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CASE REPORT

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Hungry bones without hypocalcaemia following parathyroidectomy

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Hungry bone syndrome is a complication of parathyroid surgery where the correction of primary hyperparathyroidism is associated with rapid bone remineralization, causing severe and prolonged hypocalcaemia [1]. We present a case of hungry bones where although there was rapid bone formation, the serum calcium was maintained within normal limits owing to the development of secondary hyperparathyroidism.

Case history

A 46-year-old woman with a recent traumatic rib fracture presented to our endocrine clinic after a dual-energy X-ray absorptiometry (DXA) scan was diagnostic of osteoporosis: *T* score lumbar spine –2.9 and femur –3.3. She had no risk factors for the development of osteoporosis except for a transient 9-month period of amenorrhoea attributed to excessive exercise 20 years previously. She was on no medication, and a physical examination was normal. Blood tests showed a markedly elevated serum ionized calcium of 2.3 mmol/l (1.19–1.35), normal serum inorganic phosphate of 0.89 mmol/l (0.80–1.40), an elevated serum parathyroid hormone (PTH) level of 1267 ng/l (2–52), 25 (OH) vitamin D of 127.5 nmol/l (recommended threshold >70 nmol/l), and mild elevation in serum creatinine of 152 µmol/l (53–97).

At presentation, blood and urine were obtained between 0700 and 0900 hours following an overnight fast in order to measure bone biomarkers: urine N-terminal telopeptide of type 1 collagen crosslinks (NTX-1) as a marker of bone resorption, and serum bone-specific bone alkaline phosphatase (BALP) as a marker of bone formation. The results of bone biomarkers are given in standardised units (*T* scores) based on comparison of results to our reference range for young adult women. *T* scores for both BALP and NTX-1 were markedly elevated at +10.52 and +15.95, respectively. We represented the bone remodelling balance as the difference between the bone formation and resorption markers: *T* score BALP minus *T* score NTX-1. At presentation, bone remodelling was in a negative balance at –5.43 (Table 1).

A sestimibi scan and neck ultrasound gave images which were consistent with a solitary right-sided parathyroid adenoma. At surgery, a single parathyroid adenoma was removed, 2.5 × 1.5 cm in size and weighing 1.5 g. No other parathyroid lesions were identified. Following parathyroid adenomectomy, serum calcium and renal function normalized and remained within normal limits, serum phosphate fell transiently to a nadir of 0.57 mmol/l (0.8–1.4), whilst serum magnesium remained within normal limits. Despite normocalcaemia post surgery, parathyroid hormone concentration remained elevated (PTH = 176 ng/l), although much lower than at presentation. Bone biomarkers demonstrated a reversal in the remodelling balance, with a *T* score of +7.37 as a consequence of a marked reduction in bone resorption with a sustained elevation in bone formation (see Table 1). A repeat DXA scan 6 months after surgery showed a 20% and 14% increase in bone density at the lumbar spine (*T* score = –1.5) and femur (*T* score = –2.6), respectively. Nine months after surgery, her PTH level was within the normal reference range (PTH = 49.7 ng/l); bone biomarkers still showed a positive remodelling balance at +1.88 (see Table 1).

Comment

Hungry bone syndrome occurs in 12% of patients postparathyroid adenomectomy for primary hyperparathy-

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Table 1. Bone formation and resorption markers pre- and post-parathyroid surgery

		Parathyroid surgery			
	Reference range	Before	3 months after	6 months after	9 months after
Serum ionised calcium	1.19–1.35 mmol/l	2.1	1.29	1.30	1.31
Serum PTH	2–50 ng/l	1267	176	120.8	49.7
Serum BALP	6.1–11.8 µg/l	41.7	27.8	11.5	8.7
BALP *T* score		+10.52	+6.03	+0.77	–0.13
NTX-1	25.5–72.40 nmol/mmol/l/creatinine	276	24.2	18.3	14.4
NTX-1 *T* score		+15.95	–1.34	–1.74	–2.01
Bone balance *T* score		–5.43	+7.37	+2.51	+1.88

PTH, parathyroid hormone; BALP, bone alkaline phasphatase; NTX-1, N-terminal telopeptide of type 1 collagen crosslinks

roidism, and is characterised by prolonged severe hypocalcaemia [1]. Risk factors for the development of hungry bone syndrome postparathyroid adenomectomy include a large parathyroid adenoma, high preoperative serum calcium, serum PTH, and serum alkaline phosphatase levels, the presence of osteitis fibrosa cystica, and old age [1].

In hyperparathyroidism, hypercalcaemia is mainly due to both increased bone turnover with predominant osteoclastic bone resorption and increased renal tubular reabsorption of calcium. After parathyroidectomy, the PTH stimulus is abruptly removed. The excessive osteoclastic activity therefore stops, but osteoblastic activity continues, resulting in a marked increase in bone uptake of calcium to facilitate bone formation, predisposing the patient to symptomatic hypocalcaemia. We interpret the findings in our case to indicate that the parathyroid glands detected this excessive flux of calcium from the serum into the bone and responded by increasing PTH secretion from the remaining parathyroid glands in order to maintain serum calcium within normal limits. The hyperparathyroidism observed postoperatively did not have a deleterious effect on bone formation, but rather was an important compensatory mechanism in maintaining normal serum calcium.

Hyperparathyroid bone disease entails an increase in bone turnover, usually with a negative bone balance per remodelling cycle such that primary hyperparathyroidism may be associated with bone loss that can be recouped following parathyroidectomy [2]. In our case of severe hyperparathyroidism, we noted a marked increase in indices of bone resorption and bone formation, but with a marked negative balance. Following successful parathyroid surgery the remodelling balance according to bone biomarkers was positive. The anticipated gain in bone mass was confirmed by the substantial increase in bone density of 14% at the spine and 20% at the femur on DXA after only 8 months. It is worth noting that the patient had a greater degree of bone loss at the femur than at the spine, and after surgery had a greater increase in bone mineral density at the femur than at the spine. This is in keeping with the presumed greater effect of PTH on cortical bone, which predominates at the femur, than on cancellous bone, which predominates at the spine.

One previous report demonstrated a similar finding of hyperparathyroidism in hungry bone syndrome persisting for 27 weeks postsurgery [3]. This case differed from our own as their patient developed hypocalcaemia in the immediate postoperative period, requiring intravenous calcium and vitamin D supplementation, unlike our patient who was able to maintain normocalcaemia throughout the postoperative period. The incidence of hungry bone syndrome following parathyroidectomy is decreasing because of earlier diagnoses of hyperparathyroidism, appropriate treatment before the development of significant bone disease, and improved preoperative care, with early recognition of the condition. Preoperative treatment with calcitriol for 5–10 days, with careful monitoring of the serum calcium particularly in patients with tertiary hyperparathyroidism [4], or the use of bisphosphonates [5] which inhibit osteoclastic bone resorption, may prevent the development of hungry bone syndrome post-parathyroidectomy.

The presence of normocalcaemia postparathyroidectomy for primary hyperparathyroidism does not exclude the phenomenon of hungry bones. Measurement of the bone remodelling balance allowed us to diagnose the condition and increased our understanding of our patient's bone turnover before and after parathyroid adenomectomy, as well as reassuring us that the postoperative hyperparathyroidism was a compensatory mechanism rather than the persistence of primary hyperparathyroidism.

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