ANAESTHETIC MANAGEMENT OF PRIMARY HYPERPARATHYROIDISM WITH RARE PRESENTATION OF MULTIPLE BROWN’S TUMOUR

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INTRODUCTION

Hyperparathyroidism (HPT) is a disease in which there may be a complex of biochemical, anatomic and clinical abnormalities resulting from increased secretion of parathyroid hormone (PTH). Hyperparathyroidism may be primary due to idiopathic hyperplasia which involves all four glands or parathyroid adenoma which is isolated involving only one gland or as a part of MEN1 with resultant hypercalcemia. Secondary hyperparathyroidism is usually secondary to electrolyte imbalance (Ca2+, PO43−) & CRF. Tertiary hyperparathyroidism is due to deficient response to parathyroid hormone at the level of receptor in kidney (renal resistance) in long standing cases of hyperparathyroidism and CRF with resultant autonomous function of parathyroid. A fourth type occurs due to ectopic hyperparathyroidism in patient with malignancy. Brown tumors are uncommon in secondary HPT and extremely rare in normocalcemic hyperparathyroidism patients. It has become increasingly rare to find multiple focal areas of demineralization of the skull; or ostitis fibrosa cystica (Brown tumour) as manifestations of the disease and it may be mistaken for primary skeletal neoplasm. Hence we review our experience of anesthetic management and systemic association of hyperparathyroidism with multiple brown’s tumour.

CASE REPORT

A 30 yrs female weighing 42 kg presented with multiple swellings over different areas of body since 6 months; which followed after pregnancy. There was no other associated complaints or any significant family history. On examination there were multiple bony swellings present as follows: a) Hard and mildly tender swelling right side body of mandible. b) Hard and non tender swelling present in left frontal region. c) Hard and non tender swelling present below left knee joint. Radiological evaluation of the above areas revealed an osteolytic lesion at all sites (Figure 1, 2, 3). Her serological investigation - Serum Alkaline phosphate: - 1080 IU/Lit (normal 245-770 IU/Lit) were also suggestive of increased osteoclastic activity. Serum Calcium was 10.2 mg/dl (borderline high) & serum phosphorous was 2.1 mg/dl (borderline low) raising the possibility of hyperparathyroidism which was confirmed by a markedly elevated assay of serum parathyroid hormone {>1900 pg/ml (normal: 11.1-79.5 pg/ml)}. USG neck (figure 4) revealed presence of hyperechoic lesion of size 21x10x11 mm on posterior-inferior aspect of left lobe of thyroid gland. A whole body CT scan for complete skeletal survey revealed multiple lytic expansile lesions involving whole skeleton and increase in size of parathyroid glands on left side (figure 5). The typical salt and pepper appearance on skull radiology and periarticular osteopenia on radiology of the hands was not very obvious. All other routine blood investigations were normal. Pre-operatively one day prior to surgery patient was given tab. Furosemide (20 mg) bd and inj. NS (0.9%) with inj.KCL (10 ml, equivalent to 20 meq of potassium) overnight.

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and morning serum calcium was done which was 8.2 mg/dl. Her hydration status and serum electrolytes were monitored during this forced saline diuresis therapy. The patient was then placed for left parathyroidectomy. Preoperatively, the patient was kept nil per orally after 10 pm. In the operating room, intravenous access was secured. The patient was connected to multipara monitor and monitored for electrocardiogram (ECG), non-invasive blood pressure (NIBP), oxygen saturation (SpO₂) and end tidal carbon dioxide (EtCO₂). Neuromuscular function was monitored with peripheral nerve stimulator. Premedication was given with inj. Ranitidine 50 mg iv, inj. Glycopyrrolate 0.2 mg iv, inj. Ondansetron 4 mg iv and inj. Midazolam 1mg iv. The patient was pre-oxygenated for 3 minutes, and was induced with inj. Thiopentone sodium 250 mg iv, inj. Succinylcoline 70mg iv administered to facilitate tracheal intubation. Anaesthesia was maintained with 66% nitrous oxide, oxygen 33% and isoflurane (0.5-1 vol%) and inj. Atracurium. Patient's ECG was continuously monitored to detect any change in cardiac rhythm due to altered calcium metabolism. Further boluses of atracurium were given on the basis of neuromuscular monitoring. Patient's heart rate and blood pressure were stable throughout the period of surgery. The surgery lasted for 1 hour 45 minutes. After completion of surgery, neuromuscular block was reversed with inj. Neostigmine 2 mg and inj. Glycopyrrolate 0.4 mg. During extubation the position of vocal cords was checked to assess any damage to recurrent laryngeal nerve. Postoperatively, the patient was kept in post anaesthesia care unit and was closely observed for signs and symptoms of hypocalcaemia. The patient was given a slow intravenous infusion of calcium gluconate after 24 hours postoperatively and then put on oral calcium with active vitamin D3 (calcitriol) to tide over the temporary hypocalcemia. Further boluses of atracurium were given to facilitate tracheal intubation. Anaesthesia was maintained with 66% nitrous oxide, oxygen 33% and isoflurane (0.5-1 vol%) and inj. Atracurium. Patient's ECG was continuously monitored to detect any change in cardiac rhythm due to altered calcium metabolism. Further boluses of atracurium were given on the basis of neuromuscular monitoring. Patient's heart rate and blood pressure were stable throughout the period of surgery. The surgery lasted for 1 hour 45 minutes. After completion of surgery, neuromuscular block was reversed with inj. Neostigmine 2 mg and inj. Glycopyrrolate 0.4 mg. During extubation the position of vocal cords was checked to assess any damage to recurrent laryngeal nerve. Postoperatively, the patient was kept in post anaesthesia care unit and was closely observed for signs and symptoms of hypocalcaemia. The patient was given a slow intravenous infusion of calcium gluconate after 24 hours postoperatively and then put on oral calcium with active vitamin D3 (calcitriol) to tide over the temporary hypocalcaemia that may occur after removal of the parathyroid tumour due to suppression of normal parathyroid activity. The parathyroid assay done postoperatively was now within normal range (23.5 pg/ml). Serum calcium levels were checked regularly. Her postoperative course was uneventful; the patient was discharged home with regular follow up at ENT outpatient department.

DISCUSSION

For unknown reasons hyperparathyroidism tend to present either with bone disease or with renal stones but never both. It is more common in the female gender with the majority of cases in the third to fifth decade as in our case. Skeletal involvement in “classical” primary hyperparathyroidism reflects a striking increase in osteoclastic bone resorption and is accompanied by a cellular repair process that results in the accumulation of fibrillar stroma and connective tissue cells along with multilnucleated giant cells and spicules of osteoid deposits. Thus the classical “brown tumor” of hyperparathyroidism is a collection of osteoclasts mixed with innocuous spindle cells and poorly mineralized woven bone. Even though the “brown tumor” can localize anywhere in the skeleton, the preferential locations are the head bones (particularly the mandible), and the ends of long bones and ribs. The rarity of multiple such lesions led us primarily to the differential diagnosis of fibrous dysplasia or less commonly a metastatic lesion. However the characteristic feature as in our case was the haemorrhage and haemosiderin deposits which impart the brownish colour and hence the term. Treatment of brown tumour is dependent on the treatment of hyperparathyroidism. Once serum calcium is normalized, the brown tumour may regress, or may require surgical resection. Resection is carried out in the majority of cases to achieve a definitive diagnosis. Primary hyperparathyroidism can be divided pathologically into adenomas (85%), hyperplasia (15%) and carcinomas (<1%). Histologically distinction between adenomas and hyperplasia is virtually impossible with an increased cell to fat ratio in both. Adenomas involve only one gland as in our case (left inferior parathyroid). Double adenomas are rare (5% cases). The major areas of debate surrounding primary hyperparathyroidism include a) Differentiation between adenomas and hyperplasia b) Whether medical therapy in mild cases of primary hyperthyroidism is appropriate c) Value of preoperative localization studies d) Unilateral versus bilateral neck dissection as a surgical approach. Melton concluded that long term medical therapy with calcitonin and bisphosphonates to reduce calcium level was costly and possible only in few cases of mild primary hyperparathyroidism with reversal of symptoms and bone density loss. 90-95% of adenomas can be found at neck exploration. Hence preoperative localization techniques like Thallium-Technetium subtraction scan, USG, CT, MRI and Arteriography, which are expensive are required in revision cases only. There are two schools of thought regarding surgical approach. Unilateral neck exploration with preoperative localization as in our case minimizes risk of recurrent laryngeal nerve injury and postoperative hypocalcaemia due to loss of vascularity to the normal parathyroid. Bilateral thorough neck exploration (including superior mediastinum and posteriorly upto prevertebral fascia) by an experienced surgeon even without preoperative localization increases cure at initial surgery. Variability in site and number of glands occurs in 20% cases. Gilmour found 4 glands in 80%; 3 glands in 13% and 5 in 6% cases. Wang noted aberrant parathyroid in mediastinum.
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in 18% cases. However the most common ectopic site was retroesophageal in the neck. Although there are no specific guidelines to conduct anaesthesia in patients with primary hyperparathyroidism with multiple brown’s tumour. One needs to be vigilant about various factors that might alter serum calcium levels. It is important to correct malnutrition and low albumin levels in the preoperative period. Preexisting hypertension, which is more common in primary hyperparathyroidism should be controlled if present. In the intraoperative period, special focus needs to be made on the acid base status and transfusion of large amounts of citrated blood; least life threatening hypocalcaemia may ensue. Continuous ECG monitoring in these patients is imperative as hypercalcaemia may be associated with disturbance in cardiac rhythm, although there is evidence that QT interval may not be a reliable index of changes in serum calcium concentrations during anaesthesia. Coexisting skeletal muscle weakness may decrease the requirement of muscle relaxant in this group of patients. A reduction in the duration of action of rocuronium has been reported in a patient with normocalcaemic hyperparathyroidism, hence neuromuscular monitoring is mandatory, if available, in this group.

Our patient was also monitored for neuromuscular blockade, although there was no alteration in the duration of action of muscle relaxant. Acidosis decreases calcium binding to albumin thus increasing the levels of ionized calcium, which can cause life threatening hypercalcaemia, hence it is important to maintain normocarbia. This is a point of concern while managing patients with hypercalcaemia. One of the serious complications in these patients is recurrent laryngeal nerve injury. Hence assessment of vocal cord movement during extubation is imperative. Other severe problems encountered during surgery are bleeding and permanent hypoparathyroidism. Postoperative hypoparathyroidism needs to be monitored carefully. A high index of suspicion may avert life threatening respiratory failure and concomitant ECG changes. Serum calcium level usually normalizes by 3rd - 4th day and thus needs to be checked at regular postoperative intervals.

Patients with primary hyperparathyroidism usually develop less severe hypocalcaemia that is amenable to calcium therapy and it should be routinely initiated following subtotal parathyroidectomy.

Our patient received IV calcium gluconate infusion after first 24 hours. Subsequently oral calcium therapy was instituted. Further, in the postoperative period, nonsteroidal anti-inflammatory drugs should be avoided for pain control in case there is renal function impairment. The following factors and their anaesthetic implications play a major role in successful outcome of patient of hyperparathyroidism with BROWN tumor Table 1.

CONCLUSION

In conclusion, it may be worth emphasizing that successful anaesthetic management of a patient with hyperparathyroidism requires vigilance for several factors that might potentiate adverse effects of hypo- and hypercalcaemia. These factors and their anaesthetic implications are summarized in Adequate preoperative assessment and preparation, close monitoring of the signs and symptoms of hypo and hypercalcaemia, restoration and keeping ionized calcium within normal limits during perioperative period can go a long way in the successful anaesthetic management of patients with abnormal calcium metabolism.

FIGURES & LEGENDS

Figure 1: OPG showing multilocular radiolucent lesion (arrow) present on right side of mandible involving body. Typical loss of lamina dura was not very evident.

Figure 2: X-RAY skull A/P view showing osteolytic lesion in left frontal region (arrow).
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Figure 3: X-RAY Left knee joint A/P & lateral view showing osteolytic lesion (arrow)

Figure 4: USG Colour Doppler of neck shows presence of hypo echoic lesion at inferior pole of left thyroid gland.

Figure 5: C.T.scan neck (axial view) showing (white arrow) parathyroid adenoma on left side posterior to thyroid gland.

Figure 6: Arrow showing parathyroid adenoma stained blue with methylene blue seen on posterior aspect of left lobe of thyroid (pulled anteriorly).

Table 1: Factors and their anaesthetic implications

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<thead>
<tr>
<th>Phase of operation</th>
<th>Anatomic/Physiologic Issue</th>
<th>Anaesthetic Implication</th>
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<tbody>
<tr>
<td>Preoperative</td>
<td>Factors influencing serum calcium: Malnutrition Low albumin • Hypertension • Renal function impairment</td>
<td>Correct nutrition and albumin level Control blood pressure Assess renal function</td>
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<td></td>
<td>Altered acid-base status (may lead to hypo-or hypercalcemia)</td>
<td>Citrated blood transfusion Continuous ECG monitoring May need less muscle relaxant Neuromuscular monitoring Care during positioning of patients Assess vocal cord movement during extubation</td>
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<tr>
<td></td>
<td>Skeletal muscle weakness</td>
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<td></td>
<td>Osteoporosis, pathological fractures</td>
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<td>Recurrent laryngeal nerve injury</td>
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<tr>
<td>Postoperative</td>
<td>Postoperative hypoparathyroidism</td>
<td>Check serum calcium regularity till 3-4 postoperative days Calcium therapy (IV/Oral) if needed Avoid NSAIDs</td>
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<tr>
<td></td>
<td>Renal function impairment</td>
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REFERENCES


