Osteomalacia in the Elderly

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There is a dearth of studies on the long-term effects of treatment of osteomalacia in the elderly. This report describes the response of 20 patients treated with vitamin D for at least a year. Of the 20 patients, 18 were women. Ages ranged from 59-94, with a modal range of 80-89.

Diagnostic Criteria

The diagnosis was based on biochemical criteria and histological and/or X-ray findings. The subsequent changes in serum alkaline phosphatase (AP) in response to treatment with vitamin D may also be used as a retrospective criterion.

The pre-treatment biochemical data were based on an average of two estimations. The mean level of AP 314 iu/litre (range 109-720 iu/litre) was above the upper limit of normal (mean + 2 SD) for this age group[1] in all cases except one. In the one case with a serum AP at the upper limit of normal, the corrected serum calcium was 2.0 mmol/litre and the phosphate was 0.8 mmol/litre.

The mean serum calcium was below normal in 14 patients. Correction of the serum calcium on the basis of the total protein measured at the same time produced a level below normal in nine patients and a level at the lower limit of normal in five. Serum protein measurements were not available in the other six patients. The mean serum phosphate was 0.8 mmol/litre (range 0.4-1.5 mmol/litre) and was below the lower limit of normal (0.8 mmol/litre) in nine cases.

Eight patients had a bone biopsy showing a great excess of osteoid tissue, eight had X-rays showing Løsers zones, while four had both a 'positive' bone biopsy and Løsers zones. Levels of 25-hydroxycholecalciferol were not available for this series.

Causes of the Osteomalacia

The cause was established in a few cases only (Table 1).

| Cause            | Patients |
|------------------|----------|
| Malabsorption    | 4        |
| Postgastrectomy  | 1        |
| Gluten-sensitive enteropathy | 1 |
| Dietary          | 1        |
| Anticonvulsant   | 2        |

Table 2. Biochemical data prior to, and after, one year’s treatment.

|                      | Base Line | 1 Year |
|----------------------|-----------|--------|
|                      | Mean      | Range  | Mean  | Range   |
| AP (iu/litre)        | 314       | 109-720| 100   | 50-249  |
| Calcium (mmol/litre) | 2.1       | 1.6-2.5| 2.4   | 2.0-2.8 |
| Corrected calcium    | 2.1†      | 1.8-2.3| 2.4*  | 2.0-2.6 |
| Phosphate (mmol/litre)| 0.8      | 0.4-1.5| 1.2   | 0.7-1.6 |

†14 patients
*11 patients

Expressed as a percentage of the baseline AP, 13 patients showed an initial rise of 10-90 per cent so that after one month’s treatment the mean AP level for the whole group was 117 per cent of the baseline. This showed a steady fall so that in one year the mean level for the whole group was 36 per cent (Tables 2, 3 and Fig. 1). In 14 patients it took 3 months to one year for the level to reach normal, in four patients it took 2 years, while in one patient it took 2½ years. In two cases it had not fallen to normal at the time of death, while in one patient with concomitant Paget’s disease it did not reach normal even after 6 years, though the level fell by nearly 50 per cent in the first year.

Treatment

Initial treatment was with calciferol 1.25 mg daily, in 15 patients; smaller doses of calciferol in four patients and 1α-hydroxycholecalciferol 1 µg daily in one patient. Subsequent treatment was adjusted according to the results of regular biochemical estimations. These were carried out at approximately fortnightly intervals for the first month, monthly for the next 5 months, six-monthly for the next 18 months and thereafter annually. Any tendency to hypercalcaemia would necessitate more frequent estimations.

Biochemical Response

The serum phosphate was back to normal within one month of starting treatment in seven patients and within 4 months in the remaining two. The serum calcium was back to normal within one month in eight patients, within 4 months in three and in up to 3 years in the remaining three cases.

The serum AP fell in all patients so that after one year’s treatment the mean level was 100 iu/litre (Table 2).
Table 3. Serum alkaline phosphatase expressed as percentage of base line level in 20 patients on treatment with vitamin D.

| Time      | Mean and range | Standard deviation | Number of observations |
|-----------|----------------|--------------------|------------------------|
| 1 month   | 117 (60-182)   | 35                 | 18                     |
| 3 months  | 83 (41-149)    | 30                 | 10                     |
| 6 months  | 54 (14-91)     | 24                 | 16                     |
| 1 year    | 36 (12-80)     | 17                 | 18                     |
| 2 years   | 34 (16-59)     | 14                 | 11                     |
| 3 years   | 27 (13-50)     | 13                 | 11                     |

Subsequent Vitamin D Therapy

Response to treatment was satisfactory in 17 patients. Of 15 patients started on 1.25 mg calciferol orally daily, three were reduced within 3 months of starting, six between 3-12 months of starting and three between 1-2 years, but two were still on 1.25 mg calciferol daily after 3 years. One patient started on 0.25 mg calciferol daily remained on this same dose for 3 years, while one man with an obvious dietary osteomalacia was started on vitamin D 500 iu/daily. After 2 years this was reduced to 500 iu twice a week. One patient was treated with 1α-hydroxycholecalfetor (1α-HCC) 1 µg daily. Three patients showed a poor biochemical response. In one case the initial dose was doubled and then trebled and as there was still no response at 6 weeks, a single intravenous injection of 5 mg of calciferol was given. In a second patient the calciferol was doubled after 4 months. The patient started on 1µg of 1α-HCC was increased to 2 µg after 2 months and to 3 µg after 3 months. In all cases the subsequent biochemical response was satisfactory. Only two patients showed a transient hypercalcaemia of up to 2.7 mmol/litre necessitating temporary withdrawal of calciferol. In one case this occurred after 4 months’ treatment and in the other after 2 years. The return to normal was rapid and subsequent treatment was uneventful.

Clinical Response

Fourteen patients were immobile at the time of diagnosis, 11 were mobilised over periods of up to 3 months, while three patients remained immobile due to general frailty and conditions other than osteomalacia. The six patients who were mobile at the time of diagnosis had minor or no symptoms attributable to osteomalacia.

Discussion

The symptomatic response in this group was most gratifying, with 11 of the 14 immobile patients being mobilised over the course of 3 months. The three ‘failures’ appeared to be due to general frailty and other conditions. Rosin[3], in his study of osteomalacia in a geriatric unit, showed that in 10 patients who survived long enough for treatment bone pain went in 2 to 4 weeks and bone tenderness in 2 to 3 months.

The changes in AP may be used as supporting the initial diagnosis. The progressive fall was preceded by a ‘flare’ in 13 cases. Morgan et al.[4] showed a fall in serum AP in post-gastrectomy osteomalacia treated with vitamin D. Smith and Dick[5] in a study of 10 patients aged 19-75 showed a preliminary rise in AP in three patients, while Stamp[6], in a series of 45 patients (of whom all but two were Asian and all but six were under the age of 60) with nutritional osteomalacia, noted a preliminary rise in AP in about a quarter of the cases.

In the nine cases where analysis of the AP isoenzymes was available, it was shown that both the initial elevation and the subsequent fall was due to changes in the bone isoenzyme. This was of considerable interest in the
support it gives to the use of polyacrylamide gel electrophoresis in the analysis of AP isoenzymes[2], though it did not materially influence the clinical diagnosis and management in this series.

The initial dose of calciferol 1.25 mg daily would be regarded by many as high. However, with careful follow-up, only two transient episodes of hypercalcaemia occurred; the average follow-up period was 3½ years, with a range of 1 to 8 years. The calciferol was gradually reduced to as low as 1.25 mg per month. Annual blood checks were continued indefinitely.

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References
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Raynalde published at Venice in 1551 a work entitled Oyle Imperial which was printed by J. Grypihus. It seems unlikely Raynalde, the printer, would have been responsible for a work printed in Venice by another printer, while his press was issuing books in London. It is, of course, possible that the printer and physician were related. An interesting suggestion is that the physician was a graduate of Merton College, where he was a Fellow in 1520, and is known to have visited Paris. Through the influence of John Chamber, physician to Henry VIII, he became chaplain to Queen Jane Seymour. The fact that he was in orders would not necessarily prevent him from being a physician. Another of the same name was also a Fellow of Merton College and subsequently succeeded John Chamber as Warden of that College.

The title-page of the first edition of The Byrth of Mankind is of interest for its ornamental border, in particular the top-panel, which consists of a rose and cable with an empty shield, and illustrates how such devices passed from one printer to another. This border was first used by Wynkyn de Worde in 1521, when the shield included his device; it is known to have been used by four other printers before Thomas Raynalde, by which time the whole panel had been turned upside down and the shield became blank. The first edition, of which there were two issues, is not common, and copies with the birth figures are rare. They represent the first use of copper plate illustrations in England. The copy in the College library belonged to Samuel Merriman, consultant physician-accoucheur to the Middlesex Hospital, 1810-1825, who gave it to his son, Samuel William John in 1848; he was physician to the Royal Infirmary for Children. Dr Merriman had acquired the book from the sale of the library of Dr Combe in 1808. This same Dr Combe had also possessed the original manuscript of the translation which Jonas had presented to Queen Katherine; but its present whereabouts is unknown.

This English translation went through numerous editions in the age of Elizabeth and the early Stuarts; it survived through the Civil War and Commonwealth, greeting the Restoration and blossoming into its last edition in 1676. The German original had an even longer life; published in 1513, it was still in use in the eighteenth century, the last edition appearing in 1730. All this in spite of the fact that it was largely a compilation from the work of Soranous of Ephesus, an authority on obstetrics who practised in Rome about 100 AD.

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