Case Report

The diagnostic and therapeutic challenges in the management of a double giant parathyroid adenoma

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ABSTRACT

Primary hyperparathyroidism is a common endocrine disorder of the parathyroid gland. It is mostly seen as a single gland adenoma in up to 85% of the cases with the excess production of parathyroid hormone. Double adenomas although reported are very rare and double giant parathyroid adenomas are even rarer. We possibly report the second case in the literature of primary hyperparathyroidism caused by double giant parathyroid adenomas, presenting with severe symptomatic hypercalcemia and review the diagnostic and therapeutic challenges in its management. The presentation with severe hypercalcemia and the presence of atypia in one of the adenomas added to its uniqueness. A combination of the neck ultrasound and a parathyroid scintigraphy should be used for preoperative localization and selection of the right surgical approach for patients undergoing parathyroidectomy. The parathyroid scintigraphic protocols keep getting refined; it is hence vitally important and practical to adapt the diagnostic algorithms in accordance with local availability and expertise.

Keywords: Atypical parathyroid adenoma, double giant parathyroid adenoma, primary hyperparathyroidism, single photon emission computed tomography-computed tomography, Tc99 m SestaMIBI scintigraphy

INTRODUCTION

Primary hyperparathyroidism is a condition characterized by the inappropriate secretion of parathyroid hormone with respect to the extracellular calcium concentration. It may result from the enlargement of a single gland (solitary parathyroid adenoma) in approximately 85% of cases, parathyroid hyperplasia in 15–20% of patients, and parathyroid carcinoma in about 1% of patients.[1] Double parathyroid adenomas have been reported to very rarely occur.[2] We possibly report the second case in the literature of primary hyperparathyroidism caused by double giant parathyroid adenoma,[3] presenting with severe symptomatic hypercalcemia and discuss the diagnostic and therapeutic challenges in its management.

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CASE REPORT

A 34-year-old man was evaluated by his general physician for generalized body pains, malaise, and fatigue for 6 months. Further evaluation revealed a right pelvi-ureteric junction calculus and multiple other calculi in the inferior calyx of a nonfunctional right kidney for which he had undergone a laparoscopic right nephrectomy. Persistence of his symptoms prompted further clinical evaluation by a magnetic resonance imaging of the spine which showed diffusely altered marrow signals in all vertebrae and a mild disc bulge at D6–D7 level. Computed tomography (CT) scan of the neck and chest revealed two lesions, one in the left upper paratracheal and the other in the pretracheal region (reported as enlarged lymph nodes) measuring 4 cm × 2 cm and 3 cm × 2 cm in addition to minimal bilateral basal atelectasis [Figure 1a and b].

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He was subsequently referred to our center for ruling out a possible malignancy. Biochemical evaluation at our center revealed severe hypercalcemia (serum calcium: 15.2 mg/dl); the levels of serum parathormone (PTH) were also elevated (1789 pg/ml). An ultrasound of the neck picked up the lesions in the left lower neck and anterior mediastinum as seen in the CT scan suggesting a possibility of double giant parathyroid adenoma. A Tc99 m SestaMIBI scintigraphy done subsequently demonstrated only a solitary persistent retention of the SestaMIBI tracer in the region of the left inferior parathyroid gland [Figure 2]. The second adenoma was interestingly not captured in the conventional anterior planar MIBI scintigraphy possibly as the adenomas were seen to be overlapping (as also demonstrated in Figure 1a and b CT scan images). A lateral/oblique imaging was unfortunately not available for confirmation of the same. It would be prudent to mention that the facility for a hybrid Tc99 m SestaMIBI single photon emission computed tomography/computed tomography (SPECT/CT) imaging was not available and this modality could also have possibly picked up both the adenomas. A provisional diagnosis of a double giant parathyroid adenoma (one from the inferior parathyroid and the other ectopic in the anterior mediastinum) was made.

The severe hypercalcemia was temporarily controlled by a hydration and forced diuresis, and the patient was subsequently taken up for surgery. The patient underwent a successful resection of both the enlarged parathyroid glands through a transcervical approach after carefully safeguarding the left recurrent laryngeal nerve [Figure 3a and b]. A formal exploration of the remaining parathyroid glands demonstrated no abnormality.

The patient needed correction for biochemical hypocalcemia in the immediate postoperative period, the same which normalized after a couple of weeks. The postoperative serum PTH levels also normalized. The final histopathology confirmed the diagnosis of a giant double parathyroid adenoma; the parathyroid adenoma on the anterior mediastinum was an atypical adenoma with features such as broad fibrous septa and suspicious areas of vascular and capsular infiltration [Figure 4a-d]. The patient continues to be on regular follow-up finally having a remission of his bony and renal symptoms.

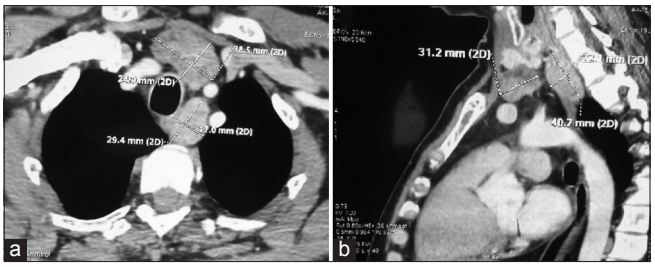

Figure 1: Computed tomography scan of the neck and chest ([a] axial section, [b] sagittal section) revealed two lesions, one in the left upper paratracheal (left inferior parathyroid adenoma) and the other in the pretracheal regions (ectopic mediastinal parathyroid adenoma)

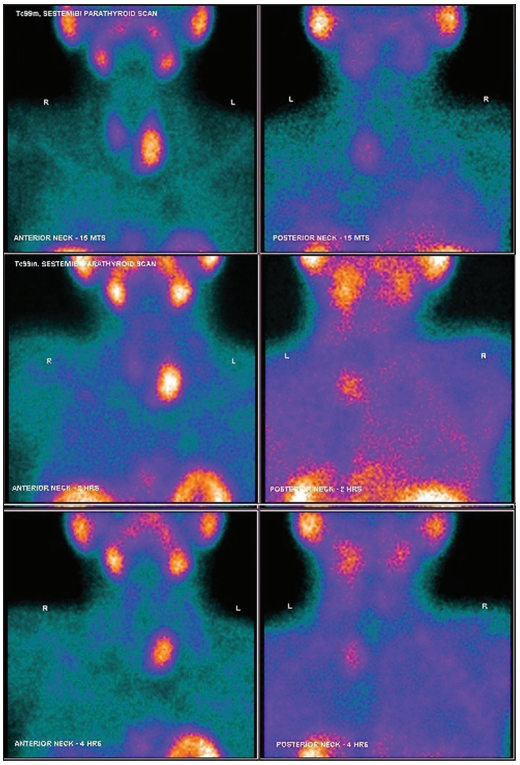

Figure 2: 25 mCi of 99mTc-SestaMIBI was given intravenously followed by the acquisition of early (15 min postinjection) and delayed images (1, 2, and 4 h after the injection) at of the neck and thorax. The scan demonstrated a persistent retention of the SestaMIBI tracer in the region of the left inferior parathyroid gland

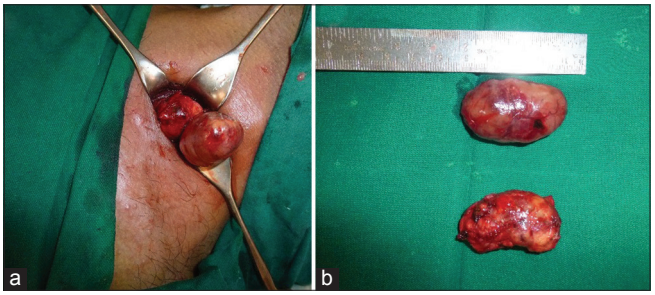

Figure 3: (a and b) Intraoperative photograph showing resection of both the parathyroid adenomas

DISCUSSION

Primary hyperparathyroidism is a common endocrine disorder of the parathyroid gland and mostly results from parathyroid adenoma with excess production of parathyroid hormone. It is mostly seen as single gland adenoma in up to 85% of the cases. Double adenomas although reported are very rare and double giant parathyroid adenomas are even rarer.[2,3] Considerable debate exists as to whether double adenomas are a distinct entity or represent early stages of 4 gland hyperplasia.

Primary hyperparathyroidism is known to present with protean manifestations which include asymptomatic presentation and also symptoms pertaining to renal, skeletal, gastrointestinal, and neuropsychiatric symptoms, often leading to misdiagnosis in the initial stages of the disease.[4] Primary hyperparathyroidism is often associated with borderline or mild hypercalcemia (serum

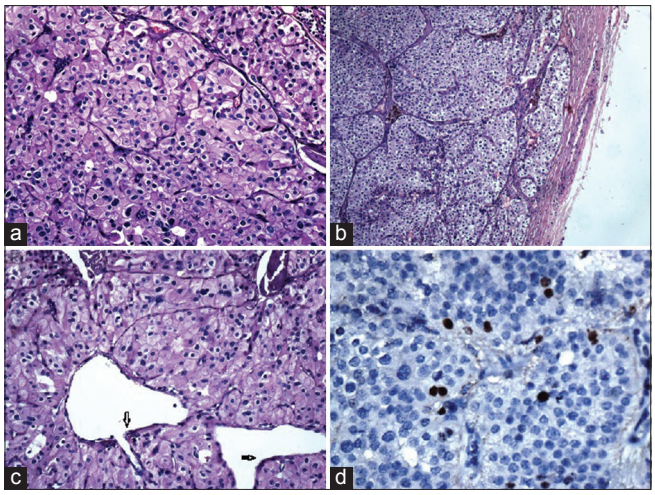

Figure 4: (a) The ectopic anterior mediastinal lesion with findings suggestive of atypical parathyroid adenoma. (b) Showing capsular invasion. (c) Showing vascular invasion (d) showing low expression of Ki-67 (H and E, ×20)

calcium concentration often below 11 mg/dl). Values >13 mg/dl are considered unusual in primary hyperparathyroidism although they do occur and are more common in patients with malignancy-associated hypercalcemia.[5] Although the secretion of parathyroid hormone is modulated by levels of serum calcium, many studies have suggested a direct correlation between gland weight and serum PTH levels and the corresponding levels of serum calcium. Further, it has been found that an increased glandular mass correlates with the severity of hyperparathyroidism and the subsequent risk of postoperative hypocalcemia.

Parathyroid scintigraphy is the modality of choice for localization of parathyroid adenomas, and Tc-99 m-labeled SestaMIBI scintigraphy is the most widely used modality for localization of parathyroid adenomas.[1] The limitations of a conventional planar scintigraphy can be overcome by the incorporation of SPECT-CT as a component of a hybrid imaging which enables a high spatial resolution three-dimensional (3D) image that has shown to improve the ability of detecting the parathyroid lesions.[6] Parathyroid scintigraphy is usually complemented by neck ultrasound or 4D-CT scans which can identify adenomas with a high sensitivity and specificity. A recent study showed dual isotope pinhole subtraction parathyroid scintigraphy to have the highest diagnostic accuracy when compared with the other imaging modalities such as dual-phase parathyroid scintigraphy, 4D-CT scan, and ultrasound as the first-line imaging study in primary hyperparathyroidism.[7]

Parathyroid carcinoma and atypical parathyroid adenoma can be differentiated relatively easily from typical parathyroid adenomas, but distinguishing them from each other is a challenge in the absence of well-defined clinical and histological criteria. Some authors have tried to define atypical parathyroid adenoma by the presence of two or more of the following criteria: Clinical or intraoperative adherence, fibrotic bands, trabecular growth, and mitotic rate of >1/10 high-power field without indisputable signs of malignancy.[8] Low number of tumor cells staining for Ki-67 and MIB-1 is also consistent with a diagnosis of atypical parathyroid adenoma.

The conventional surgical approach for parathyroidectomy is bilateral exploration of the neck via a collar incision to examine all four glands and remove any diseased glands, with intraoperative frozen section confirmation. However, based on the fact that most cases of primary hyperparathyroidism are caused by single gland disease, it is argued that a more limited and focused surgical examination of the neck is also possible.[9] A parathyroid scintigraphy coupled with intraoperative parathyroid hormone monitoring can additionally aid in the performance of a focused approach and this has been suggested as a viable alternative.[10] Further estimation of intraoperative PTH levels after the removal of each of the adenomas can nail the fact as to whether either or both of the adenomas were PTH secreting.

CONCLUSION

Primary hyperparathyroidism, with its varied manifestations and indolent course, is a condition well known to pose a diagnostic dilemma to the clinician. A double parathyroid adenoma albeit extremely uncommon may further complicate the issue. A combination parathyroid scintigraphy and a neck ultrasound should be used for preoperative localization and selection of the right surgical approach for patients undergoing parathyroidectomy. The parathyroid scintigraphic protocols keep getting refined; it is hence vitally important and practical to adapt the diagnostic algorithms in accordance with local availability and expertise.

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Conflicts of interest
There are no conflicts of interest.

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