Hungry Bone Syndrome due to Primary Parathyroid Adenoma with Multiple Bone Fractures

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ABSTRACT
Hungry bone syndrome (HBS) refers to the rapid, profound, and prolonged hypocalcemia associated with hypophosphatemia and hypomagnesemia which follows parathyroidectomy in patients with severe primary hyperparathyroidism (PHPT) and preoperative high bone turnover. It is a relatively uncommon, but serious adverse effect of parathyroidectomy. The severe hypocalcemia is believed to be due to increased influx of calcium into bone, due to the sudden removal of the effect of high circulating levels of PTH on osteoclastic resorption, leading to a decrease in the activation frequency of new remodeling sites and to a decrease in remodeling space, although there is no good documentation for this. Various risk factors have been suggested for the development of HBS, including older age, weight/volume of the resected parathyroid glands, radiological evidence of bone disease and vitamin D deficiency. The syndrome is reported in 25 to 90% of patients with radiological evidence of hyperparathyroid bone disease vs only 0 to 6% of patients without skeletal involvement. There is insufficient data-based evidence on the best means to treat, minimize or prevent this severe complication of parathyroidectomy. Treatment is aimed at replenishing the severe calcium deficit by using high doses of calcium supplemented by high doses of active metabolites of vitamin D. Preoperative treatment with bisphosphonates has been suggested to reduce postoperative hypocalcemia, but there are to date no prospective studies addressing this issue.

Keywords: Bisphosphonates, Hyperparathyroid bone disease, Osteoclastic resorption, Parathyroidectomy, Postoperative hypocalcemia.

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INTRODUCTION
The primary hyperparathyroidism is characterized by hypercalcemia due to increase of osteoclastic bone resorption. Parathyroid resection is the treatment of choice for patients of hyperparathyroidism with declining cortical bone density, nephro lithiasis and severe hypercalcemia.1 One of the common complications of parathyroid surgery is the development of hypocalcemia. It is hypocalcemia varies, due to the possible surgical removal of all parathyroid tissue and long-term hypercalcemic suppression of nonadenomatous parathyroid glands.1,2 Alternatively, hypocalcemia may be due to hungry bone syndrome (HBS), which is caused by massive calcium deposition in the bones after surgical treatment for PHPT.1 We report a case of prolonged HBS in a 16-year-old female with a parathyroid adenoma.

CASE REPORT
A 16-year-old girl came to the Emergency department on 16th December 2013 with the complain of severe pain in lower limbs with shortening of right lower limb. There was no familial history of any form of hyperparathyroidism. Patient was admitted 2 years back with a 6-month history of intermittent abdominal pain and easy fatigability operated for acute pancreatitis. Two months after the surgery suffered femur neck fracture following a trivial fall. The fracture was treated with closed reduction with internal fixation at MGM Hospital, CBD Belapur, Navi Mumbai, India. On physical examination, there was a bilateral genu varus, bilateral tibia vara, ulnar deviation at both wrists, bilateral valgus elbow deformity and spine deformity with anterior neck swelling in the region of thyroid which was soft and smooth surfaced. Her height was 132 cm, weight 22 kg, and blood pressure 96/68 mm Hg. Biochemical investigations are shown in Table 1. Elevated serum calcium levels, decreased serum phosphate concentrations, together with increased PTH level confirmed the diagnosis of PHPT. Ultrasound demonstrated large parathyroid adenoma of size 3.5 × 1.2 cm on the left side. Computerized Tomography (CT) neck confirmed the ultrasound findings. It showed a 2.1 × 2.1 × 2.3 cm mass on left side of neck displacing left thyroid gland anteriorly. Roentgenogram of the long bones of upper and lower extremities and spine revealed demineralization with cystic lesions and multiple fractures (Fig. 1). She underwent surgery where on neck exploration, a well defined mass of parathyroid, 2 × 3 × 2.5 mm

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One previous report demonstrated HBS persisting for 27 weeks postsurgery. Smith et al recommended that preoperative treatment with calcitriol for 5 to 10 days may prevent HBS in the postparathyroidectomy state.

In primary hyperparathyroidism, 25-hydroxy vitamin D concentration tends to below normal, while 1,25-dihydroxy vitamin D tends to be high normal. Bisphosphonates have a negative effect on bone remodeling and some authors recommended their use to prevent HBS in patients with PHPT. Hungry bone syndrome secondary to PHPT is transient. In this period, calcium supplementation is preferred over bisphosphonate treatment in children.

Brasier et al followed 198 adult patients after surgery for PHPT and studied the risk factors for the development of HBS. They reported a positive correlation with ageing, larger adenoma size, increased serum alkaline phosphatase levels, and elevated blood urea nitrogen levels. There has been no report on predictive risk factors for HBS in children with PHPT. Because bone metabolism is more active in children than in adult patients, HBS is more severe and frequent in young patients with PHPT.

Although, most patients with primary hyperparathyroidism demonstrate preserved vertebral bone marrow density (BMD), which mainly reflects cancellous bone, but this patient showed a significant loss of vertebral bone

### DISCUSSION

Hungry bone syndrome is considered to be present if the serum calcium levels are below 8.5 mg/dl and the serum phosphate levels are normal or below 3 mg/dl on the third day after parathyroidectomy. The predominant feature of the present case was the marked and a longstanding postoperative HBS. It can be explained by the long period of hypercalcemia secondary to parathyroid adenoma that resulted in atrophy of the healthy parathyroid glands.

**Table 1: Biochemical characteristics of the patient**

<table>
<thead>
<tr>
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<th>Parathyroid surgery</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum total calcium (mg/dl)</strong></td>
<td>12.62</td>
<td>8.8–10.6 mg/dl</td>
</tr>
<tr>
<td><strong>Serum alkaline phosphatase (U/L)</strong></td>
<td>2356</td>
<td>80–300 U/L</td>
</tr>
<tr>
<td><strong>Serum PTH (pg/ml)</strong></td>
<td>&gt;1900</td>
<td>15–68.3 pg/ml</td>
</tr>
<tr>
<td><strong>Blood urea nitrogen (mg/dl)</strong></td>
<td>6.1</td>
<td>5–15 mg/dl</td>
</tr>
<tr>
<td><strong>Serum vitamin D3 (ng/ml)</strong></td>
<td>25.490</td>
<td>30–100 ng/ml</td>
</tr>
<tr>
<td><strong>Spot urine Ca/Cr</strong></td>
<td></td>
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**Fig. 1:** Pretherapy X-ray pelvic both hips showing gross osteoporosis

**Fig. 2:** Post-therapy X-ray pelvic both hips showing mineralization and improved bone density

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in size, weighing 12 gm was excised. Light microscopic examination of the mass revealed a parathyroid adenoma. On the first postoperative day, the serum calcium level fell rapidly to 6.2 mg/dl.

Despite intravenous intermittent calcium supplementation, the serum calcium level remained less than 70 mg/dl and urinary calcium/creatinine ratio was consistently less than 0.05. Continuous intravenous and oral calcium supplementation was given for 20 weeks in form of injectable calcium gluconate in four divided doses of 200 mg per kg per day intravenously and calcium carbonate in two divided doses of 1 gm per day per orally respectively was given for 20 weeks and stopped. When serum phosphorus and alkaline phosphatase levels returned to normal limits 5 months after the operation, she had no symptoms and radiological evidence of mineralization of bone (Fig. 2).
density along with appendicular skeleton. There are a few reports on severely affected lumbar spine bone densitometry in adults with PHPT, but no report in children with PHPT is available. This finding may indicate that severely affected lumbar spine BMD at the diagnosis of PHPT may be used as one of the additional preoperative predictors of HBS in children. The presentation of PHPT in children is different from PHPT in adults, in whom the disease is usually less severe.10

CONCLUSION

It has been found that there was a reversible cancellous BMD loss in our patient with PHPT. Overt bone disease, raised alkaline phosphatase, decreased cancellous BMD and a large parathyroid adenoma may be used as preoperative predictive risk factors of HBS in pediatric patients with PHPT.

REFERENCES