Annals of Clinical Cases

ISSN: 2692-7993

Case Report

Severe Hypercalcemia: Diagnostic Challenge: Parathyroid Carcinoma or Atypical Parathyroid Adenoma?

Faten Hadj Kacem[1], Abir Derbel[1], Wajdi Safi[1], Sidina Mohamed Elmoctar[1], Mouna Zghal[2], Naoures Gouia[2], Nadia Charfi[1], Tahya Boudawara[2] and Mohamed Abid[1]*

[1]*Department of Endocrinology, CHU Hedi Chaker, Sfax, Tunisia*

[2]*Department of Anatomopathology, CHU Habib Bourguiba, Sfax, Tunisia*

Abstract

Atypical parathyroid adenoma and parathyroid carcinoma were rare <1%. Clinico-biological and anatopathologic features were overlapped. Diagnosis will be established difficultly. A 52-year-old man was admitted to our endocrinology department with complaints of intense weakness, headaches, polyuro polydipsic syndrome and digestive symptoms. He had severe hypercalcemia (serum calcium: 5.25 mmol/L), normal phosphatemia, renal failure and an elevated parathyroid hormone level. The patient was treated by intravenous hydration, diuretic and bisphosphonate treatment. Also a session of hemodialysis was performed. In neck, ultrasonography revealed parathyroidien nodule in the in the lower pole of the right thyroid. Technetium-99 m-sestamibi scintigraphy showed fixed MIBI abnormality in the projection of the inferior region of right thyroid lobe. Hybrid-fusion SPECT/CT systems found heterogeneous and hypodense nodule with calcifications and areas of necrosis located below the lower right pole of the thyroid. Surgical treatment was performed and parathyroid adenoma was excised with right thyroidectomy (lobo-isthmectomy) and ipsilateral mediastinal recurrent nerve dissection. Histopathological results found atypical adenoma. In the postoperative period, serum calcium dropped to 2.14 mg/dl. Oral calcium and vitamin D replacements were commenced. The patient was regularly followed.

Keywords: Hypercalcemia; Parathyroid adenoma; Parathyroid carcinoma; Intravenous hydration

Introduction

Parathyroid tumors are a heterogeneous group of tumor affecting 0.1% to 0.3% of general population. Primary hyperparathyroidism is most commonly due to solitary parathyroid adenoma. Atypical parathyroid adenoma and parathyroid carcinoma were rare <1% [1]. Clinico-biological features and anatopathologic findings were overlapped on both diseases. That's why, diagnosis was established difficultly. A definitive diagnosis of malignancy could only be made relying on histological results. There are no definite criteria to distinguish between carcinoma and atypical adenoma [2]. In this manuscript, we report an exceptional case of severe hypercalcemia linked to atypical adenoma in basis on histological findings.

Case Presentation

A 52-year-old man who had no medical history of nephrolithiasis nor bone disease was hospitalized in our department of endocrinology, Sfax, Tunisia, for severe hypercalcemia. He presented one month ago intense weakeness, headaches, polyuro-polydipsic syndrome and digestive symptoms including epigastralgia and vomiting. In our department, he was signs of extra and intracellular deshydration. His blood pressure was 90/50 mmHg and his pulse was at 112 battement/minute (bpm). He had clinical euthyroidism and eucorticism. Electrocardiogram revealed tachycardia at 130 bpm and normal corrected QT interval. Serum biochemistries revealed that his serum calcium was at 5.25 mmol/L, serum phosphore was at 0.84 mmol/L, serum alkaline phosphatase was normal, serum levels of sodium was (159 mmol/L), serum pancreatic enzyme level was normal and kidney failure was found (serum creatinin: 158 umol/L, urea=13 mmol/L). 24-hour urine calcium excretion was at 0.66 mmol/ kg/day. Serum Parathyroid Hormone (PTH) was elevated at 1207 ng/mL. 25-OH vitamine D was normal at 30ng/ml. The diagnosis of primary hyperthyroidism was retained. Kidney ultrasound was performed and hadn't show nephrocalcinosis. Bone densitometry of femur and spine showed osteoporosis with T-score value <-2.7. Cervical ultrasound examination disclosed an oval nodule with lobulated contours measuring 36 mm × 23 mm × 23 mm, hypoechoic with heterogeneous echostructure and additional display of vascularisation in colour-coded ultrasonography in the lower pole of the right thyroid. It was completed by Technetium-99 m-sestamibi scintigraphy which revealed fixed MIBI abnormality in the projection of the inferior region of right thyroid lobe. Hybrid-fusion SPECT/CT systems found that this focus was heterogeneous and hypodense nodule with calcifications and areas of necrosis located below the lower right pole of the thyroid measuring 31 mm × 22 mm × 38 mm (Figure 1).

Face to this severe hypercalcemia, intravenous hydration and furosemide were started. Serum calcium level didn't decrease indicating administration of 4 mg IV zoledronic acid. Then, a session of hemodialysis was performed. At 24 hours, serum calcium dropped to 3 mmol/L and right hemi thyroidectomy with parathyroid adenoma excision and ipsilateral mediastinal recurrent

Citation: Kacem FH, Derbel A, Safi W, Elmoctar SM, Zghal M, Gouia N, et al. Severe Hypercalcemia: Diagnostic Challenge: Parathyroid Carcinoma or Atypical Parathyroid Adenoma? Ann Clin Cases. 2021; 2(2): 1030.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Feb 17th, 2021

***Corresponding author:** Abir Derbel, Department of Endocrinology, CHU Hedi Chaker, Sfax, Tunisia, E-mail: abirderbel@gmail.com

nerve dissection were performed. Patient was closely monitored. The pathology report showed grossly nodule measured 3.5 cm × 2 cm × 2 cm. It was a fleshy lobulated with fine and intact capsule without necrosis. Histopathological results found well-circumscribed parathyroid nodule with lobular architecture. Lobules were separated by dense fibrotic bands which were sometimes thick and calcified (Figure 2). Tumor cells were of medium size, round or cuboids. They were arranged in clusters, acini and sometimes in pseudo-follicular structures (Figure 3). The cytoplasm was abundant clear or eosinophilic. The nucleus was atypical, hyperchromatic and voluminous (Figure 4). There were sometimes prominent nucleoli. No marked pleomorphism and mitotic figures were present. The invasion of the capsule wasn't been observed; few vascular emboli were detected within the tumor proliferation without invasion of extra-capsular vessels (Figure 3).

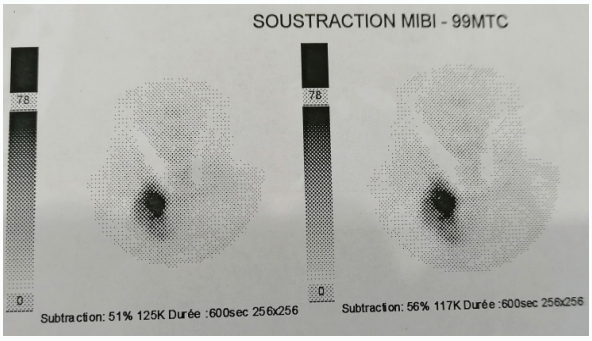

Figure 1: Technetium-99m-sestamibi scintigraphy revealed fixed MIBI abnormality in the projection of the inferior region of right thyroid lobe.

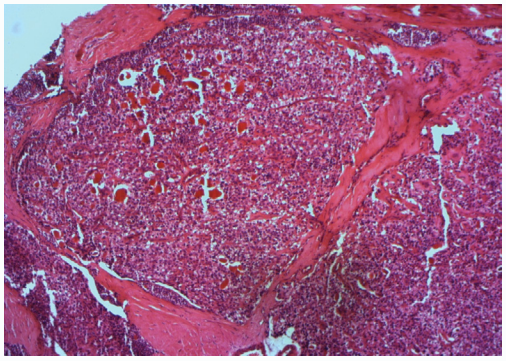

Figure 2: Tumor proliferation with lobular architecture separated by thick fibrous bands (HE × 50).

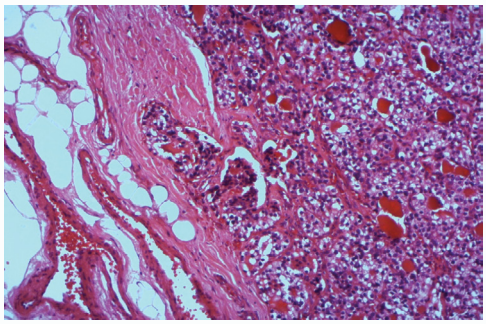

Figure 3: Tumor cells arranged in clusters, acini and pseudo-follicular structures. Presence of lymphatic emboli within the tumor proliferation without extra-capsular angio invasion or capsular effraction (HE × 100).

Immunohistochemical analysis was positive for Parathyroid Hormon (PTH) and negative for Thyroglobulin (Figure 5). The high volume of nodule, the dissecting fibrosis observed in the tumor, the elevated cell density and the presence of prominent nucleolus guided us to caracterise the adenoma as atypical. But, the absence of extra-capsular angio invasion and perineural invasion eliminated the parathyroid carcinoma. On the first postoperative day, serum calcium levels were dropped to 2.14mg/dl. On the second postoperative day, serum Ca level was found to be decreased to 2.11 mg/dl, and oral calcium and vitamin D replacements were commenced. The patient was followed regularly.

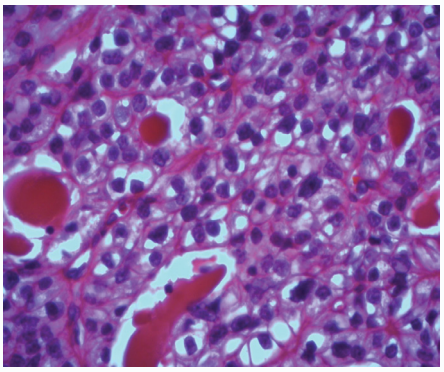

Figure 4: higher power reveals round tumor cells with atypical, hyperchromatic and voluminous nucleus. Mitotic figures were absent (HE × 400).

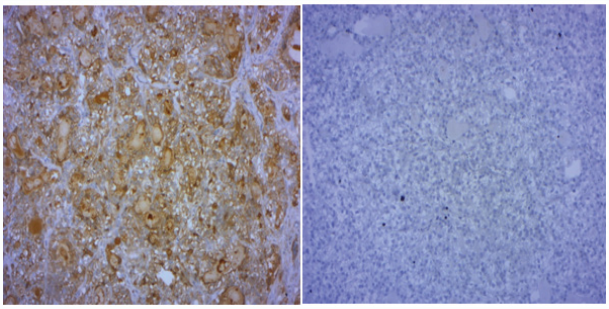

Figure 5: Tumor cells positive for Parathyroid Hormon and negative for thyroglobulin.

Discussion

Primary hyper parathyroidism was the third most common endocrine disorder after diabetes and thyroid disorders [3]. It represents the most frequent cause of hypercalcemia [4]. It affects more frequently women than men [3,5]. It may be diagnosed in asymptomatic stage [6]. The major cause was single adenoma in up 89% of cases [7]. Other causes include hyperplasia of four glands (6%), double adenomas (4%), and, rarely, parathyroid carcinoma [8]. Distinction between carcinoma and atypical parathyroid adenoma was difficult in preoperative evaluation. There are no specific clinical, biological or radiological manifestations. More frequently, the diagnosis is retrospective. However, some clinical findings allow us to think to benign or malignant etiology. Among conditions which associated with higher risk of parathyroid carcinoma and must draw the clinician's attention we cite: young age, male gender, severe hypercalcemia with albumin-corrected calcium levels more than 3.0 mmol/L, hypercalcemic crisis, concomitant renal failure or bone involvement and palpation of a big mass in the neck more than 3 cm.

All of these signs should raise the suspicion of parathyroid carcinoma [9,10]. Hoarseness, a sign of recurrent laryngeal nerve palsy due to local invasion is highly suggestive of malignancy, since it is very uncommon in benign hyperparathyroidism [11]. Parathyroid levels could increase twelve times higher than normal levels in patients with carcinoma in contrast to benign disease in which PTH level increased approximately two-fold higher than normal values [12]. Our patient presented high level of serum calcium not improved by simple therapy and required hemodialysis. Ultrasonography revealed large sized tumor more than 3 cm. All of these arguments were rather suggestive of malignancy.

Neck ultrasound and 99 mTecnitium-MIBI scintigraphy represent the dominant imaging techniques for preoperative location of parathyroid tumor. Imaging findings allow surgeons to choose the most appropriate invasive approaches [13]. Lobulated tumor and non-homogenous echogenity on ultrasonography are often associated with carcinoma [14]. Parathyroid carcinoma appears as a large hypoechoic lesion, with irregular borders [15,16]. Also, among criteria predicting malignancy we found: infiltration of adjascent structure and presence of calcifications [17]. In the other side, the absence of suspicious intra-tumoral vascularisation and a thick capsule were predictive of benignity [17]. In our case the nodule was lobulated, heterogeneous with additional display of vascularisation. Then, preoperative evaluation couldn't exclude parathyroid carcinoma. That's why histological examination represents the objective tool to distinguish between parathyroid carcinoma and adenoma. In fact, several signs are found in both carcinoma and atypical adenoma such us: atypical nuclear features, broad fibrous bands, mitotic features, trabecular or solid growth patterns. Although, they are not pathognomonic [18]. Malignancy is confirmed in the presence of extra-capsular vascular emboli, perineural invasion or invasion of the capsule or adjacent structures according to Ippolito et al [19].

The most effective treatment in parathyroid carcinoma was resection "en bloc" [20]. Parathyroidectomy should be performed with ipsilateral thyroid loboisthmectomy and removal of contiguous lymph nodes (paratracheal and central lymph node dissection). There is no consensus for the surveillance of patients with atypical parathyroid adenomas after parathyroid surgery so far. Authors were based on their own experience.

Conclusion

Parathyroid atypical adenoma is an exceptional entity. Long term prospective study of cases is needed to enlighten the course of this rare disease and determine the risk of occurrence of carcinoma and recurrence of hypercalcemia after surgical therapy.

References

1. Cetani F, Pardi E, Marcocci C. Update on parathyroid carcinoma. J Endocrinol Invest. 2016;39(6):595-606.
2. Baser H, Karagoz A, Okus A, Cayci M, Karanis MIE, Burnik FS, et al. Differential Diagnosis of Atypical Parathyroid Adenoma and Parathyroid Carcinoma in a Case with Severe Hypercalcemia. J Med Cases. 2013;4(6):357-61.
3. Rao SD. Epidemiology of parathyroid disorders. Best Pract Res Clin Endocrinol Metab. 2018;32(6):773-80.
4. McDow AD, Sippel RS. Should Symptoms Be Considered an Indication for Parathyroidectomy in Primary Hyperparathyroidism? Clin Med Insights Endocrinol Diabetes. 2018;11:1179551418785135.
5. Lal G, Clark OH. Diagnosis of primary hyperparathyroidism and indications for parathyroidectomy. In: Clark O, Duh QY, Kebebew E, editors. Textbook of Endocrine Surgery. Philadelphia: Elsevier; 2005. p. 384-92.
6. Silverberg SJ, Clarke BL, Peacock M, Bandeira F, Boutroy S, Cusano NE, et al. Current issues in the presentation of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3580-94.
7. Fraser WD. Hyperparathyroidism. Lancet. 2009;374(9684):145-58.
8. Ruda JM, Hollenbeak CS, Stack BC. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. Otolaryngol Head Neck Surg. 2005;132(3):359-72.
9. Shane E. Parathyroid carcinoma. J Clin Endocrinol Metab. 2001;86(2):485-93.
10. Talat N, Schulte KM. Clinical Presentation, Staging and Long-Term Evolution of Parathyroid Cancer. Ann Surg Oncol. 2010;17(8):2156-74.
11. Betea D, Ptorac I, Beckers A. Parathyroid carcinoma: Challenges in diagnosis and treatment. Ann Endocrinol (Paris). 2015;76(2):169-77.
12. Chen Q, Kaji H, Nomura R, Sowa H, Yamauchi M, Tsukamoto T, et al. Trial to predict malignancy of affected parathyroid glands in primary hyperparathyroidism. Endocr J. 2003;50(5):527-34.
13. Johnson NA, Tublin ME, Ogilvie JB. Parathyroid Imaging: Technique and Role in the Preoperative Evaluation of Primary Hyperparathyroidism. Am J Roentgenol. 2007;188(6):1706-15.
14. Hara H, Igarashi A, Yano Y, Yashiro T, Ueno E, Aiyoshi Y, et al. Ultrasonographic features of parathyroid carcinoma. Endocr J. 2001;48(2):213-7.
15. Tamler R, Lewis MS, LiVolsi VA, Genden EM. Parathyroid carcinoma: ultrasonographic and histologic features. Thyroid. 2005;15(7):744-5.
16. Sidhu PS, Talat N, Patel P, Mulholland NJ, Schulte KM. Ultrasound features of malignancy in the preoperative diagnosis of parathyroid cancer: a retrospective analysis of parathyroid tumours larger than 15 mm. Eur Radiol. 2011;21(9):1865-73.
17. Stojadinovic A, Hoos A, Nissan A, Dudas ME, Cordon-Cardo C, Shaha AR, et al. Parathyroid neoplasms: clinical, histopathological, and tissue microarray-based molecular analysis. Hum Pathol. 2003;34(1):54-64.
18. Ippolito G, Palazzo FF, Sebag F, De Micco C, Henry JF. Intraoperative diagnosis and treatment of parathyroid cancer and atypical parathyroid adenoma. Br J Surg. 2007;94(5):566-70.
19. Fang SH, Lal G. Parathyroid cancer. Endocr Pract. 2011;17(Suppl 1):36-43.