Treatment of vitamin D deficient osteomalacia may unmask autonomous hyperparathyroidism

AVG Taylor, PH Wise

Summary

Two cases of vitamin D deficient osteomalacia with secondary hyperparathyroidism are presented. In both cases treatment with vitamin D replacement therapy resulted in elevated calcium levels and a failure of parathormone levels to normalise, indicating autonomous parathyroid activity. Subsequent surgery in one case resulted in removal of a parathyroid adenoma. The importance of osteomalacia and its complications are discussed.

Keywords: osteomalacia, vitamin D, hyperparathyroidism, Asians

The prevalence of osteomalacia in the British Asian community, its associated morbidity and the availability of simple treatment indicate that there is a continued need to identify and eliminate the disorder within this community. However, vitamin D replacement therapy may unmask autonomous hyperparathyroidism and monitoring of serum calcium levels is therefore mandatory. Two cases are presented.

Case reports

Case 1

A 43-year-old Kenyan Asian woman who had been living in the UK for 21 years was referred to the endocrine out-patients department by her general practitioner, with a two-year history

of generalised aches and pains and limping due to left hip pain. There was no history of joint swelling or fractures and investigations performed by the general practitioner suggested the possibility of osteomalacia, with a raised alkaline phosphatase of 988 U/l (reference values 90–250), a low serum phosphate of 0.1 mmol/l (0.6–1.4) and a normal corrected calcium of 2.4 mmol/l (2.15–2.55). She was not a vegetarian but her only dairy product was yoghurt. There was no history of liver or renal disease but recurrent iron deficiency anaemia had been treated with ferrous sulphate, although not further investigated. She described no abdominal symptoms and her periods were regular but heavy. Examination was unremarkable. A diagnosis of osteomalacia with secondary hyperparathyroidism was confirmed by a raised parathyroid hormone level of 560 ng/l (10–50) and a low 25-OH vitamin D level of 5 nmol/l (15–100). A bone scan showed multiple areas of increased uptake. X-Rays were normal, as was serum electrophoresis. Malabsorption was excluded by subsequent investigations and the cause of her iron deficiency was found to be dietary in nature.

Treatment was commenced with calcitriol 0.25 µg twice daily resulting in a fall in parathyroid hormone levels: however levels remained elevated above the normal range. Concurrently, serum calcium levels rose, indicating the unmasking of autonomous hyperparathyroidism; this is illustrated in figure 1. She was referred for surgery which resulted in excision of a left parathyroid adenoma.

Figure 1 Corrected calcium and parathyroid hormone (PTH) levels following vitamin D replacement therapy

Department of
Endocrinology,
Charing Cross
Hospital, London
W6 8RF, UK
AVG Taylor
PH Wise

Correspondence to
Dr AVG Taylor,
Consultant Physician &
Endocrinologist, Horton
General Hospital NHS
Trust, Oxford Road,
Banbury, Oxon
OX16 9AL, UK

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Figure 2 Corrected calcium and parathyroid hormone (PTH) levels following vitamin D replacement therapy

Following surgery, serum calcium and parathyroid hormone levels returned to the normal range. The patient remains well on vitamin D supplements but has made no attempt to alter her diet.

Case 2

A 54-year-old Asian man with insulin-dependent diabetes mellitus complained of lower limb pains during a consultation for review of his diabetes in 1989. There was no evidence of peripheral neuropathy or peripheral vascular disease. In view of his vegetarian habits 25-OH vitamin D levels were checked and found to be less than 5.0 nmol/l.

Renal function and repeated serum calcium levels were normal. He was commenced on alfacalcidol 0.5 µg daily with symptomatic improvement, although medication was only taken intermittently over the next five years. In 1994, hypercalcaemia was first noted in association with raised parathyroid hormone levels, as illustrated in figure 2, and this prompted discontinuation of alfacalcidol. Unsuppressed serum parathyroid hormone in association with raised calcium levels indicated autonomous parathyroid activity. Management is currently conservative in view of the only mildly elevated calcium levels.

Discussion

Osteomalacia is still a common problem in the British Asian community, affecting up to 20% of adult Asians.¹ It is also common in the institutionalised elderly.² The pathogenesis is multifactorial and involves reduced UV radiation exposure and dietary factors.³ The diagnosis can be made biochemically by the finding of low 25-OH vitamin D levels associated with elevated parathyroid hormone levels, but is often delayed because of non-specific symptoms and a lack of awareness. In case 1, two years elapsed from the onset of symptoms to presentation and others have reported similar findings.⁴

Prolonged or severe vitamin D deficiency

results in secondary hyperparathyroidism and the clinical syndrome of osteomalacia, which was present in both these patients. Correction of vitamin D deficiency usually results in normalisation of raised parathyroid hormone levels. The development of tertiary hyperparathyroidism, although well recognised in chronic renal failure, has only rarely been described in solar/nutritional vitamin D deficiency.^{5,6} It is indicated by persistently raised parathyroid hormone levels in association with hypercalcaemia following vitamin D replacement. The predominant histological findings are usually those of parathyroid hyperplasia,⁷ but adenomata have been described as in case 1.⁸ The finding of an adenoma also raised the possibility of primary hyperparathyroidism associated with vitamin D deficiency.⁹ It is for this reason that the term autonomous parathyroid activity is preferred.

Efficient methods of preventing vitamin D deficiency are now being implemented, particularly involving the annual or bi-annual administration of high-dose oral or intramuscular calciferol to major at-risk populations of Asians and elderly institutionalised patients. Whether primary or tertiary hyperparathyroidism, it is likely that the phenomenon represented by these two patients is occurring more frequently than is currently recognised, with potentially serious consequences. Vitamin D repletion may prevent the develop-

Summary points

- osteomalacia is still a common problem in the British Asian community, affecting up to 20% adult Asians
- prolonged osteomalacia is associated with autonomous hyperparathyroidism. This may only become apparent following vitamin D replacement therapy
- monitoring of serum calcium levels is mandatory in the treatment of osteomalacia for early detection of autonomous parathyroid activity

ment of autonomous parathyroid activity. However, it may also reveal it in those with either prolonged vitamin D deficiency or previously unrecognised primary hyperparathyroidism, a condition now known to be

present in at least 1:1000 of the population. Regular screening for hypercalcaemia in populations receiving such vitamin D repletion regimens is therefore considered to be mandatory.

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Meningismus, fever and macular rash as presenting features of the primary antiphospholipid syndrome?

Tim Houghton, Aeron G Davies

Summary

We report here, we believe for the first time, the primary antiphospholipid syndrome, presenting with fever, meningismus and skin rash. Serology was positive for antiphospholipid antibodies but negative for antinuclear factor. Such presentations, once meningitis has been excluded, should be screened for antiphospholipid antibodies. If serology proves to be positive, anticoagulation for life should be considered to avoid thrombotic episodes and death due to pulmonary embolism.

Keywords: antiphospholipid syndrome, meningismus, thrombosis

The antiphospholipid syndrome is a rare but increasingly recognised clinical entity. It was first described by Hughes in 1983¹ as a clinical condition presenting with widespread venous and arterial thrombosis in the presence of antiphospholipid antibodies. Features of this syndrome are widespread and varied, and include stroke, chorea, migraine, transient cerebral ischaemic attack,² livedo-reticularis,³ pulmonary hypertension,⁴ recurrent abortion,⁵ epilepsy, transverse myelopathy, valvular heart disease and ocular ischaemia.⁶ This list will probably be added to, as serological testing for antiphospholipid antibodies is now more general.

We describe the case of a young woman who presented with meningismus, fever and

macular rash and who was found to have positive serology for antiphospholipid antibodies.

Case report

A 21-year-old woman was admitted as an emergency with a 24-hour history of severe generalised headache and photophobia, neck-stiffness and rigors. She had a history of three miscarriages and a previous admission two years previously with headache and meningismus, with a normal computed tomography scan of brain.

Examination revealed an ill-looking woman with a pyrexia of 39.2°C, neck-stiffness, Kernig's sign and a generalised macular erythematous rash. There were no other neurological signs. Initial investigations revealed a polymorphonuclear leukocytosis of $12.1 \times 10^9/l$ (82% polys). C-Reactive protein (CRP) was >150 mg/l (normal range 1–15). Lumbar puncture and other haematological parameters were normal.

Initially a working diagnosis of possible meningococcal meningitis was made and the patient was commenced on high-dose intravenous benzylpenicillin. The following day she was much better and afebrile, but she still had the headache and macular rash. In view of the normal lumbar puncture and clinical improvement, the intravenous antibiotics were stopped. She continued to improve and on the day of discharge was well except for a low-grade pyrexia. Haematological parameters such as white cell count had returned to

Department of
General Medicine,
Bronglais General
Hospital, Aberyst-
wyth, Wales, UK
T Houghton
AG Davies

Correspondence to Dr
Tim Houghton, Royal
Hull Infirmary, Anlaby
Road, Hull HU3 2JZ, UK

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