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Case Report

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Atypical cystic parathyroid adenoma masquerading as a thyroid nodule and presenting with severe hypercalcemia

Abstract

Background: Primary hyperparathyroidism occurs as a result of isolated parathyroid adenoma in 80% to 85% of all cases. Severe hypercalcemia due to cystic atypical parathyroid adenoma is rare entity.

Method: We report a rare case of severe hypercalcemia associated with cystic atypical parathyroid adenoma.

Result: 27 year old female presented with nausea, vomiting and abdominal pain. A serum calcium level of 15.8 mg/dl with PTH of 413 was noted on admission. She was initially treated with IV hydration and had ultrasound of neck which showed 2.8 cm complex nodule in right thyroid lobe. After appropriate work up, she underwent a surgical resection of parathyroid adenoma found on CT with 3D reconstruction. Pathology showed a mixed picture more consistent with possible atypical adenoma.

Conclusion: Parathyroid cyst is known but rare entity, which is usually nonfunctional. However, atypical cystic parathyroid adenoma with severe hypercalcemia is very rarely reported. It may exhibit some pathologic features of carcinoma, but angio-invasion and/or metastases are not present. Severe hypercalcemia with a large, cystic neck mass should prompt thoughts of cystic atypical parathyroid adenoma versus carcinoma. In both cases, long-term follow up would be prudent. Also, our case emphasizes the importance of knowing ultrasonographic features to differentiate parathyroid adenoma appearing as thyroid nodule.

Keywords: atypical adenoma; hypercalcemia; parathyroid adenoma; thyroid nodule; ultrasonographic features; hypercalcemia; cystic neck mass; ultrasound; thyroglobulin; parathyriodectomy; hyperparathyroidism; neoplasm; vitamin d; immunohistochemistry; carcinoma

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Abbreviations: HPT, hyperparathyroidism; PHPT, primary hyperparathyroidism; IV, intravenous

Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia. Majority of cases are related to single gland adenoma. Parathyroid carcinoma, atypical parathyroid adenoma, parathyroid cysts and parathyromatosis are rare conditions that account for approximately 2% of all patients with PHPT. We report an unusual case of severe hypercalcemia due to cystic atypical parathyroid adenoma,[1] which appeared as thyroid nodule on ultrasound. Such a case is rarely described in literature.

Case report

A 27-year old Caucasian woman with history of mental retardation presented with severe nausea, vomiting and abdominal pain of 1 day duration. No similar episodes were reported in the past. There was no prior history of renal stones or fractures. On examination, she was afebrile, with BP 130/75mm Hg and HR 90-100 beats/minute. She was confused and had generalized tenderness over her abdomen. Laboratory data (Table 1) revealed hypercalcemia secondary to primary hyperparathyroidism. Neck ultrasound (Figure 1A & 1B) revealed a right dominant 2.8cm complex, solid and cystic nodule with intranodular and peripheral vascularity. She was admitted and was treated with intravenous (IV) normal saline. She received 1 dose of IV pamidronate 60mg. Her calcium level improved to 9.8mg/dl and was subsequently discharged. She underwent biopsy of the right thyroid nodule, which was consistent with parathyroid neoplasm possibly adenoma with immunohistochemistry negative for Thyroglobulin, TTF 1, Calcitonin and S 100. She was subsequently referred to endocrine surgery for evaluation of parathyriodectomy. CT scan of neck with 3D imaging reconstruction[2] (Figure 2) study confirmed a large well defined nodule with peripheral enhancement suspicious for large right parathyroid adenoma. She underwent minimally invasive parathyriodectomy with fluid aspiration and intra-operative PTH levels fell from 289 pg/ml to 15.8 pg/ml. Pathology (Figure 3) was supportive of the diagnosis of atypical parathyroid adenoma with fragments of hyper cellular parathyroid neoplasm consisting of neoplastic cells with solid nest and trabecular growth patterns with focal capsular distortion and increased mitotic activity. Immunohistochemistry revealed Ki-67 proliferation index 1-3%, bcl-2 positive, diffuse strong and focal weak positive p 53. Post operatively; she was started on calcium and vitamin D supplementation. She is doing well and remains normocalcemic for 2 years following surgical resection with most recent calcium of 9.3mg/dl.

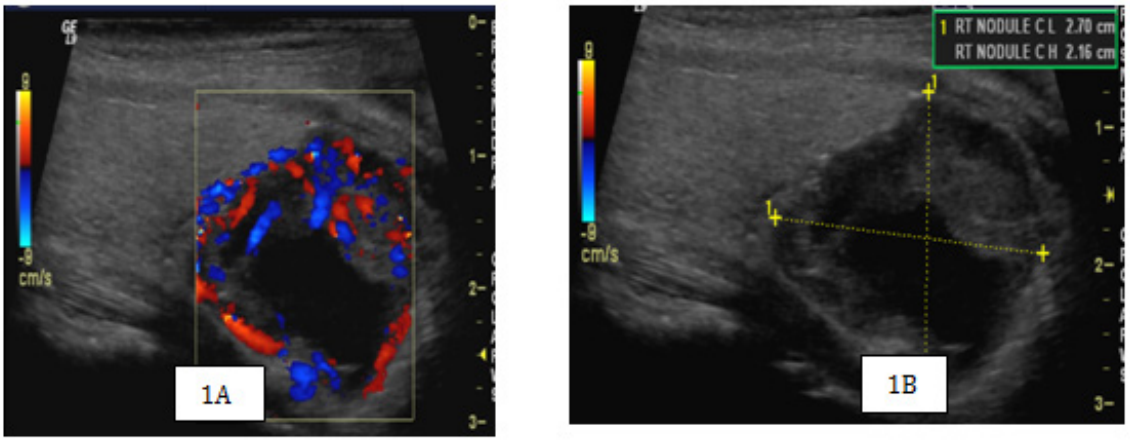

Figure 1A: Ultrasonographic findings consistent with right thyroid nodule with solid and cystic component. 1B: prominent peripheral and intranodular vascularity.

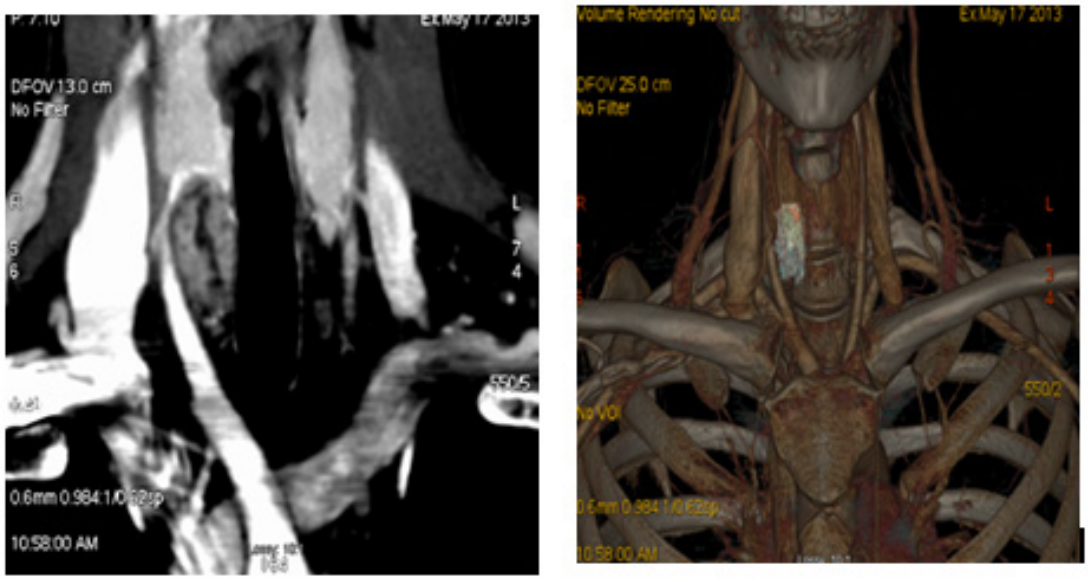

Figure 2 Localization of parathyroid adenoma on CT of neck with 3 D reconstruction.

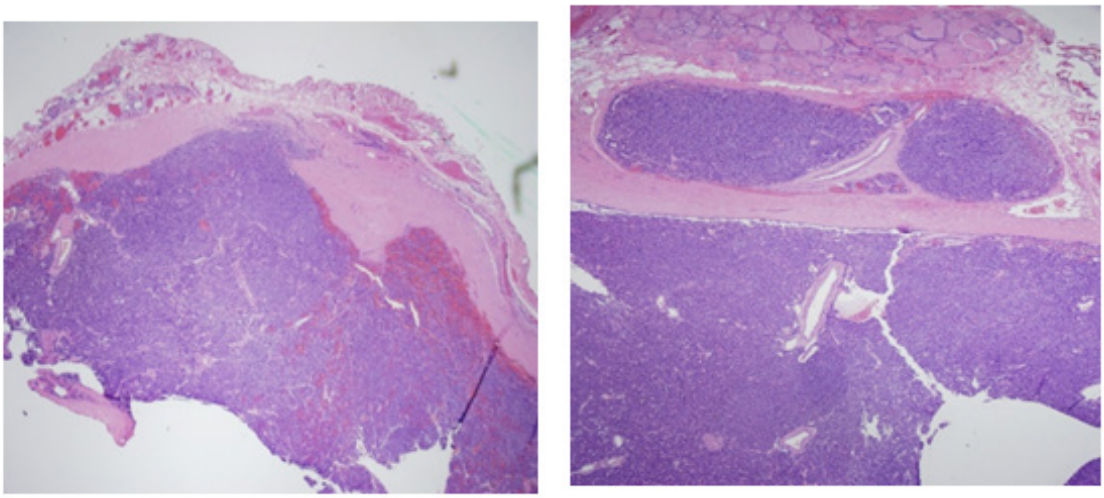

Figure 3 Hyper cellular neoplastic cells with solid nest and trabecular growth pattern separated by thick fibrous tissue band.

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Table 1 Laboratory parameters

Labs	Admission	Post-surgery
Total Ca	15.8 (8.5-10.5 mg/dl)	9.4 mg/dl
Ionized Ca	N/A	
PTH Intact	413 (12-72 pg/ml)	15.7 pg/ml
25-OH Vitamin D	9 (30-100 ng/ml)	23 ng/ml
1-25 Hydroxy Vitamin D	N/A	
Phosphorous	3 (2.5-4.8 mg/dl)	3.8 mg/dl
24 Hour Urinary Calcium	N/A	
BUN/Creatinine/E-GFR	16/0.76/>60	
Sodium	144 (135-145 mmol/L)	138 mmol/L

Discussion

Parathyroid cysts are rare lesions found in neck and anterior mediastinum. They are often nonfunctional (>90%) and rarely in functional form.[3–6] However, cases of sever hypercalcemia with calcium level of 15-23mg/dl due to parathyroid cysts have been reported.[1,3–5,7,8] Formation of parathyroid cysts remain a question and different hypothesis have been postulated including persistence of vestigial branchial clefts/Kurtsteiner canal. Many investigators believe that functional cysts are due to degenerative changes in preexisting parathyroid adenoma.[9–11]

Similarly, atypical adenoma is a rare cause of primary hyperparathyroidism. It is certainly uncommon for an atypical parathyroid adenoma to present with severe hypercalcemia, although calcium level of 23.3 has been reported by due to an adenoma.[12] The majority of patients with parathyroid carcinoma and atypical adenoma can be easily distinguished from patients with primary hyperparathyroidism due to classic adenoma, but distinguishing these conditions from each other is more difficult because of lack of precise clinical and histologic criteria. Those tumors with worrisome features but not diagnostic of malignancy, fall under category of "atypical adenoma." Clinically, parathyroid cancer more commonly presents with palpable neck mass, hoarseness of voice and profound Hypercalcemia.[13] Histopathologically, atypical adenoma and parathyroid cancer share features such as fibrous capsule, fibrous trabeculae, trabecular growth pattern and mitotic figures, however true capsular, tissue and vascular invasion along with recurrence is exclusive to parathyroid cancer.[14] Existence of local recurrence or metastatic disorder is the single and reliable characteristic in distinguishing between benign and malignant parathyroid disorders.[15]

Our patient had thick capsule with some focal distortion associated with mitotic activity but no vascular or local invasion was noted. Although, our patient had positive markers, the role of prognostic markers as Ki-67, p53, bcl-2 that may assist in evaluating aggressive behavior in these tumors has not been fully studied and is limited because of lack of consistent difference in their expression.[16] Absence of nuclear staining for parafibromin and presence of protein gene product 9.5 (PGP 9.5) has been postulated as diagnostic of parathyroid carcinoma. Also, some patients with sporadic parathyroid carcinoma have germline HRPT2 mutations,[17] but unfortunately, in our case, both parafibromin/PGP 9.5 staining and genetic testing were not done. Interestingly, our patient had both rare features of 'cyst' and 'atypia' together. Co-existence of these two entities makes this case extremely rare. To our knowledge, so far only one similar case has been described in literature. It is important to report such cases to estimate the true prevalence of cystic atypical parathyroid adenoma and broaden the differential diagnosis of a cystic mass with hypercalcemia.

Also, in our patient, the parathyroid adenoma was masquerading as a thyroid nodule on ultrasound images. Certain ultrasound characteristics used to distinguish a parathyroid adenoma from thyroid nodule include solid composition, hypo echoic appearance and presence of a feeding polar vessel.[18] Ultrasound is inexpensive and noninvasive technique for localization but it needs experienced hands to identify and distinguish parathyroid adenoma from thyroid pathology. Sometimes, US directed biopsy with PTH analysis is required for confirmation.

Conclusion

Atypical cystic adenoma are rare, they have some features of carcinoma but lacks the clear evidence of malignancy like invasion or metastasis. They have unpredictable clinical course, hence long-term follow up is prudent to assess for local recurrence and distance metastases to distinguish between benign and malignant parathyroid disease. Also, it can rarely present with severe hypercalcemia as in our case. This case also highlights the importance of suspecting parathyroid adenoma mimicking a thyroid nodule and emphasizes on appropriate follow up imaging or procedure for confirmation.

Acknowledgments

None.

Conflicts of interest

The auhtor declares there is no conflicts of interest.

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