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Case Report

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Primary Hyperparathyroidism Due to Parathyroid Carcinoma of Ectopic Origin a Case Report

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Abstract

The following is a rare case of a 43-year-old woman who arrived at the emergency department with symptoms associated with hypercalcemia that were caused by primary hyperparatoriodism secondary to ectopic parathyroid carcinoma. The diagnostic difficulty and management of these patients is discussed below.

Keywords: Primary Hyperparathyroidism, Ectopic Parathyroid Carcinoma, Hypercalcemia

Introduction

Parathyroid carcinoma is a malignant neoplasm that affects 0.5-5% of the patients that suffer from primary hyperparathyroidism [1]. This type of cancer remains a challenge in diagnosis and treatment due its rareness.

Case: A 43-year-old Hispanic woman, with no past medical history, who presents with arthralgias, myalgias, and generalized weakness. She started four days before admission with generalized headache, pressure-like and subjective fever associated with gingivorrhagia. Physical examination revealed a non-pruriginous maculopapular rash, predominantly in upper and lower extremities and diffuse abdominal tenderness on deep palpation diagnosing at that time dengue by positive serology. Within the initial assessment, the presence of hypercalcemia of 11.4 mg/dl called attention, thrombocytopenia of 45,000 and a mixed cholestatic and hepatocellular liver injury (AST 178 U/L, ALT 137 U/L, ALP 300 U/L, and GGT 345 U/L) with preserved renal function. Complimentary laboratory test revealed ionized calcium of 1.56 mmol/L, elevated PTH of 680.5 pg/ml, and low 25-hydroxyvitamin D of 4.7ng/dl. Tc-99m sestamibi scintigraphy reported abnormal focal uptake in the mediastinum (Figure 1). CT of the chest showed a mass in superior mediastinum, in the paratracheal region, 5.3 x 3.4 x 3.3 cm in size, with a solid and cystic component, and with heterogenous uptake of radiotracer, predominantly in the solid component (Figure 2). Supportive treatment is given for dengue, with clinical improvement and discharged with cinacalcet 30mg every 12 hours and follow up with Endocrinology. Fifteen days after discharge, patient presented to the ED with generalized weakness and drowsiness. On physical exam: Vital signs BP 113/98 mmHg, HR 94bpm, RR 21 rpm, Temp 36°C, alert and oriented x4, with bradypsychia, and diminished sensitivity and muscle strength 3/5 in upper and lower extremities, with mild tachycardia, and lungs clear to auscultation. Upon admission, laboratory tests revealed Hb 15.2 g/dl, MCV 86.2 fL, Hct 41.1%, leukocytosis of 22.26 K/uL, with ANC 20.03, platelets 339,000 K/uL, glucose of 181mg/dL, Cr 1.04 mg/dL BUN 15.5 mg/dL Urea 33.2 mg/dL AST 26 U/L, ALT 37 U/L, ALP 271 U/L, GGT 149 U/L, Na 137 mmol/L, K 2.42 mmol/L, Cl 91.8 mmol/L, Phosphorus 2.1 mg/dl, Calcium 19.3 mg/dl, PTH: 2791 pg/ml, and normal thyroid function test. She was started on IV hydration, cinacalcet, denosumab and intermittent renal replacement therapy in 4 sessions, without lowering serum calcium levels. PTH increased > 5000, surgical intervention was decided, but nevertheless, patient died 8 hours after surgery, in (Figures 3 & 4) are showed the patient's PTH and calcium levels during hospitalization.

Figure 1. Sestamibi parathyroid scintigraphy with CT scan reconstructions where during the thyroid gland phase shows adequate thyroid gland uptake with a homogeneous distribution, with evidence of a large focal area of abnormal uptake, in the anatomical projection of the mediastinum, right of the midline probably pedicle. Parathyroid phase (2 hours): the late images show efficient clearance of the radiotracer by thyroid gland with evidence of a large focal area of abnormal uptake in the anatomical projection of the mediastinum to the right of the probably pedicle midline.

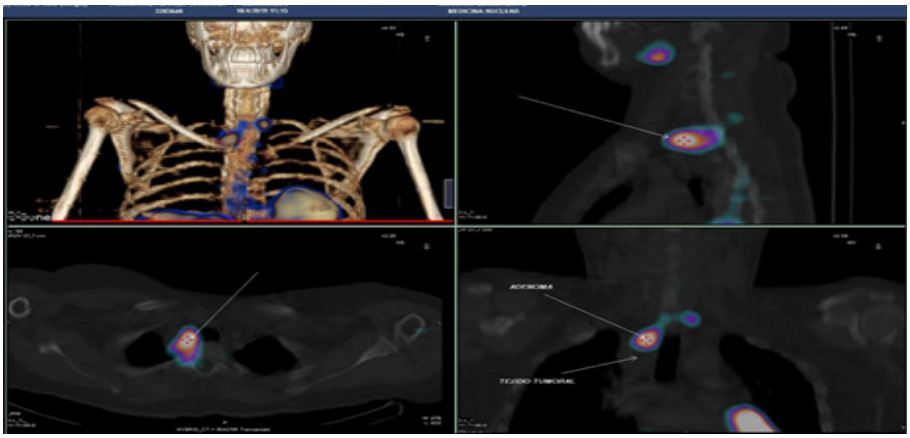


Figure 2. Chest CT with and without contrast in coronal and sagittal view demostrating a mass located towards the superior mediastinum, paratracheal with dimensions 5.3 x 3.4 x 3.3 cm with heterogeneous enhancement after contrast mainly of the solid component of 2.0 x 1.5 cm and cystic component that shows few thin septa with enhancement.

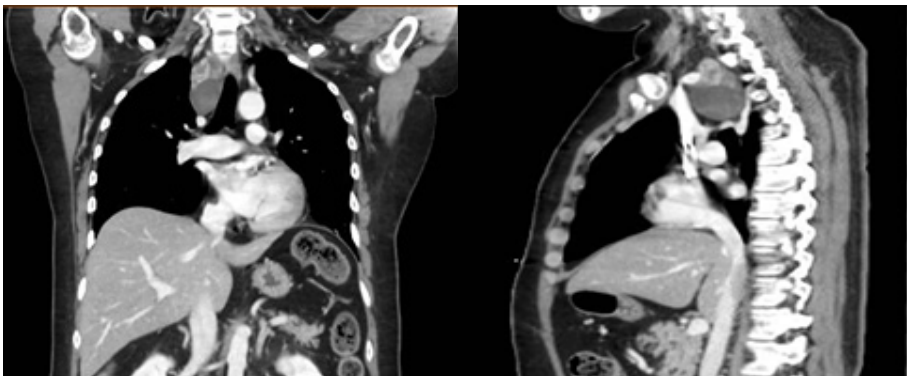


Figure 3. The serum calcium level in mg / dl during the days of hospital stay, note that during her first admission the patient went home with calcium levels of 10.8 mg / dl and 15 days later returns with levels of 19.3 reaching a level of maximum of 19.9 mg / dl during her second hospitalization.

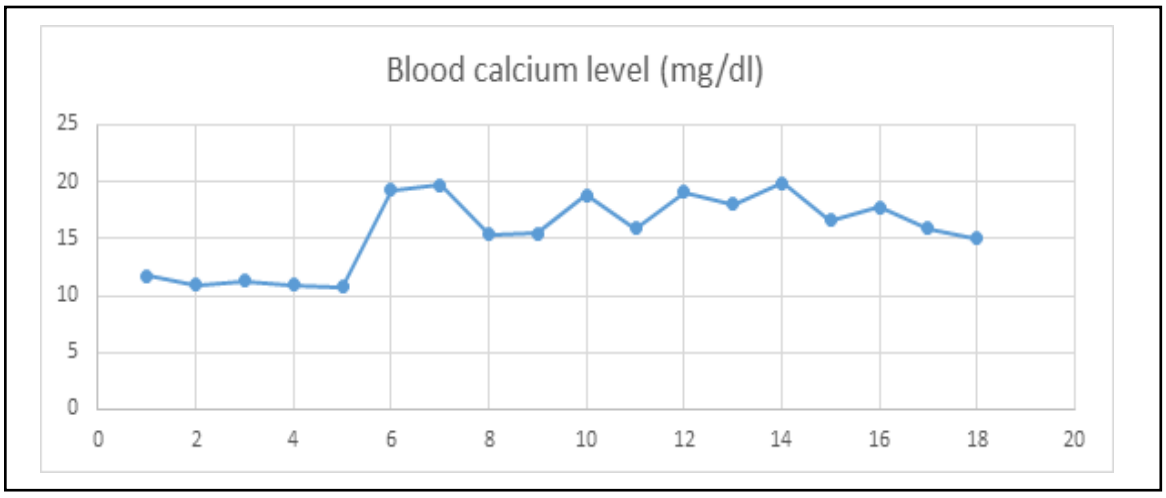
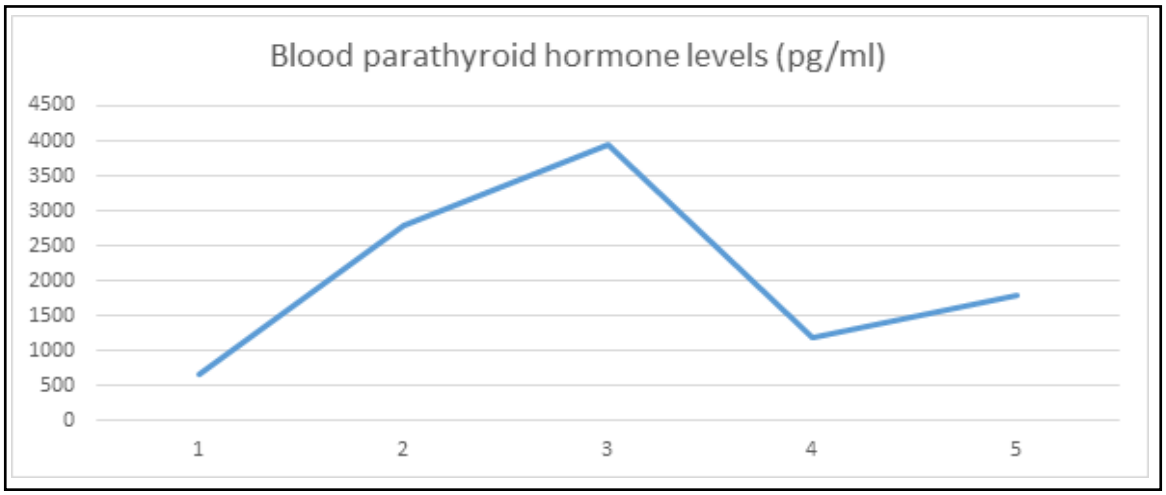


Figure 4. The level of serum PTH expressed in pg / ml in the y-axis is observed in relation to the blood samples taken preoperative, and perioperative in the x-axis. Observe as in the fourth sample that was made which corresponds to one minute after the removal of the tumor and sample 5 was performed 5 minutes after removal.



Discussion and Conclusions

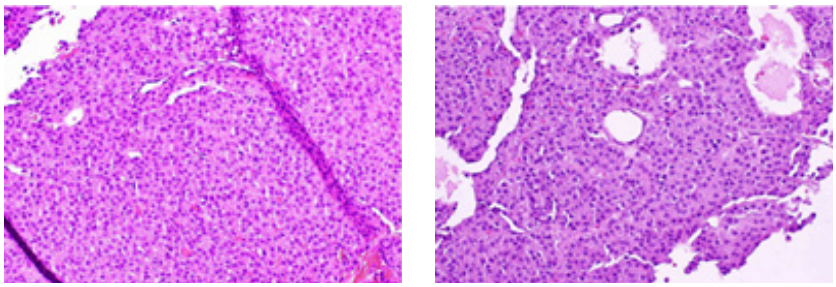
As is usually the case of parathyroid carcinoma, the diagnosis in this case was difficult. In the first admission the diagnosis of Dengue with incidental hypercalcemia, create questions, since the abdominal pain and generalized weakness can be explained by hypercalcemia, the presence of fever, gingivorrhagia, rash and thrombocytopenia can't be attributed by hypercalcemia. In addition levels of hypercalcemia where slightly above the upper limit of normal.

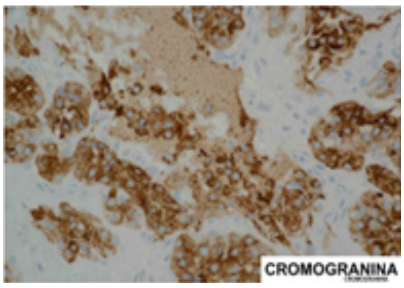
The first diagnostic possibility of primary hyperparathyroidism was a parathyroid adenoma, representing 80 to 85% of the causes [2]. Although the clinical characteristics of parathyroid adenoma and a parathyroid carcinoma can overlap, there are certain characteristics that can distinguish them; carcinoma tends to have more symptomatic, larger size, renal and bone involvement, as well as very high levels of calcium and PTH, as in our case [3]. To make a histopathologic diagnosis, although the presence of a trabecular pattern, mitosis, and thick fibrous bands are highly suggestive of carcinoma, there are two criteria that allow a more definitive diagnosis: the local invasion of adjacent structures and the presence of lymphatic nodules or distant metastases [3].

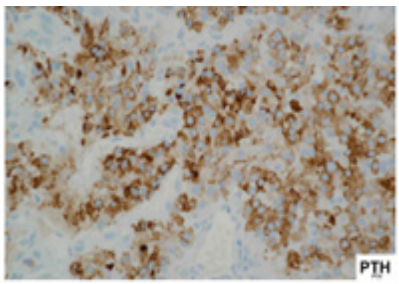
In this case, the diagnosis was even more challenging because the mass was localized in the upper mediastinum, which we must remember that the embryological origin of the parathyroid comes from the third and fourth pharyngeal pouch. The inferior parathyroid share their origin in the third pharyngeal pouch with the thymus, which they can migrate a greater distance; for this reason the inferior parathyroid can be located in ectopic sites. The four glands are located in the upper and lower poles of the thyroid gland; however, they can be located anywhere in the upper portion of the mediastinum due to its embryological origin [4].

The histopathologic diagnosis was a challenge in our patient; it reported infiltration of adjacent soft tissues of mediastinum, indicative with carcinoma. Several markers have been evaluated such as parafibromin, galectin-3, PGP9.5, Ki67 and cyclin D1, which have proved to be a good immunohistochemical panel to aid in the diagnosis of parathyroid cancer [5, 6]. In our case, despite we did not have access to all markers, chromogranin A, parathyroid hormone and prolactin positive (Figure 5) with the sum of clinical signs and symptoms, helped with the diagnosis [6].

Figure 5. Histological sections of the tumor with hematoxylin and eosin staining (superior) and immunohistochemical staining (lower). A neoplastic parathyroid lesion is seen infiltrating soft tissues of the mediastinum with permeation of small caliber vessels (venules), Immunohistochemical studies demonstrated chromogranin A, parathyroid hormone and prolactin positive. Data in favor of malignant parathyroid gland lesion: carcinoma.







The treatment of parathyroid carcinoma when it is resectable is surgical, helping to control hypercalcemia, which is the main cause of morbidity and mortality. Carcinomas may grow slowly but sometimes can be very aggressive. 30% of patients are cured with surgery, 49 to 60% recur after free of disease and need surgery again and 30% experience a short and aggressive time of the disease [5, 7].

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