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LETTERS TO THE EDITOR

Parathyroid crisis due to a cystic parathyroid adenoma

Crisis paratiroidea por adenoma quístico de paratiroides

To the Editor:

Parathyroid crisis (PC), also known as parathyroid storm or acute primary hyperparathyroidism, is a clinical sign of primary hyperparathyroidism (PHP) that represents an endocrine emergency, characterized by severe hypercalcemia (>15 mg/dL). PC sometimes occurs in patients with known hyperparathyroidism, but in other cases it is the first evidence of parathyroid disease.

We report the case of a 53-year-old female patient who experienced a PC which evidenced parathyroid disease. The patient had a history of endometriosis with left oophorectomy and menopause at 40 years. Her family history was unremarkable. She attended the emergency room for constipation and pain in the epigastric region and left renal fossa. Laboratory tests revealed creatinine levels of 2.12 mg/dL and urea levels of 60 mg/dL, and an abdominal ultrasound showed bilateral renal stones with hydronephrosis and right renal atrophy. She was therefore admitted to the urology department for ureteral catheterization. Clinical signs consistent with an acute abdomen were observed on the following day, with 17,000 WBCs and neutrophilia in laboratory tests and pneumoperitoneum in a computed tomography (CT) scan of the abdomen. During emergency surgery, colonic perforations by scybala were found, and a colectomy with discharge ileostomy was therefore performed. On her second day in the intensive care unit she experienced neurological impairment leading to stupor. Tests were performed to rule out pharmacological (negative urinary tests for benzodiazepines and opiates), infectious (germ-free lumbar puncture), and neurological causes (no acute intracranial disease in CT, normal electroencephalogram). On the fifth day, laboratory tests showed serum calcium levels of 18.2 mg/dL (8.1-10.2), phosphorus levels of 2.4 mg/dL (2.7-4.5), protein levels of 55.1 g/L (66-87), and albumin levels of 23 g/L (35-50), with a corrected calcium level of 19.5 mg/dL. Her urinary calcium level was 1,734 mg (100-230), with a urine output of 6,200 mL. Serum parathormone (PTH) levels were 1,933 pg/mL (12-72). PHP was diagnosed, and treatment was started with an intravenous infusion of 4 L of 0.9% saline, furosemide, calcitonin, and bisphosphonates (zoledronic acid). The patient recovered from stupor in 24 hours. Thyroid ultrasound examination, a cervical CT, and MRI of the neck and chest revealed a mixed 2-3 cm nodule in the right thyroid lobe (RTL) with no typical parathyroid characteristics, although an atypical parathyroid adenoma could not be ruled out. A technetium-99m sestamibi (^{99m}Tc-MIBI) scan did not show any hyperfunctional parathyroid glands, and an octreoscan showed hyper-uptake at the RTL nodule. The patient was transferred to the endocrinology department for ultrasound-fine needle aspiration (FNA) and to complete the work-up. The ultrasound showed a mainly cystic mixed nodule in RTL with a solid isoechogenic area, well delimited, 1.71 x 2.34 cm in size, and apparently intrathyroid in location (Fig. 1). FNA of the solid and cystic area (3 mL of colloid, blood-stained fluid) revealed a morphological and immunocytochemical pattern consistent with parathyroid cellularity. Thyroid hormone levels were normal: thyrotropin (TSH) 0.46 μIU/mL (0.35-5.5) and free thyroxine (T4L) 0.84 ng/dL (0.84-1.76). PTH concentration in 7 mL of fluid drawn in a second aspiration was > 19,000 pg/mL. X-rays of the hands and skull were normal, and bone densitometry showed osteopenia in the femur and lumbar spine with T-score values of −1.8 and −2.2 respectively. Renal function normalized, but not calcemia (11.3 mg/dL), and an additional dose of zoledronic acid was therefore given. One month after the crisis, the patient underwent surgery consisting of right hemithyroidectomy and right inferior selective parathyroidectomy. Serial PTH measurements done before and 5 and 10 minutes after resection found values of 550, 183, and 83 pg/mL respectively. Gross examination by the pathological laboratory revealed a whitish, fleshy nodule, 3.5 cm in diameter and 4 g in weight identified as a parathyroid adenoma, and microscopic examination revealed a circumscribed, encapsulated tumor consisting of polygonal cells with wide and clear cytoplasms and round nuclei with no atypia arranged in nests or macrofollicles, with a solid appearance at the periphery and a cystic appearance at the center consistent with a cystic parathyroid adenoma. No vascular or capsular invasion was observed (Fig. 2). After one month, the patient was asymptomatic and with a calcemia of 9.3 mg/dL.

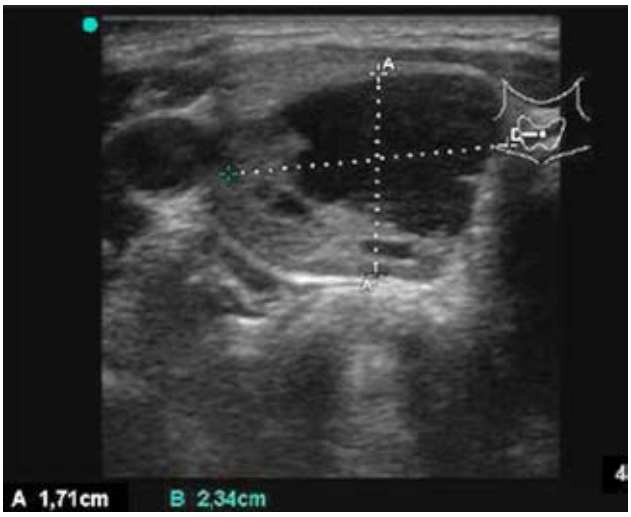

Figure 1 Predominantly cystic mixed nodule, 1.7 x 2.3 cm in size, in right thyroid lobe.

The most frequent cause of PHP is an isolated adenoma, most common in the lower parathyroid glands, 1-3 cm in size, 0.3-5 g in weight, and in post-menopausal women aged 50-60 years[1].

Currently, 70%-80% of patients diagnosed with PHP have few or no symptoms. PC is a rare manifestation of PHP caused by an adenoma, cystic adenoma, atypical adenoma, or parathyroid carcinoma. PC has a 100% mortality rate without treatment and a 20% mortality rate when medical treatment and surgery are combined[2].

Both intrinsic factors (degeneration or acute infarction of a pre-existent adenoma) and extrinsic factors (immobilization or a concomitant disease causing dehydration and decreased calcium excretion, promoting crisis development, especially in the case of a pre-existent asymptomatic hyperparathyroidism) appear to be involved in PC[3,4]. These factors coexisted in our patient, who had undergone colectomy and was immobilized, with drains and catheters that promoted dehydration, had bilateral kidney stones suggesting a long-standing pre-existent hyperparathyroidism which could not be documented because no prior calcium levels were available, and also had a cystic parathyroid adenoma similar to those reported by other authors[5-8].

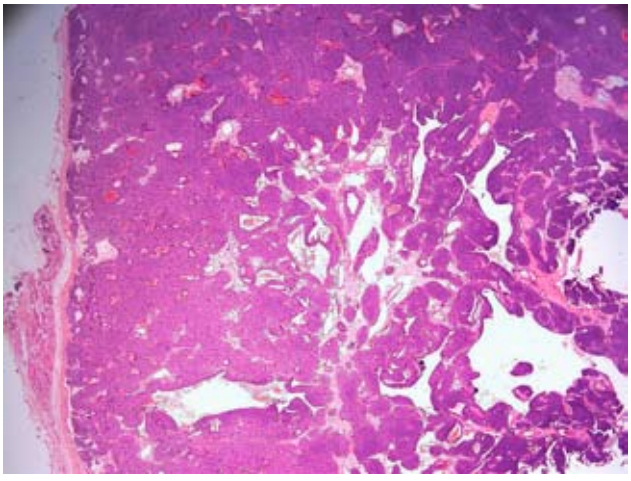

Figure 2 Pathological study showing parathyroid adenoma with a solid part at its periphery and a cystic part at its center.

Parathyroid cysts are classified as non-functional and functional. Functional cysts account for 10%-15% of all parathyroid cysts and are associated with hyperparathyroidism, hypercalcemia, and hypophosphatemia. Non-functional cysts usually contain a clear, transparent fluid, while the fluid in functional cysts is usually brown or hemorrhagic.

There are different theories concerning the etiology of parathyroid cysts, including retention of gland secretions, embryological remnants of the third and fourth pharyngeal pouch, cystic degeneration of the parathyroid glands, the enlargement or coalescence of microcysts, and the persistence of Kursteiner canals, but none of them is applicable in all cases. There is however greater agreement about the etiology of functional cysts, which result from cystic degeneration, infarction, or bleeding from a pre-existent adenoma[7].

Differential diagnosis of adenoma, cystic adenoma, atypical adenoma, and carcinoma is mainly histological, and is difficult from the clinical viewpoint. Very high PTH and calcium levels are more commonly seen in cystic and atypical adenomas and carcinoma. The finding of a rapidly growing palpable cervical mass and local compressive symptoms such as paralysis of the recurrent laryngeal nerve suggests carcinoma. Histologically, adenoma has no mitotic activity or capsular or vascular invasion. A typical adenoma shares some characteristics with carcinoma such as the presence of fibrous bands, capsular invasion, and mitotic activity, but not vascular invasion or metastases, which are found only in carcinomas[7,8].

Parathyroid cystic adenomas cannot be distinguished from thyroid cysts by imaging techniques. Fine needle aspiration and measurement of intracystic PTH and thyroglobulin levels may therefore be of help in differentiating them[3]. Functional cysts have higher intracystic PTH levels as compared to non-functional cysts, sometimes reaching up to several million pg/mL[8].

Cervical ultrasound and ^{99m}Tc-MIBI scan are the most commonly used location techniques. According to different studies, their sensitivity and specificity range from 74%-79% to 96% respectively for ultrasound and from 58%-88% to 96% for scans. Tublin et al suggested that ultrasound should first be performed by experienced clinicians, followed by a scan when ultrasound results are negative or equivocal[9]. The absence of parathyroid tissue at the periphery of the cystic adenoma and the rapid clearance of the radiotracer may explain false negative results with ^{99m}Tc-MIBI scans[8].

Because of the lack of conclusive results from the cervical ultrasound and ^{99m}Tc-MIBI, and to rule out ectopic PTH production[10], an octreoscan was performed, showing uptake at the RTL, but not at other levels. Although some parathyroid adenomas express somatostatin receptors[11], octreoscan is not a routine procedure for locating PHP. Subsequent FNA and the measurement of intracystic PTH levels confirmed the parathyroid origin of PTH.

As regards the treatment of PC,rapid recognition of the condition and the early management of hypercalcemia are

essential for reducing the mortality rate[12]. Medical treatment rarely restores normal calcium levels. Surgery is the definitive treatment, with a 98% cure rate and a 2.3% complication rate when performed by qualified surgeons. While waiting for elective surgery, the patient should be stabilized by intravenous infusion of 2-4 L of 0.9% saline, furosemide, calcitonin, and bisphosphonates. Hemodialysis may be required in some cases.

The reported case demonstrates the need for measuring calcium levels in patients with no remarkable history in whom renal function impairment and kidney stones are found in order to rule out an associated primary hyperparathyroidism. Metabolic changes, including hypercalcemia, should also be considered as the cause of impaired consciousness so that immediate intensive medical treatment may be started.

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Cervical chylous fistula after lymphadenectomy for papillary thyroid carcinoma treated with somatostatin analogs

Fístula quilosa cervical tras linfadenectomía por carcinoma papilar de tiroides tratada con análogos de la somatostatina

To the Editor:

The occurrence of a chyle fistula due to injury to the thoracic duct or one of its affluents following cervical dissection and/or lymphadenectomy is an uncommon complication during surgery for thyroid carcinoma. Various treatment approaches have been described, of which surgery is reserved as the final option when all other approaches have failed. We report a chyle fistula occurring after thyroidectomy with lymphadenectomy for papillary thyroid carcinoma which was resolved with conservative management using somatostatin analogues (octreotide).

A 34-year-old female patient with an unremarkable history attended the clinic for subclinical hypothyroidism. A physical examination revealed the presence of a hard stone nodule, approximately 2 cm in size, in the left thyroid lobe. No cervical adenopathies were palpated. Tests for thyroid hormone and anti-thyroid antibody levels were performed before surgery but showed no significant changes. An ultrasound examination showed the presence of an 11-mm nodule in the left thyroid lobe with gross calcification inside. Fine needle aspiration of the lesion revealed a papillary carcinoma of the thyroid gland. Surgery consisting of total thyroidectomy with excision of the central cervical and bilateral jugular lymph nodes was performed. The final histological study confirmed the presence of a 1.7-cm papillary thyroid carcinoma involving one of the nodes in the central compartment and one node in each jugular chain. One week after surgery, the patient reported a lump, fluctuating upon palpation, in the left cervical region. Upon puncture (fig. 1), a whitish fluid (lymph) was collected. After three fluid evacuations, one per week, combined treatment was started with a diet rich in middle-chain fatty acids plus octreotide (0.1 μg/8 hours subcutaneously), and the fistula healed in the first week of treatment.