developed a painful tender rib, and in January 1969 a painful tender area developed in the left humerus. These were the only abnormal physical findings in a thin cheerful elderly lady with no muscle weakness.

Investigations. Serum calcium 8·0 mg/100 ml, inorganic phosphate 2·8 mg/100 ml, alkaline phosphatase 16 KA units. Serum proteins—total 6·4 g/100 ml, albumin 4·1 g/100 ml. X-rays of the chest, pelvis, spine, humeri and hands revealed osteoarthritis of the right hip, lumbar spondylosis with a narrowed L1/2 intervertebral disc space, and diminished bone density. No fractures or pseudo-fractures were seen. Calcification of the aorta was present. A bone biopsy from the left iliac crest showed osteoporosis and moderately severe osteomalacia (Figs. 1 and 2). Blood urea, serum electrolytes and urine examination were normal.

Haemoglobin concentration 14·6 g/100 ml, white blood cells 3700 mm³ with a normal differential count, erythrocyte sedimentation rate 3 mm in the first hour (Westergren). Serum folic acid level 1·4 and 2·5 μg/ml. Red cell folate level 144 and 174 μg/ml. Serum vitamin B₁₂ level > 400 μg/ml. Bone marrow examination showed partially megaloblastic erythropoiesis with a few metamyelocytes and occasional hypersegmented polymorphs. Stainable iron was present in the erythroblasts. Serum iron 244 μg/100 ml.

Faecal fat excretion 8·7 g/day. Xylose excretion,
vitamin A absorption, glucose tolerance test and jejunal mucosal biopsy were normal. A small bowel meal showed stasis and flocculation of the barium in loops of gut which were dilated and in which the mucosal pattern was abnormal.

Dietary assessment showed that she consumed 1700 calories daily made up of 200 g protein and 71 g fat. Daily intake of calcium was 894 mg, vitamin D 114 i.u., iron 6.41 mg and folic acid 45·4 µg (cooked).

Progress. 10 mg vitamin D₃ was administered intramuscularly, and 2 g calcium with 15 mg folic acid were given by mouth daily. The biochemical results are shown in Fig. 3. After an initial rise, the serum alkaline phosphatase level fell to within normal limits by 3 months, by which time the serum calcium and inorganic phosphate had risen to normal. Total serum proteins and serum albumin levels remained unchanged. The serum calcium and inorganic phosphate product ranged from 17·6 to 24·4 before treatment commenced, and rose to above 30 thereafter.

The rib tenderness disappeared soon after treatment commenced; the tender area of the left humerus improved but is still present, and the left sacral pain and tenderness have remained unchanged. A repeat iliac crest bone biopsy was performed in March 1970 and showed normal calcification of bone (Figs. 4 and 5).

Discussion

The diagnosis of osteomalacia was suggested by spontaneous bone pain, and was confirmed biochemically and histologically. The absence of radiological changes, other than skeletal rarefaction, does not invalidate the diagnosis, and has been noted when this condition occurs after partial gastrectomy (Deller et al., 1964, Thompson, Lewis & Booth, 1966). The final confirmation of the diagnosis, and the demonstration that this was due to simple vitamin D deficiency, was the biochemical response to a small dose of vitamin D, as suggested by Morgan et al. (1965a), and return of the bone histology to normal. The initial increase in the level of serum alkaline phosphatase was noted also by Morgan et al. (1965b) in their patients. Recently Whittle et al. (1969) have described a rise in serum phosphate level following vitamin D (in their patients given intravenously) as a sensitive means of detecting deficiency of this vitamin.

Simple dietary deficiency of vitamin D causing osteomalacia in women has been increasingly recognized in Britain, most frequently in the elderly (Gough, Lloyd & Wills, 1964; Anderson et al., 1966; Exton-Smith, Hodkinson & Stanton, 1966; Chalmers et al., 1967) but occasionally in younger women (Dent & Smith, 1969). Where the dietary vitamin D
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FIG. 3. The results of serial serum alkaline phosphatase, calcium and inorganic phosphate estimation related to treatment.

FIG. 4. Biopsy 2. Lower power view of iliac crest material. Note absence of grey marginal osteoid seams shown in Fig. 1. There is now no evidence of osteoporosis. von Kossa, × 20.

FIG. 5. Higher power view of material shown in Fig. 4. Absence of osteoid seams is confirmed. von Kossa, × 80.
intake was estimated, it was found to be below 70 i.u. daily, which Dent & Smith (1969) regard as the minimum that would prevent the development of osteomalacia. Dietary analysis in our patient showed a daily intake of 115 i.u. vitamin D.

Simple deficiency of vitamin D can result also from malabsorption. In our patient steatorrhoea, together with an abnormal small bowel radiological pattern, was present. Preoperatively her measured body weight had remained steady for many years, while postoperatively marked loss of weight occurred. In the presence of an adequate caloric intake, this suggests malabsorption. Diarrhoea occurred postoperatively but this does not necessarily indicate the presence of steatorrhoea (Logan, 1964; Kraft et al., 1965). Folate deficiency was demonstrated by low serum and red cell folate levels, together with a partially megaloblastic bone marrow. Dietary folate intake was low at 45.4 μg daily and is likely to be the explanation (Neale & Hoffbrand, 1967), although malabsorption of folate has not been excluded. No cause, other than the vagotomy and pyloroplasty, was found to explain the malabsorption.

Osteomalacia is a recognized late complication of partial gastrectomy. Initial reports were of single cases (Pyrah & Smith, 1956; Hartley, 1957; Ellman & Irwin, 1959; Klipstein, 1962) or small series (Baird & Oleskey, 1957 (five cases); Melick & Benson, 1959 (two cases); Harvald, Krogsgaard & Louis, 1962 (three cases)). Surveys of postgastrectomy patients (Jones et al., 1962; Jones, Williams & Nicholson, 1963; Clark et al., 1964; Deller et al., 1964) then demonstrated a high incidence of skeletal abnormalities. The incidence of osteomalacia varied according to the criteria used for diagnosis, but abnormalities of calcium metabolism were found in 19–28%, with histological evidence of osteomalacia in a large proportion of those examined. A most comprehensive study by Morgan et al. (1965a) failed to confirm these findings, an incidence of less than 1% being claimed, but was disputed by Clark & Crooks (1965) because the rigid criteria used only recognized overt osteomalacia, the exclusion of patients with Paget's disease of bone ignored the possibility of coexisting disease, and because, if the unexplained elevated levels of serum alkaline phosphatase were due to osteomalacia, an incidence of more than 4% in males would result. This last hypothesis receives support from the subsequent finding (Thomson et al., 1966) that elevated serum alkaline phosphatase levels in post-gastrectomy patients were frequently due to osteomalacia and associated with low levels or absence of serum vitamin D. Too much emphasis must not be put on the serum alkaline phosphatase level, however, as there is evidence that the upper limit of normal rises with age (Roberts, 1967), and conversely, histologically proven osteomalacia may occur without secondary hyperparathyroidism and hence normal levels (Thalassinos, Wicht & Joplin, 1970). Support for the conclusion of Morgan et al. (1965a) was provided by Higgins & Pridie (1966) who, while following for 2 years those of 210 post-gastrectomy patients with biochemical or radiological abnormalities, found only one to deteriorate and require treatment. Coexistent Paget's disease of bone had confused the initial assessment of this patient. The incidence of osteomalacia following partial gastrectomy remains uncertain.

Postgastrectomy osteomalacia is caused by malabsorption of vitamin D. Duodenal bypass has been claimed to be of prime importance (Hillemand, Mialaret & Boutelier, 1960) on the basis of a patient's cure by conversion of his Billroth II to a Billroth I anastomosis. However, this patient received also vitamin D. Other experience with conversion operations has not confirmed the claim (Jones et al., 1962; Thompson et al., 1966; Williams, 1966). The site of vitamin D absorption in the human is not known, but Schacter, Finkelstein & Kowarski (1964) found the greatest absorptive capacity for vitamin D in the midjejunum of rats. Certainly, vitamin D malabsorption cannot be due to duodenal bypass alone, and the commoner association with Polyta as opposed to Billroth I gastrectomy may be because it is more frequently done (Thompson et al., 1966) and is more liable to cause steatorrhoea (Shingelton et al., 1957).

Steatorrhoea may also follow vagotomy associated with pyloroplasty (Logan, 1964), and there is no significant advantage for selective over truncal vagotomy in this respect (Baldwin et al., 1965; Kraft et al., 1965). Osteomalacia is thus to be expected following vagotomy and pyloroplasty (Wastell, 1967) but was not conclusively demonstrated in a survey of the nutritional states of patients after the operation (Wastell, 1969), and has apparently not yet been reported. Osteomalacia occurs years following partial gastrectomy, and it is thought to increase with the length of time from the operation (Jones et al., 1963). Vagotomy and pyloroplasty became an established surgical procedure years after the widespread use of partial gastrectomy, and the recognition of this complication might be expected following a similar time-interval. It was to be expected that this complication should first be described in a woman. The increased prevalence of osteomalacia in females was confirmed by the finding of postgastrectomy osteomalacia in four of 165 females as compared to two of 681 males (Morgan et al., 1965a). Clark et al. (1964) found a disturbance of calcium metabolism in five of seven females as compared to ten of forty-six males after partial gastrectomy.
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