

Recognition and Management of Hungry Bone Syndrome - A Case Report

A N Hisham, MS, E N Aina, MS, H Zanariah, MRCP*, Breast and Endocrine Surgical Unit, Departments of Surgery and *Medicine, Hospital Kuala Lumpur, 50586 Kuala Lumpur

Summary

Hungry bone syndrome (HBS) following successful parathyroid surgery is a well described phenomenon. However, few studies have clearly addressed this syndrome or looked at the outcome of perioperative management. We report a case of HBS following successful parathyroid surgery. The perioperative management is discussed and literature pertaining to this interesting case is reviewed.

Key Words: Primary hyperparathyroidism, Hungry bone syndrome, Bisphosphonates

Case Report

A 36 year-old Chinese man presented with generalised bone and joint pains for fifteen years. The pain had worsened progressively over the last six months and was associated with polyuria, polydipsia, malaise and weight loss. There was no previous history of renal calculi, pancreatitis or peptic ulcer disease. Clinical examination revealed an alert but anxious looking man. There was a palpable mass measuring 4 by 4cm at the left lower pole of thyroid gland.

Serum calcium was elevated to 2.98mmol/L (N: 2.1 - 2.6) whereas the serum phosphate was low 0.69mmol/L (N: 0.8 - 1.60). Serum alkaline phosphatase was 1607 IU/L (N: 53 - 128) and parathyroid hormone was markedly elevated to 804pgmol/1 (N: 10 - 60). Full blood count, serum electrolytes and renal profile were within normal limits. Skeletal radiograph showed florid metabolic bone changes of hyperparathyroidism. Ultrasound of the neck showed a large solid homogenous mass in the left lower pole of thyroid. Neck computed tomography (CT) scan confirmed of a large mass without evidence of local invasion. A presumptive diagnosis of primary hyperparathyroidism most likely due to a left inferior parathyroid adenoma was made.

Preoperative preparation was aimed at controlling the hypercalcaemia. He was hydrated with 6 - 8L of saline infusion daily and was given subcutaneous calcitonin two weeks prior to surgery. Postoperative hungry bone syndrome was predicted due to extensive bone involvement, marked elevation of serum alkaline phosphatase and parathyroid hormone. Hence, calcitonin and dihydroxy-vitamin D₃ (calcitriol) were instituted to reduce demineralisation of the bone. Although his bone pain resolved, the biochemical derangement remained unchanged (Fig. 1). However, when 60mg of intravenous bisphosphonate (disodium pamidronate) was added serum calcium level dropped further, whereas serum phosphate level normalised just before surgery. Serum alkaline phosphatase level also dropped after treatment (Fig. 2).

At surgery the parathyroid tumour was removed without much difficulty. The tumour weighed 15 grams and histological examination confirmed the diagnosis of parathyroid adenoma. As expected serum calcium dropped within first 48 hours of surgery to 1.8mmol/L and was associated with low serum phosphate of 0.43mmol/L (Fig.1). These biochemical indices were strongly suggestive of hungry bone syndrome. He was treated with intravenous calcium infusion, oral calcium

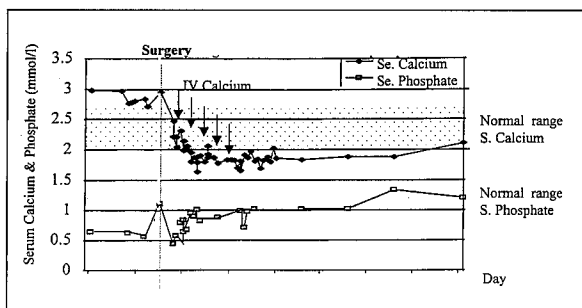


Fig. 1 Serum calcium and phosphate levels.

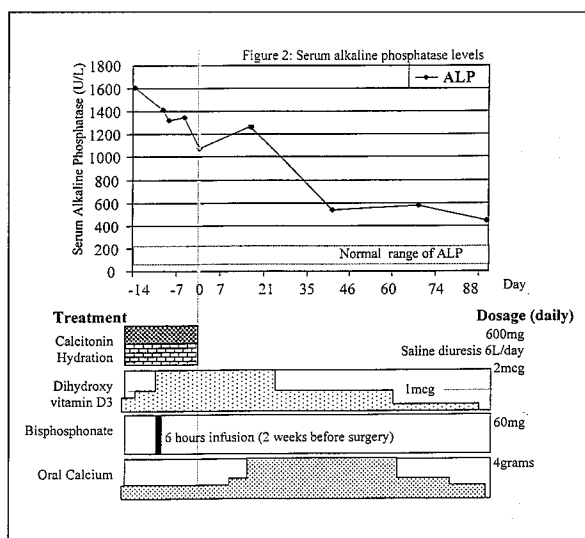


Fig. 2 Serum alkaline phosphatase levels.

supplements and dihydroxy-vitamin D₃. After three weeks serum calcium reached near normal levels whereas serum phosphate normalised within a week. Four weeks after surgery he was mildly hypocalcaemic but clinically asymptomatic.

Serum calcium normalised only after nine weeks and this may be attributed to the suppressive effect of the non-adenomatous parathyroid glands. It is interesting to note that alkaline phosphatase levels increased further after the surgery reflecting accelerated osteoblastic activity and bone remineralisation (Fig. 2). Alkaline phosphatase returned to normal only after three months.

Discussion

Hungry Bone Syndrome (HBS) following successful parathyroid surgery is not uncommon. In a study by Brasier et al, the incidence of HBS was 12.6% of 198 patients with primary hyperparathyroidism¹. Over the years it has been given less emphasis, as florid metabolic bone complications of hyperparathyroidism become a rarity.

HBS is characterised by prolonged and severe postoperative hypocalcaemia and hypophosphataemia as a result of extensive and accelerated remineralisation of bone following sudden decrease of parathyroid hormone^{1,2}. This syndrome should be anticipated when there is evidence of severe parathyroid bone disease with marked elevation of serum alkaline phosphatase and serum parathyroid hormone³. Risk factors predicting the development of HBS include age, high levels of alkaline phosphatase, blood urea nitrogen and size of adenoma¹. The size of the adenoma is the most important predictive factor.

We would like to emphasise the importance of appropriate preoperative management. A well-balanced approach is necessary to prevent preoperative fatal hypercalcaemic crisis and at the same time reduce the postoperative hypocalcaemic consequence of HBS. In most instances the metabolic derangement of HBS following successful surgery can be minimised or reduced by prophylactic preoperative treatment. This avoids prolonged and vigorous postoperative intravenous calcium infusion. However, no reports have examined the duration of the preoperative management and we would suggest at least two weeks preparation prior to surgical intervention. However, prolonged medical therapy is not always necessary or advantageous. It should be abandoned in favour of early operation if the patient's condition is deteriorating with recalcitrant hypercalcaemia⁴.

Preoperative treatment with dihydroxy-vitamin D₃ (calcitriol) has been used but its effect is variable^{2,3,4}. It is important to note that despite treatment with dihydroxy-vitamin D₃ and calcitonin, the occurrence of severe HBS has been documented². The preoperative management with inorganic phosphate has been abandoned because of lethal complications of pulmonary, soft tissue and intravascular calcium

CASE REPORT

deposition⁸. Bisphosphonates on the other hand which are commonly used in treatment of malignancy-related hypercalcaemia and Paget's disease have been shown to be beneficial in treating hypercalcaemia in primary hyperparathyroidism and hungry bone syndrome⁹.

Bisphosphonates are structurally related to pyrophosphates. They are safe and effective in controlling parathyroid-induced hypercalcaemia⁷. They have been used in treating symptomatic patients who require re-operation, whilst allowing time for localisation studies and also as an alternative to surgery in elderly patients who are old or fragile⁶. Furthermore, when force diuresis and other means of controlling hypercalcaemia fail, bisphosphonates provide optimal treatment.

The use of bisphosphonates in prevention of HBS has only recently been highlighted⁹. Although the exact mechanism is not well understood, bisphosphonates are known to have a potent osteoclastic inhibitory effect on bone. Moreover, they have a transient inhibitory effect

on mineralisation¹⁰. It has been postulated that in bisphosphonate-induced inhibition of mineralisation, reduction of calcium uptake by bone occurs and therefore indirectly reduces the likelihood of acute postoperative hypercalcaemia⁹.

It is interesting to note that preoperative bisphosphonate therapy not only reduces the severity of HBS but also shortens the course of postoperative calcium replacement following successful parathyroid surgery. In conclusion, this case report illustrates the need for careful perioperative management and emphasises the importance of anticipating HBS prior to surgical intervention.

Acknowledgements

The authors wish to thank Professor Dato' Khalid BAK for his assistance. We also thank the Director-General of Health Services, Malaysia, for his kind permission to publish this article.

References

1. Brasier AR, Nussbaum SR. Hungry bone syndrome: clinical and biochemical predictors of its occurrence after parathyroid surgery. *Am J Med* 1988; 84: 654-60.
2. Hisham AN, Meah FA, Abdullah T, Khalid BAK, Sakinah O, Tan TT. Hungry bone syndrome in a child following parathyroid surgery. *Asian J Surgery* 1995; 18(2): 147-49.
3. Cruz DN, Perazella MA. Biochemical Aberrations in a dialysis patient following parathyroidectomy. *Am J Kidney Dis* 1997; 29, (5): 759-62.
4. Murphy JP. Fatal hypercalcaemic crisis. *Hospital update* 1992; 18: 677-78.
5. Kaye M. Hungry bone syndrome after surgical parathyroidectomy. *Am J Kidney Dis* 1997; 30(5): 730-31.
6. Jansson S, Tisell LE, Linstedt G, Lundberg PA. Disodium pamidronate in the preoperative treatment of hypercalcaemia in patients with primary hyperparathyroidism. *Surgery* 199; 110: 480-86.
7. Goode AW. Parathyroid surgery. In: Taylor I, Johnson CD (eds). *Recent Advances in Surgery* 18. Churchill Livingstone 1995; 99-116.
8. Vernava AM, O'Neal LW, Palermo V. Lethal hyperparathyroid crisis: hazards of phosphate administration. *Surgery* 1987; 102: 941-48.
9. Kumar A, Ralston SH. Bisphosphonates prevent the hungry bone syndrome. *Nephron* 1996; 74 (4): 729.
10. Adamson BB, Gallacher SJ, Byars, Ralston SH, Boyle IT, Boyce BF. Mineralisation defects with pamidronate therapy for Paget's disease. *Lancet* 1993; 342: 1459-60.