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Case Report

Hyperparathyroidism with Melaena a Rare Presentation – Case Report with Review of Literature

Ankit Raikhy[1], Sanjeev Kumar Choudhary[1], Annu Babu[1*], Karthik Shetty[2], Abhishek Bhartia[3], V. K. Bhartia[4]
[1]Senior Resident, Department of Minimal Access and Bariatric Surgery, CMRI , Kolkata, India
[2]Junior Resident, Department of Minimal Access and Bariatric Surgery, CMRI , Kolkata, India
[3]Consultant, Department of Minimal Access and Bariatric Surgery, CMRI, Kolkata, India
[4]Head of Department, Department of Minimal Access and Bariatric Surgery, CMRI, Kolkata, India

***Corresponding author**
Annu Babu
Email: drannubabu@yahoo.co.in

Abstract: Hyperparathyroidism presenting with a Gastrointestinal bleed is a rare occurence, and is mostly associated with an parathyroid adenoma. In primary hyperparathyroidism, the incidence of gastrointestinal bleeding is greater in patients with MEN syndrome and is rarely seen in patients with only a parathyroid adenoma/hyperplasia . In case of tertiary hyperparathyroidism, it is known that CKD patients have a significantly deranged clotting mechanism due to altered nitrous oxide (NO) metabolism and uraemic toxemia. Also erosive gastritis and angiodysplasia are frequent causes of upper G.I bleeding in these patients. We here by present a case report of 63 years old male presented with complaints of passing blackish stools along with multiple episodes of nausea and vomiting since 15 days with a background of known case of hypertension , with chronic kidney disease which was recently diagnosed and being treated. Per rectal examination done was having stool mixed with black colored blood. The upper G.I endoscopy was suggestive of ulcer at the duodenum part one with no active bleed and colonoscopy was normal . Further investigations were done and it was found that patient had a raised 24hr urinary calcium levels of 294 mg\dl and a parathyroid hormone levels of 1732.1 pg\ml. Tc 99 sestamibi scan shown single left lower parathyroid nodule, hence diagnosis of primary hyperparathyroidism was made and patient underwent an open parathyroidectomy . The HPE of the resected specimen revealed a parathyroid adenoma. In post operative follow up patient is doing well. This type of case report is very less reported in literature.
Keywords: Chronic kidney disease, Duodenal ulcer, Hyperparathyroidism, Melaena.

INTRODUCTION

Usually there are four parathyroid all situated posterior to the thyroid gland. A few number of patient may have 3-5 glands. The inferior parathyroid is derived from third pharyngeal pouch. It has embryonic relation with the thymus. The superior parathyroid is more consistent in the position and located superior to the intersection of inferior thyroid artery and recurrent laryngeal nerve. Embryologically originates from the fourth pharyngeal pouch. There are instances where the superior gland is found in the thyroid stroma.

Hyperparathyroidism occurs due to the increased production of parathyroid hormone [1]. Occurs either the parathyroid gland is making too much of the hormone or there is increased production due to the factors (secondary hyperparathyroidism) [2]. Mostly the patients rarely present with the symptoms [3]. The kidney stones are the most common symptom, other symptoms include weakness ,depression ,bone pains, confusion, and increased frequency of urination [2]. The bones are weak in both type of hyperparathyroidism. Primary hypothyroidism occurs in 80% cases are due to parathyroid adenoma. Most of the cases due to multiple benign tumors. The parathyroid cancer is rare. Secondary hyperparathyroidism occurs in due to vitamin D deficiency, CKD, and low blood sodium. The primary disease is diagnosed by high Parathyroid hormone (PTH) and high calcium level [4]. Tertiary hyperthyroidism occurs in patients with long standing chronic renal disease.

CASE REPORT

A 63 years old male patient was brought to our hospital with complaints of passing blackish stools along with multiple episodes of nausea and vomiting since 15 days with a background of known case of hypertension with chronic kidney disease which was recently diagnosed and being treated. Patient had a history of generalized body ache and fever few weeks back. On examination, patient was found to have tachycardia (100 beat per minute) and a blood pressure of 120/70 mm of Hg with Pallor. On per abdomen examination patient had soft abdomen, no tenderness,

no guarding , no rigidity and no palpable lump. Per rectal examination done showed stool mixed with black colored blood. Systemic examination was within normal limits. On routine blood investigations, Hb-8.3 gm\dl , calcium-13.36 mg\dl , albumin-3.1 gm\dl, potassium-5.4 mmol\L, urea-40 mg\dl, creatinine-2.64 mg\dl, phosphate-2.1 mg\dl, Vitamin D3-8ng\dl. Patient was put on conservative management with IV fluids , Antibiotics, Pantroprazole infusion, Analgesics, Packed Red Blood Cell transfusion and admitted in ICU care for further investigation and monitoring .

On radiological investigation USG of abdomen shows - B\L Renal medullary calcifications, whereas the upper G.I endoscopy was suggestive of ulcer at the duodenum part one (Figure 1) and Colonoscopy was normal. Patient stabilised in next 24 hours and was shifted to ward . Where his blood electrolyte was done which was suggestive of Hyperclacemia with Serum Calcium level of 13.36mg/dl . Further investigations were done and it was found that patient had a raised 24hr urinary calcium levels of 294 mg\dl and a parathyroid hormone levels of 1732.1 pg\ml. A Tc 99m sestamibi parathyroid scan was done showing sustained enhanced uptake at the lower pole of left lower lobe of thyroid gland (Figure 2) which was suggestive of a solitary parathyroid tumor or hyperplasia . Hence, a diagnosis of primary hyperparathyroidism was made since the renal condition of the patient was detected very recently and that the parathyroid adenoma in a tertiary hyperparathyroidism case is seen only in advanced cases of End stage renal disease (ESRD) .

Subsequently, patient underwent an open parathyroidectomy (Figure 3) with a transverse cervical incision after examining the rest of the parathyroid glands. Intraoperatively, post-excision of diseased gland, parathyroid hormone values dropped to 124.2 pg\ml within first 10 minutes. The HPE of the resected specimen (Figure 4) revealed a parathyroid adenoma. Post operative period was uneventful .Serial monitoring of serum calcium was done and the serum calcium level was normal . Wound was healthy (Figure 5) and patient was discharged on post operartive day four . In follow up period patient is doing well .

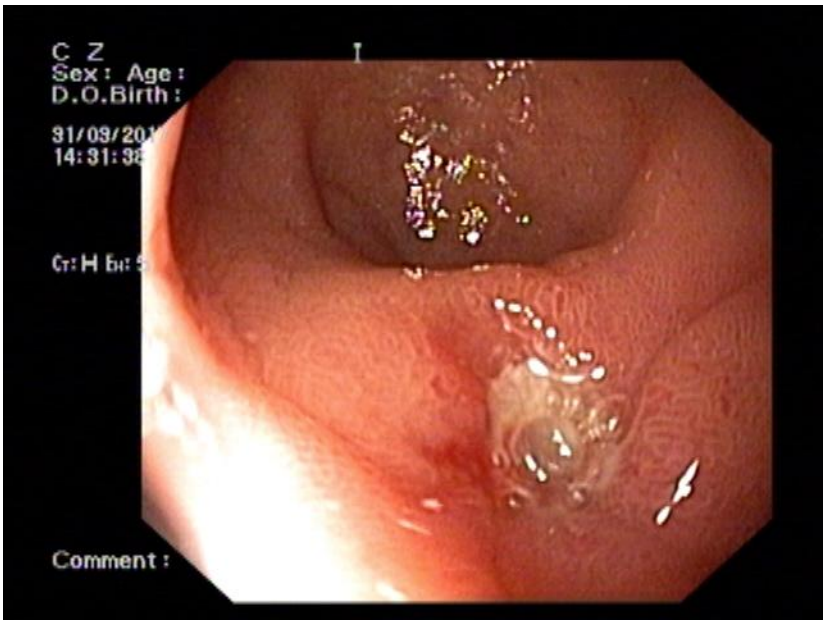

Fig-1: Upper G I endoscopy showing ulcer in duodenum

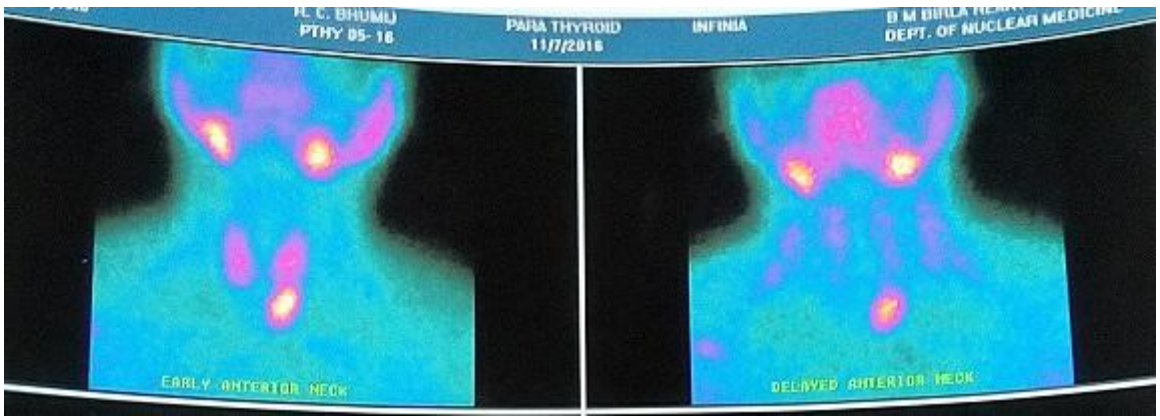

Fig-2: Tc 99m Sestamibi scan showing the increased uptake at the left lower thyroid

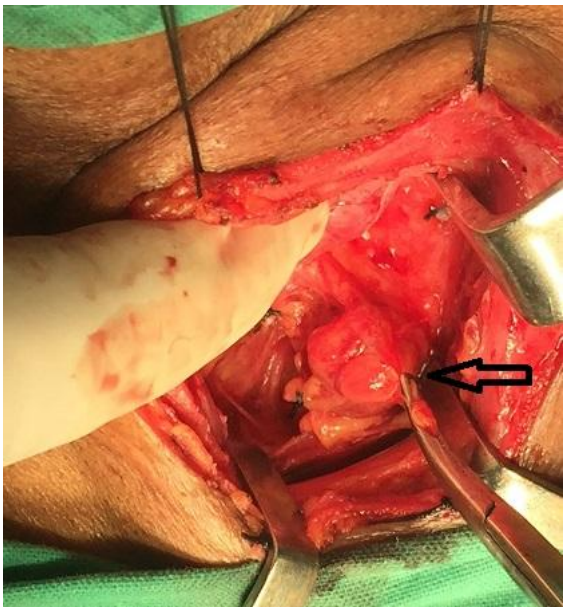

Fig-3: Intraoperative enlarged left lower parathyroid gland

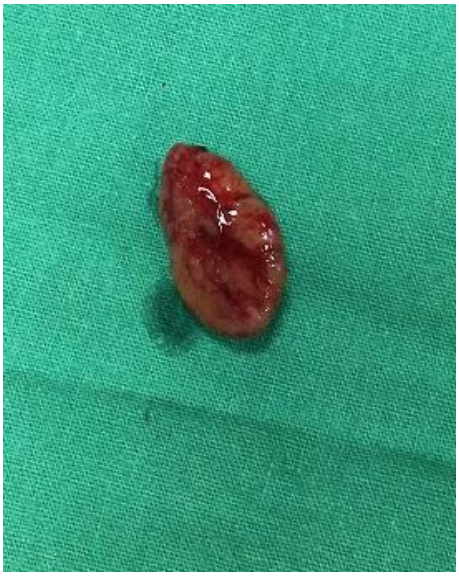

Fig-4: Resected specimen of left lower parathyroid

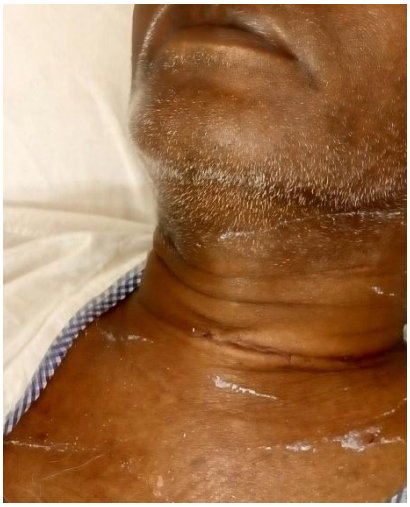

Fig-5: Post operative wound

DISCUSSION

Greep [5] in 1963 as well as Pang and Epple [6] in 1980 brought into light that parathyroid gland originally appeared 100 million years ago, with the evolution of amphibians. This development of gland led transition of life to the terrestrial from the marine life which had high calcium content in aquatic life. The parathyroid glands first noted by Remark (1815-1865) [7] and in 1863 by Virchow(1821-1922) [8]. The correlation of parathyroid activity with disease of bone was by Schlagenhaufer [9]. He suggested that in patients with osteitis fibrosa cystica only one parathyroid was enlarged and its removal would cure disease. The was tested by a Viennese surgeon Felix Mandl [4] who removed the parathyroid gland from the patient with osteitis fibrosa cystica , which resulted in the correction of condition. The disease recurred in the patient seven year later and patient finally died of the disease. Sir Richard Owen (1804-1892) [10] Professor at Royal College of Surgeons of England, first described the parathyroid gland in 1852. In his honour the parathyroid gland was named Gland of Owen by Cave in 1953. Swedish born Sandstrom (1852-1889) was credited in discovering and naming the glands [11]. He studied the neck anatomy of various animals, cat, dog, rabbit, Ox and then finally humans where he found pea shaped glands at the inferior margin of thyroid. He named it "glandulae Parathyroidae".

His study was published in the local journal of Sweden. These findings were not taken serious until brought to light by Gley (1857-1930) [12] who studied the significance of parathyroid gland.

The first time description of the harmone was made by Moussu [13] 1898, by treating the tetany in dogs following parathyroidectomy with horse parathyroid extracts. In 1909 MacCallum and Voeghin (1879-1960) proposed the calcium level in plasma is controlled by parathyroid harmone. In 1909, Berkeley and Beebe [14] prepared the extract for the treatment of tetany due to parathyroidectomy. The pure form of parathyroid was extracted by Rasmussen and Gravy 1959 [15]. The purity of substance was sufficiently high and research confirmed it to be polypeptide hormone.

It was in 1864 that Engel [16] described the parathyroid adenoma and skeletal disease. Albright (1900-1969) and Bloomberg *et al* [17] described that the primary hyperparathyroidism was due to a single adenoma of one gland and also the parathyroid carcinoma. The first operated patient of parathyroidectomy was Charles Martell. Martell was operated twice in 1926 but without success. He was again operated fifth time for parathyroid in 1932 by Churchill [18] and Cope. This time they removed 3cm parathyroid tumor from the mediastinum after opening the chest. Unfortunately the patient died and this was followed by the era of parathyroid surgeries.

Normal gland measure the ionized calcium level in the blood, the PTH hormone secretion is inversely related to the ionized calcium levels [19]. The parathyroid hormone is 84 amino acid polypeptide. The half life of parathyroid hormone is 5 min. The main role of parathyroid hormone is to increase plasma level of calcium, increase absorption of calcium from the gut and kidneys. It also increases the level of calcitriol which also plays role in the absorption of calcium from gut.

The primary hyperparathyroidism is commonest form [2]. In developed world 1-4 per 1000 people are affected[20]. Women tend to have common occurrence about 3 times more common than man. Typical age of presentation is 50-60 years. There is 85% prevalence of primary hyperthyroidism due to adenoma in western population. In 15%cases, multiple glands are involved (hyperplasia or adenoma) [2]. The familial causes include Multiple endocrine neoplasia syndrome (MEN 1 and MEN 2a), hyperparathyroidism Jaw Tumor syndrome, or familial isolated hyperparathyroidism (FIHPT). Familial hypocalciuric hypercalcemia and neonatal severe hyperparathyroidism also belong to this category. The inactivation of MEN1 gene is the cause of molecular basis of this MEN 1 mutation, located on 11q13. MEN 2a is caused due to mutation in germ line of Ret proto-oncogene on chromosome ten [20]. The parathyroid adenoma/hyperplasia is the most common manifestation MEN 1 syndrome. Hyperparathyroidism occurs in 95% MEN1 syndrome this may be associated with pancreatic tumors and pituitary adenoma. The pancreatic tumors may be functional with elevated pancreatic polypeptide, gastrin or insulin levels. The pancreatic tumors in MEN 1 may be non functional too. The radiation exposure is also known to increase the risk of primary hyperparathyroidism and also associated with MEN syndrome [2].

In primary hyperparathyroidism the normal feed back due to extracellular calcium is lost results in change in set point. In case of primary hyperparathyroidism due to hyperplasia there is increase in number of cells. This chronic absorption can result in osteopenia, resulting in osteitis fibrosa cystic, with sub periosteal bone resorption and salt pepper appearance of the skull.

The secondary hyperthyroidism occurs due to the renal failure with decreased vitamin D levels and low calcium levels and high parathyroid hormone level. Cinacalcet is drug for controlling the parathyroid hormone levels in secondary hyperparathyroidism. The tertiary hyperparathyroidism occurs in patients with end stage renal disease. At the end stage renal disease the patient has resistance to Cinacalcet and PTH hormone is consistently high , It needs surgery for parathyroid gland removal.

Symptoms depends on whether the disease is primary or secondary. In 75% patient with primary disease are asymptomatic [2]. Many patients have non specific complaints. Symptoms related to the hypercalcemia is more common in malignant disease. These symptoms are weakness, fatigue, depression, myalgia, decreased appetite, feeling of nausea, vomiting, constipation, polyuria, congnitive impairment, osteoporosis and kidney stones [21]. Bone resorption can be indicated by examining the nails which may be Raquet nails (brachyonychia) [22]. Surgical removal of gland treats the symptoms in most of the patient. In the secondary hyperparathyroidism the parathyroid gland is normal and the serum calcium levels may be low or normal. Clinically the problem of bone syndromes occur such as rickets, osteomalacia, and renal osteodystropy [22].

In our case patient presented with very unusual combination of symptoms of passage of black tarry stools for which patient was evaluated with UGI endoscopy showing ulcer at duodenal part one and colonoscopy that was normal. The further diagnosis was made on the high calcium levels and high parathyroid levels. The peptic ulcer disease is poorly related to primary hyperparathyroidism, pathophysiology is still not known. However there have been few cases of peptic ulcer bleed due to primary hyperparathyroidism [23, 24].

Dan Xie *et al* [25] reported a case of Peptic ulcer bleeding due to Primary Hyperthyroidism in a 42 year old male. Patient had to under go the angiographic embolisation of bleeding vessel and Billroth 2 Gastrointestinal anastomosis was done. A complete work up showed that patient had primary Hyperparathyroidism with duodenal ulcer bleeding. Patient was then taken up for elective parathyroidectomy and the histology was confirmatory of a typical adenoma of parathyroid gland. Another study done by Sato H *et al*. [26] was suggestive of abnormally high pH in the stomach in patients with primary hyperparathyroidism and patient having positive H.pylori. The author further suggested that in H.pylori infected patient the Hypercalcemic conditions due to hyperparathyroidism promoted gastroduodenal diseases through induction of proinflamatory cytokines or increasing the attachment of H.pylori to the gastric epithelial cells. The pH level normalizes after the Parathroidectomy. Sarter S *et al*. [27]reported a case of female patient with upper Gastrointestinal bleeding from duodenum which was found out to be result of adenoma of parathyroid with the clinical feature of osteodystrophia fibrosa cystic generalisata. Patient was treated with parathyroidectomy. Goretzki PE *et al*. [28] investigated 61 patients with primary and 15 patients with secondary Hyperparathyroidism were operated at the surgical unit at Dusseldorf, out of which three cases of bleeding due to ulceration and one perforation of the ulceration was noted. The author suggested the role of high calcium levels in the causation of ulcer.

Here in our patient we also can take the MEN1 syndrome (WERMER Syndrome) as it is at a times associated with functional pancreatic tumors which can produce Gastrin and cause the Zollinger elison syndrome. For ruling out the diagnosis we need to have the CECT abdomen along with S. Gastrin levels. Hyperparathyroidism (HPT) presenting with a Gastrointestinal bleed is a rare occurence, and is mostly associated with an parathyroid adenoma. Adenomas, usually single, accounts for 94% cases of primary HPT [29]. Our patient suffered from acute-on-chronic renal failure, most likely due to hypercalcemia. Serum calcium concentrations from 12 to 15 mg/dl have been shown to decrease GFR by direct vasoconstriction and natriuresis leading to volume depletion and pre-renal azotemia [30]. In case of tertiary hyperparathyroidism, it is known that CKD patients have a significantly deranged clotting mechanism due to altered nitrous oxide (NO) metabolism and uraemic toxemia. Also erosive gastritis and angiodysplasia are frequent causes of upper GI bleeding in these patients [31]. In primary hyperparathyroidism, the incidence of gastrointestinal bleeding is greater in patients with MEN syndrome and is rarely seen in patients with only a parathyroid growth [32]. Excision of the abnormal parathyroid gland is the main option in primary HPT with excellent prognosis. Further follow-up can be done with serum gastrin, prolactin and calcitonin patients with clinical indications for MEN syndromes.

CONCLUSION

This case report is remarkable for its rare clinical presentation of melaena in a patient with hypercalcemia, acute-on-chronic kidney injury and markedly elevated PTH levels . We here by concluded that in a patient presented with malaena measurement of serum calcium level play important role in excluding primary hyperparathyroidism.

CONSENT

Written and informed consent was obtained from the patient for publication of this Case report and any accompanying images.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

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