

Primary hyperparathyroidism and Gougerot disease

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Abstract

Primary hyperparathyroidism (PHPT) is a common endocrine disorder caused by the overactivation of the parathyroid glands due to the autonomous production of the parathyroid hormone (PTH). The resultant hypercalcemia leads to a myriad of symptoms. Here we report the case of a 54-year-old female with a previous diagnosis of Gougerot disease, in whom clinical (diffuse bone pain, asthenia polydipsia, and polyuria) and laboratory features (calcium level, 3.1 mmol/L; phosphate level, 0.55 mmol/L; alkaline phosphatase level, 70 U/L; and intact PTH level, 1028.9 pmol/L) prompted the diagnosis of PHPT caused by a parathyroid adenoma as confirmed by anatomopathology. After treatment with renal replacement therapy, intravenous fluids and zoledronic acid, and subtotal parathyroidectomy, the patient status improved, with normal laboratory tests. However, the fortuitous nature of the association between Gougerot disease and PHPT as well as the physiopathological links between these two diseases remain to be specified.

Keywords: Gougerot disease, primary hyperparathyroidism, hypercalcemia, parathyroid hormone

Introduction

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders in the general population and is easily diagnosed by measuring the parathyroid hormone (PTH). Gougerot disease is an autoimmune disorder characterized by the lymphoid infiltration of salivary and lachrymal glands easily accessible favoring the diagnostic, and it could be primary or more often associated with another autoimmune disease (1). We report here the association between PHPT and Gougerot disease in a Moroccan patient, who was diagnosed at the department of endocrinology at the University Hospital Hassan II, Fez. We report this case in order to discuss a possible link between these two affections. Informed consent was obtained from the patient.

Case presentation

A 54-year-old woman with a 1-year history of Gougerot disease diagnosed by (xerostomy; anti-SSa- and anti-SSb-positive, and Chisholm stage IV lymphocytic sialadenitis). The etiological investigation confirmed a primary Gougerot disease without associated extraglandular manifestations and the patient received prednisone 30 mg/day.

There was no family history of thyroid/parathyroid disorders or history of previous radiation; the patient presented with a complaint of weakness and bone and joint pain, polydipsia, and polyuria. Physical examination was unremarkable.

Various additional examinations were conducted. Laboratory investigations revealed hypercalcemia (3.1 mmol/L), hypophosphatemia (0.55 mmol/L), and elevated intact PTH level (1028.9 pmol/L). The urinary calcium level was high at 210 mg/24 h, and the alkaline phosphatase level was 70 uL/L. Thyroid levels were normal; renal assessment and blood iconography results were normal.

Calcium level gradually increased. The electrocardiogram has objectify a shortening of the QT interval and the hypercalcemia was managed with renal replacement therapy, intravenous fluids, furosemide (Lasilix; Group sanofi-aventis, Casablanca, Morocco), and zoledronic acid (Zometa®; Novartis Pharmaceuticals, Casablanca, Morocco).

The cervical-thoracic magnetic resonance image revealed a nodule of 36 mm in the major axis sitting in the left parathyroidal lobe (Figure 1.A and B) evoking a parathyroid adenoma given to the clinical and biological context. A surgical treatment of the parathyroid adenoma was then indicated.



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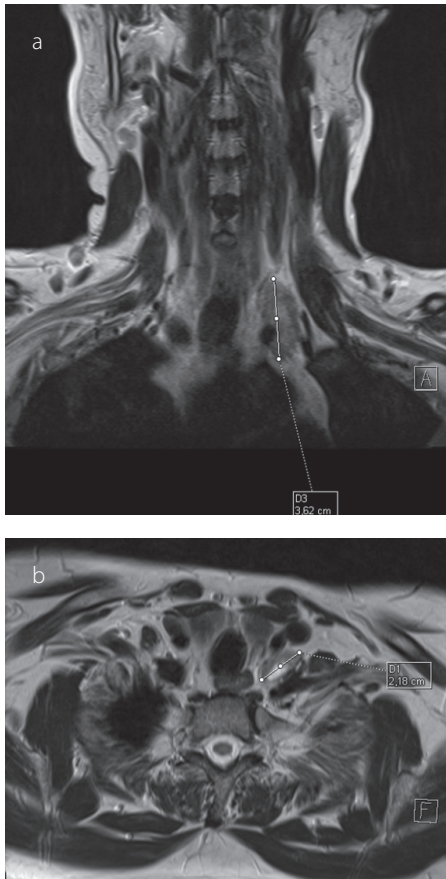


Figure 1. a, b. Axial T1-weighted magnetic resonance image shows the nodule in the left parathyroidal lobe (a); Coronal T1-weighted magnetic resonance image shows the nodule in the left parathyroidal lobe (b)

The patient underwent a successful surgical removal of the lesion. Pathology confirmed the presence of a parathyroid adenoma. The patient did not present with hungry bone syndrome in the immediate postoperative period, and postoperative PTH levels were normal [52.2 (normal range, 15-68) pg/mL]; calcium level was 91.8 (normal range, 88-106) mg/L.

Discussion

Hypercalcemia is a common electrolyte abnormality. It can result from malignancy and is caused by elevated PTH activity in more than 90% of cases.

PHPT is a common endocrine disorder in which PTH is excessively secreted from one or more of the four parathyroid glands, which leads to abnormal calcium regulation and hypercalcemia.

The parathyroid gland is the overall regulatory organ that maintains calcium homeostasis through their capacity to sense even minute changes in the level of blood calcium. External Calcium inversely regulates the release of parathyroid hormone through cell surface-bound

calcium-sensing receptors. In PHPT, Calcium is reset upward from its normal level. This defect likely arises from the increases in both the mass of pathological parathyroid tissue as well as the set point for Calcium regulated PTH release.

A single benign parathyroid adenoma is the most frequent cause of PHPT in more than 80% of patients, followed by hyperplasia in approximately 15%, and cancer in 1%-5% (2). Most cases of PHPT are sporadic and few are familial.

Many experimental findings have improved our understanding of the pathophysiology and causes of PHPT. A number of possible genetic disorders have been identified, establishing it as a multifactorial disease (2).

The association of PHPT with Gougerot disease is quite rare, with five such cases retrieved from the literature; all cases had hypercalcemia, four had moderate hypercalcemia, and only one patient had severe hypercalcemia, as in our case (3). All cases were selected according to the US-European diagnostic criteria for Gougerot disease.

Together with our case, all five patients were aged over 50 years, with a median age of 59.1 years when PHPT was diagnosed. There was a female predominance and a sex ratio of 4 females/1 male. PHPT preceded by about 1 year the Gougerot disease in only one case; the two disorders were discovered concomitantly in two cases; and PHPT diagnosis succeeded Gougerot disease in two cases. All patients, including ours, had a parathyroid adenoma. Surgery was performed in all cases. Postoperatively, all patients were relieved of hypercalcemia.

Gougerot disease, as other connective tissue disorders, is a very rare cause of hypercalcemia, with only 10 cases reported for systemic lupus erythematosus (SLE) (4, 5).

Various pathogenetic mechanisms have been proposed to explain hypercalcemia in patients with connective tissue disorders that was not attributed to an underlying disorder. The pathogenesis involves polyclonal overactivation of B lymphocytes in connective tissue disorders such as Gougerot disease and could produce anti-PTH receptor autoantibodies that might activate the PTH receptor, leading to hypercalcemia with suppressed levels of PTH and PTH-related protein (PTH-rP) (1, 6, 7). PTH-rP promotes hypercalcemia in both malignant and various benign diseases. Moreover, certain cytokines such as interleukin and prostaglandin released in patients with active SLE, might stimulate osteoclastic bone resorption, leading to hypercalcemia (8).

Endocrine symptoms are documented in up to 15% of primary Gougerot disease patients mainly due to concomitant thyroid dysfunction (9). The most common thyroid disorder found was autoimmune thyroiditis. Moreover, increased prevalence of thyroid diseases was also documented in family members of primary Gougerot disease patients, suggesting genetic susceptibility such as the presence of human leukocyte antigen-DR3 (10). Hence, it is advisable that patients with Gougerot disease should be periodically screened for thyroid function.

Two cases of a rare association of Gougerot disease with hypoparathyroidism were also reported in the literature (11, 12). The underlying pathophysiology was supposed to be either a common genetic predisposition or the extension of the autoimmune process to the parathyroid glands, which is still under debate (12).

In the present case, Gougerot disease was stable and could be safely eliminated as the main cause of hypercalcemia because PTH rate was very high and serum calcium level normalized soon after parathyroidectomy.

The present case suggests that for every patient with Gougerot disease and elevated serum levels of calcium, the presence of primary hyperparathyroidism should be searched since surgical therapy leads to a complete resolution of hypercalcemia. The fortuitous nature of the association between Gougerot disease and PHPT as well as the physiopathological links between these two diseases remain to be specified.

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