

CASE REPORTS

PARATHYROID ADENOMA: PRESENTED AS AN ACUTE ABDOMEN

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Abstract:

Primary hyperparathyroidism is a rare disease, but commonly associated with parathyroid adenoma and causes hypercalcemia with its systemic manifestations. In this case, a 23 years old women was accidentally identified as hyperparathyroidism with parathyroid adenoma by biochemical (high serum calcium and parathyroid hormone) and imaging study (sonography of neck and abdomen) while being investigated for her severe abdominal pain with vomiting and prolong history of bone and joint pain, fatigue and nonspecific systemic manifestation. Having undergone medical resuscitation for 20 days, a neck exploration revealed enlarged grayish mass near upper pole of the both thyroid., which were excised. Histological investigations revealed a parathyroid adenoma with hyperplastic changes with no features of malignancy. After complete removal of bilateral adenoma of about parathyroid hormone and serum calcium fall to normal level very quickly. This suspicious presentation of benign disease, including a marked elevation in parathyroid hormone, highlights the challenges facing the endocrine surgeon in dealing with parathyroid.

Key words: parathyroid adenoma, hyperparathyroidism, acute abdomen.

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Introduction

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder, after diabetes mellitus and thyroid disease [has an incidence between 1 in 1000 and 1 in 200]¹. Adenoma of parathyroid gland is the most common cause of hyperparathyroidism accounting for 90% of the cases. It is usually a disease of adults and more common in women (1:500) than in men (1:2000) ratio of nearly 4:1².

Most parathyroid adenomas are functional and manifest hypercalcemia causing bone fractures and urinary tract calculi³. So-called classic, specific symptoms (i.e., bone disease, renal stones, and hypercalcemic crisis) represent obvious manifestations of the disease. The clinical features associated with

primary hyperparathyroidism have changed during recent years. The relative proportion of patients with these classic symptoms has continuously decreased in clinical series because of the increase in the number of patients with nonspecific or in apparent symptoms. Nonspecific symptoms will include malaise, fatigue, depression and other psychiatric symptoms, sleep disturbance, loss of weight, abdominal pains, constipation, vague musculoskeletal pains in the extremities, and muscular weakness⁴.

Many patients are asymptomatic or have mild symptoms that may be elicited only upon questioning⁵. Parathyroid adenomas are usually so small and deeply located in the neck that they are almost never palpable; when a mass is palpated, it usually turns out to be an incidental thyroid nodule⁶. At present, over two-

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thirds of patients are detected by routine screening. Hypercalcemia of hyperparathyroidism is typically discovered accidentally by routine chemistry panels. Most patients are identified by an incidental finding of raised serum calcium during investigations for another condition.

High serum calcium is highly suggestive if unexplained but not diagnostic. But serum parathyroid hormone (PTH) concentration in the presence of hypercalcaemia confirms the diagnosis⁷. The CT and ^{99m}Tc—MIBI were more accurate than ultrasonography in locating the adenoma.

Most parathyroid adenomas are solitary and in rare cases can be multiple⁸. Differentiation between the hyperplasia and adenoma is important in terms of the clinical management. Surgery is the only curative treatment for primary HPT with parathyroid adenoma. In 80% of patients, these clinical manifestations improve or disappear after parathyroidectomy⁹. The resection of the adenoma is considered curative while the surgeon needs to remove three glands and possibly a portion of the fourth to treat hyperplasia. As a result strict criteria have been proposed for diagnosing adenomas of parathyroid gland¹⁰.

Case Presentation:

A 23 years old married nuliparous female admitted to the Department of Surgery of Dhaka Medical College Hospital, Dhaka, with the complaint of severe lower abdominal pain, more on right iliac fossa with frequent bouts of vomiting last 2 days on 11-11-2010. She was clinically diagnosed as acute appendicitis and medically managed. She had a history of generalized weakness, body ache and noticeable weight lost with a frequent episode of headache, bone pain (particularly at the epiphysial end of the long bone) and joint pain for 3 years. Her menstrual cycle was irregular and bowel not moved regularly (constipation). She also complains about frequent attack of heart burn and recurrent episode of abdominal pain with vomiting for last one years. Her attended reported that she always used to be in a depressed mood, like to sleep all day long,

fatigue easily and avoid social contact. Regarding such history and complaints she was referred to medicine department to identify concomitant medical problem.

On examination, she was found anemic, dehydrated, with normal blood pressure, heart rate, chest and abdomen (no point of tenderness, muscle guard or distension). Neck examine revealed normal finding. She had no other history of any medical conditions, previous surgery, major trauma and radiotherapy. She reported no significant family history of such shorts of problem.

On laboratory investigation, she was found anaemic (Hb%=7.5%) with increase random blood sugar level of 13.5 mmol/l. Other haematological picture and cell counts were within normal limits. Serum electrolytes were also within normal limit (Na⁺ 145 mmol/l, K⁺ 4.mmol/l, Cl⁻ 111mmol/l CO₂ 27mmol/l). Serum calcium was elevated (15.38mg/dl) with low Phosphorus level 1.6mg/dl), high urinary calcium (900mg/24hours), serum amylase, lipase, creatinine, uric acid, and albumin were found normal. Her serum parathormone (PTH) level found high (158 pg/ml) with normal thyroid hormone level (fT3=2.98pmol/l fT4=20.830pmol/l, and TSH= 0.33 iu/ml). Lipid profiles were normal. Urine out put were normal, no apparent pathology found in routine microscopic examination of urine. Urinary amylase was low (167u/l).

Ultrasonography of whole the abdomen revealed some echogenic material with posterior acoustic shadow within the lumen of gall bladder, may be granular bile or multiple calculi. There was an elongated hypoechoic area with internal irregular echogenecities, which may represent grossly swollen and edematous body and tail of the pancreas. There are multiple calcifications are also seen within the parenchyma. Both kidneys are swollen and echogenic with no evidence of calculi. Chest radiograph found normal. ECG finding showed tachycaedia with prolonged PR interval and abnormal ST segment.

Ultrasonography of the neck showed a elongated, fairly uniform hypoechoic, solid soft tissue mass, measuring about 2.6 cm x 12 cm

x 1.9 cm had seen in the region of right upper parathyroid gland. Another smaller soft tissue mass, measuring about 1.4 cm x 0.7 cm x 0.7 cm had also found in the region of left upper parathyroid gland. Thyroid gland is slightly enlarged in size. It was suggestive of bilateral parotid adenoma or hyperplasia. Thyroid scan (with intravenous Tc ^{99m} pertechnetate 2mci) revealed normal. MRI showed oval shaped well circumscribed soft tissue mass lesion in both the superior parathyroid regions. Right one was larger than left one. These mass showed isointense in T1WI and hyper-intense in T2WI. Perilesional fat plane is maintained. No intralesional calcification, necrosis or haemorrhage had seen. No ectopic mass and definite cervical lymphadenopathy were detected.

She was transferred to the Medicine unit of the same hospital on 02.12.2010 as hyperparathyroidism with hypercalcaemia. Here she was investigated and conservatively managed regarding her medical condition. She had referred to the ENT and Head-Neck surgery department on 29. 12. 2010 for surgical removal of the adenoma from both side of the parotid region. On the 2nd of January, 2011, she was operated under general anesthesia by a horizontal crease line neck incision at the level of thyroid cartilage. Per operatively there were two distinct swelling found on the both the posterior border of the upper pole of the thyroid. Both the mass were excised with intact capsule by dissection along the capsular plane from the thyroid tissue. Thyroid tissue kept intact. Right one was bigger (about 2gm) than left one (1.2gm). Homeostasis was ensured and neck wound was closed in layers. Recovery was uneventful. Histological examination revealed small nesting pattern of growth of an adenoma with uniform pattern of chief cells and disappearance of fat even in the absence of an increase in gland weight. This also showed a thin fibrous capsule with no capsular penetration. On the 2nd postoperative day, i.e. 03. 01. 2011, the serum parathyroid hormone, was found dramatically reduced from 158 pg/ml (preoperatively) to 3pg/ml (postoperatively). Serum calcium level also reduced to 9.1 mg/dl, with slight raised of serum phosphorus (1.6gm/dl to 2.2mg/dl). Subsequently her

features of GIT upset (nausea, vomiting and lower abdominal pain) were improved. Her neurological condition, mental status and well being were improving in her subsequent follow up with in two weeks. Her parathyroid hormone level, serum calcium, serum phosphorus, amylase, urinary calcium, Hb% and blood glucose level were found normal during her last postoperative visit on 15. 01. 2011.

Discussion

Primary hyperparathyroidism is a generalized disorder characterized by chronic poorly regulated excessive secretion of parathyroid hormone (PTH) by one or more parathyroid glands that results in hypercalcemia. Both familial and sporadic forms exist. The most common cause of primary hyperparathyroidism is a solitary parathyroid adenoma [90%] arising in the sporadic (nonfamilial) setting, Primary multiglandular hyperplasia (diffuse or nodular)[5% to 10%]and Parathyroid carcinoma [1%] are the other causes.¹¹

It is usually a disease of adults, most patients having adenomas are between 50 to 60 years of age.¹² The prevalence of primary hyperparathyroidism in the general population is at 0.1% to 0.3% and in women older than 60 years more than 1%.^{13,14,15} Every woman has a 1% risk of experiencing primary hyperparathyroidism during her lifetime. There is a distinct predilection for this disease to have higher incidence in women, especially those patients beyond menopause. The prevalence rate among women was approximately 13 per 1000, which represented a female/male ratio of about 4:1. This experience is similar to that of other published reports.^{16,,17,18} In our case, the patient was a young female of 23 years old married nulliparous woman.

The exact cause of primary hyperparathyroidism is unknown, although exposure to low-dose therapeutic ionizing radiation, intermittent exposure to sunshine, various diets, Lithium therapy and familial predisposition account for some cases¹⁹. The patient had no suspicious history of exposure and family history.

Parathyroid adenomas seem to be monoclonal or oligoclonal neoplasms, whereby the mechanism of propagation is thought to be clonal expansion of cells that have an altered sensitivity to calcium. The molecular events that seem to trigger clonal propagation are heterogeneous.

Parathyroid adenoma may occur in any of those four parathyroid glands but they are most often located in the inferior parathyroid glands than superior glands. In 6–10% of patients, parathyroid adenomas may be located in the thymus, the thyroid, the pericardium, or behind the esophagus. Parathyroid adenoma typically involves a single gland however multiple adenomas either unilateral or bilateral have been reported¹⁹. Patient had two sizeable adenomas on both the upper parathyroid gland. Patients with two adenomas usually have higher PTH level but here the PTH level was elevated but not so higher to be suspicious. When adenomas involve two parathyroid glands the distinction from parathyroid hyperplasia can be difficult. Parathyroid gland hyperplasia by definition involves all four parathyroid glands but hyperplasia can happen in an asymmetric form with two glands being more prominent than the others. So strict clinical criteria must be applied to diagnose double adenomas even though these criteria are sometimes confusing.^{20,21}

Adenomas are usually 0.5–5 g in size but may be as large as 20–50 g (normal glands weigh 25 mg on average). In this case right one was bigger [about 2gm] than left one [1.2gm]. Histologic examination reveals small nesting pattern of growth of an adenoma with uniform pattern of chief cells and disappearance of fat even in the absence of an increase in gland weight. This also shows a thin fibrous capsule with no capsular penetration. Chief cells are predominant in both hyperplasia and adenoma (chief cell adenoma). Variations in parathyroid adenoma includes other subtypes (oncocyctic adenoma, lipoadenoma, large clear cell adenoma, water-clear cell adenoma, and atypical adenoma).

Many patients with parathyroid adenomas are asymptomatic or have mild symptoms that may

be elicited only upon questioning. They are usually so small and deeply located in the neck that they are almost never palpable; when a mass is palpated, it usually turns out to be an incidental thyroid nodule. It has been estimated, however, that approximately 90% of people with primary hyperparathyroidism remain undiagnosed.²² At present, over two-thirds of patients are detected by routine screening. Hypercalcemia of hyperparathyroidism is typically discovered accidentally by routine chemistry panels. Most patients are identified by an incidental finding of raised serum calcium during investigations for another condition.²⁰ The screening of serum calcium has been a particularly important factor leading to the detection of patients with mild symptoms or no symptoms, especially among postmenopausal women¹³.

Historically, patients presented with long-term complications related to “stones, bones, abdominal groans, and psychic moans, with fatigue overtones.” The manifestations are categorized as urinary tract, skeletal, and those associated with hypercalcemia.¹⁵

- Renal stones/nephrocalcinosis
- Bones: aches and arthralgias, weakness, bone and joint pain.
- Groans: abdominal pain from constipation, pancreatitis, or peptic ulcer disease
- Psychic moans: mood swings, fatigue, anxiety, mild depression, or memory loss.

This patient present with severe lower abdominal pain, more on right iliac fossa with frequent bouts of vomiting which was clinically diagnosed as acute appendicitis She had a history of generalized weakness, body ache and noticeable weight lost with a frequent episode of headache, bone pain (particularly at the epiphysial end of the long bone) and joint pain. Her menstrual cycle was irregular and bowel not moved regularly (constipation). She was always in depressed mood, like to sleep all day long, fatigue easily and avoid social contact.

Primary hyperparathyroidism is commonly characterized by hypercalcemia, hypophosphatemia and excessive bone resorption.¹³ Large rises in PTH levels in benign parathyroid

disease are unusual and have been associated with more sinister diseases.¹⁷

During presentation serum calcium ($\text{Ca}^{+}=15.8$ mg/dl), PTH (161pg/ml), amylase (30-110u/l), Lipase (956 u/l) and urinary calcium (940 mg/dl) level of the patient were found high (*table-II*). Hematological report was normal (*table-III*). High serum calcium is highly suggestive if unexplained but not diagnostic. But serum parathyroid hormone (PTH) concentration in the presence of hypercalcaemia confirms the diagnosis (e.g. bone metastases of breast, renal, thyroid carcinoma have a low or inhibited PTH concentration). Very rarely reports of parathyroid adenomas that were not associated with hyperparathyroidism¹⁶ or normocalcemic²². Other associated laboratory abnormalities include: hypophosphatemia (50%), hypomagnesemia (5–10%), and an elevated alkaline phosphatase, a marker for bone disease. Many patients will have a chloride-to-phosphate ratio greater than 30. Urinary calcium levels are either normal or elevated, however, low urinary calcium level (<50 mg/24 h) in familial hypocalcuric hypercalcemia should be ruled out. Bone mineral densitometry can help determine the effects of hyperparathyroidism on bone loss and assess the need for operative intervention.

Ultrasonography of the neck showed an elongated, fairly uniform hypoechoic, solid soft tissue mass on both the upper parathyroid region, which was suggestive of bilateral parotid adenoma or hyperplasia.

MRI showed oval shaped well circumscribed soft tissue mass lesion in both the superior parathyroid regions. These mass showed isointense in T1WI and hyper-intense in T2WI. Perilesional fat plane is maintained. No intralésional calcification, necrosis or haemorrhage had seen. No ectopic mass and definite cervical lymphadenopathy were detected.

High-resolution neck ultrasound may identify tumours. ^{99m}Tc sestamibi scintigraphy (radioisotope) scanning especially when combined with SPECT used to localize adenomas (accurate in 50%)²⁰ and allows a focused approach (minimally invasive parathyroidectomy).

For the detection and localization of parathyroid adenomas and improved surgeons' ability to localize parathyroid adenomas preoperatively a double-phase imaging procedure with ^{99m}Tc sestamibi is important²¹. However, sestamibi scan may be positive in different benign and malignant thyroid tumours.²⁰ This underscores the need of an integrated approach using the combination of sestamibi scan with other imaging modalities (e.g. in our case thyroid scintigraphy) in the differential diagnosis of selected cases of primary hyperparathyroidism, especially when associated to multinodular thyroids, and/or after failure of previous parathyroid surgery. Computed tomography (CT), magnetic resonance imaging (MRI), and thallous chloride Tl 201-technetium Tc 99m pertechnetate subtraction scanning are another noninvasive preoperative localization modalities. Unfortunately ^{99m}Tc sestamibi scan was not done due to unavailability during that time.

Patients with primary hyperparathyroidism appear to have a shortened life expectancy, they have an increased risk of dying prematurely (even after surgery), mainly from cardiovascular and malignant disease. Younger patients and those with less severe disease have better prognosis¹¹.

Surgery is the only curative treatment for primary HPT with parathyroid adenoma. In 80% of patients, these clinical manifestations improve or disappear after parathyroidectomy¹⁵. However the rate of recurrence is estimated at 10%.²³ In general, surgery is contraindicated in FHH¹⁶. In this case after removal of parathyroid adenoma all the biochemical features e.g. serum calcium and PTH become normal on second postoperative day and in next follow up.

Conclusion

Bilateral parathyroid adenoma is a rare condition. Most parathyroid adenomas are functional and manifest hypercalcemia causing classic bone disease, renal stones, and hypercalcemic crisis, represent obvious manifestations of the disease. But unusual presentation also need through investigation for such condition.

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