Parathyroid carcinoma presenting as a giant mediastinal retrotracheal functioning cyst

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ABSTRACT

Parathyroid carcinoma is a rare malignancy of the parathyroid glands, and is the cause of primary hyperparathyroidism in fewer than one percent of cases. Symptoms are mainly due to local compression or hypercalcaemia secondary to markedly elevated parathyroid hormone levels. A minority of patients remain asymptomatic. Mediastinal parathyroid cysts are infrequent and may or may not be functioning. We present an 84-year-old woman with a giant functioning cystic parathyroid carcinoma located in the middle mediastinum. We performed a thorough MEDLINE and LILACS database search on published cases of parathyroid carcinoma and functioning parathyroid cysts, and found no case report with identical features to the one presented here.

Keywords: hypercalcaemia, hyperparathyroidism, mediastinal cyst, parathyroid carcinoma

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INTRODUCTION

Parathyroid carcinoma is rare, and is the cause of primary hyperparathyroidism in less than 1% of cases in most series.[1-3] Clinical manifestations are mainly due to excessive parathyroid hormone (PTH) secretion, but compression and infiltration of neighbouring structures may also play a role in morbidity. Less than 7% of the cases remain asymptomatic.

Although diagnosis is usually confirmed intraoperatively or after surgery, clinical suspicion may be aroused when calcium levels rise above 14 mg/dL, alkaline phosphatase and PTH levels are very high, kidney and bone involvement coexists, and when there is a palpable cervical mass with or without recurrent laryngeal nerve paralysis. Most reports define these kinds of tumours as solid masses ranging from 1.5 to 6 cm in diameter, but isolated cases of cystic carcinomas have also been described.

Parathyroid cysts occur very infrequently. They are usually located in the inferior parathyroid glands and are sometimes mistakenly assumed as thyroid nodules; they may occasionally be found in the mediastinum.[4-11] In 1925, De Quervein reported, for the first time, a mediastinal parathyroid cyst resection.[4,5] By 1999, 96 cases of mediastinal parathyroid cysts had been reported, 39 of which were functioning.[4,5] We report a female patient with a giant functioning cystic parathyroid carcinoma within the mediastinum.

CASE REPORT

An 84-year-old woman, maintaining full independence in the activities of daily living and who has a history of arterial hypertension, perforated gastric ulcer, chronic constipation, and severe osteoporosis with hip and vertebral fractures, presented to the hospital with complaints of progressive dyspnoea (worsening from NYHA functional class II to IV) and a dry cough over the past four weeks, despite having been treated with a ten-day course of clarithromicin. She also experienced difficulty in swallowing fluids.

Findings on physical examination included hypertension, tachypnoea with mild supraclavicular retraction, mild inspiratory stridor, bilateral basal crepitations predominating in the right lower lung field, 92% pulse oximetry saturation and breathing 21% oxygen with no signs of heart failure, although there was jugular venous distension when the patient raised both arms. Remarkable features to note included the presence of dyspnoea and hoarseness, which were exacerbated with left lateral decubitus. She had a severe dorsal kyphosis, mild diffuse goitre and no palpable lymph nodes. Relevant laboratory findings were calcium level 11.2 mg/dL (2.8 mmol/L), phosphataemia 1.6 mg/dL, albuminaemia 3.8 g/dL, TSH 2 µU/ml, alkaline phosphatase 148 UI/L (normal range 40–100 UI/L), intact PTH (iPTH) 230 pg/ml (normal range 15–65 pg/ml), and 25 OH-vitamin D levels of 18 ng/ml (normal range 14–39.3 ng/ml). Haemogram and renal function values were normal.

Chest radiograph revealed superior right-sided mediastinal widening, with tracheal displacement

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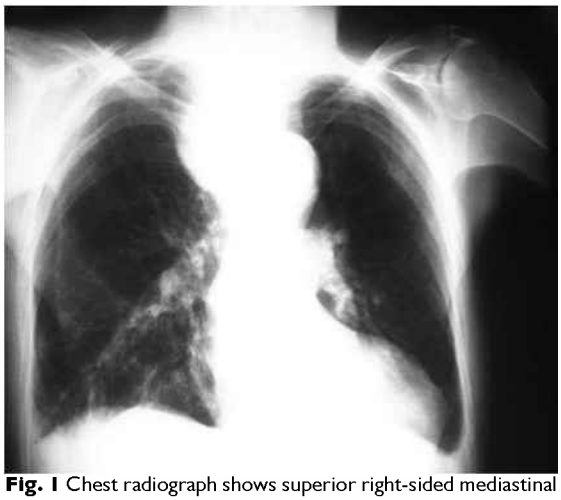

Fig. 1 Chest radiograph shows superior right-sided mediastinal widening, tracheal displacement and a mild interstitial infiltrate at the right base.

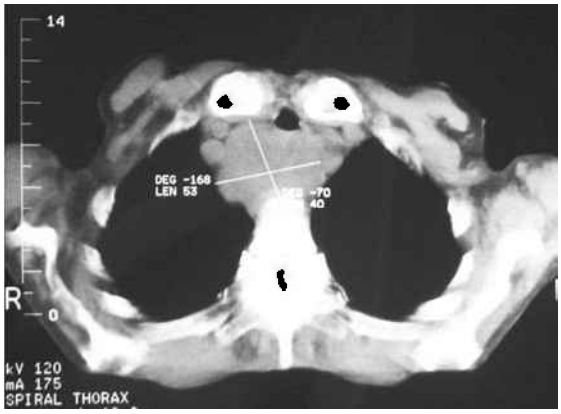

Fig. 2 CT image shows a right medial mediastinal mass with tracheal and superior vena cava displacement.

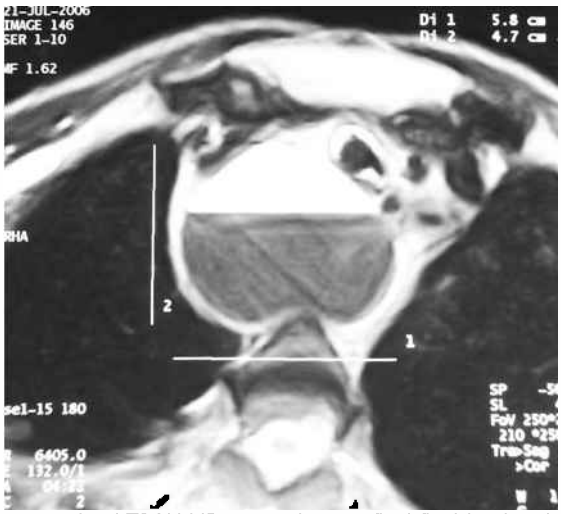

Fig. 3 Axial T2-W MR image shows a fluid-fluid level with two different intensities within the mass.

to the left and a mild interstitial infiltrate at the right base (Fig. 1). Cranial radiographs showed radiolucent areas suggesting hyperparathyroidism-related bone involvement. Computed tomography (CT) revealed a right medial mediastinal mass with tracheal and superior vena cava displacement to the left and right, respectively. Posterolateral oesophageal displacement and bilateral alveolointerstitial infiltrates predominating in the right base were also noted (Fig. 2). Due to dysphagia and suspicions of an aspiration pneumonia, an oesophageal transit using X-ray fluoroscopy was performed; this showed a remarkable lumen displacement due to extrinsic compression of the oesophagus and massive aspiration of barium contrast in the first few swallows. The procedure was therefore terminated.

During her hospital stay, the hypercalcaemia was treated with parenteral hydration, subcutaneous calcitonin and a 90-mg pamidronate infusion. In order to evaluate the tracheobronchial lumen and to perform a bronchoalveolar lavage of the infiltrate, bronchoscopy was initiated, but the procedure had to be discontinued due to excessive tracheal deviation and patient intolerance (i.e., cough, dyspnoea, and oxygen desaturation). A CT-guided fine-needle aspiration of the mass was then performed. Brownish fluid that was microscopically defined as serosanguineous was obtained, but the pathologist was unable to define its histological origin. Shortly after the procedure, the patient's dyspnoea and dysphagia worsened, and calcium levels rose.

For further evaluation, we performed a gadolinium-enhanced chest magnetic resonance (MR) angiography. The MR angiography of the neck revealed a voluminous mediastinal tumoral formation (58 mm wide × 89 mm high), which displaced the trachea forward and to the left, the aorta to the left, and seemed to compress a calibre-decreased superior vena cava. T2-weighted images showed a fluid-fluid level with two different intensities within the mass. The cyst pushed the right thyroid lobe forward and the oesophagus posteriorly (Fig. 3). Technetium-99 (Tc-99) sestamibi scintigraphy revealed an area of increased tracer uptake in the cyst limits, which is suggestive of its parathyroid origin.

In order to alleviate the patient's symptoms and obtain a diagnosis, a repeated CT-guided puncture was attempted, which produced 37 ml of brownish fluid. Symptoms improved transiently during the first 24 hours after the procedure. Part of the fluid aspirate and a blood sample were processed simultaneously for iPTH and thyroglobulin. Cytology yielded negative results for a second time. iPTH levels in the fluid aspirate were > 2000 pg/ml (maximum dilution limit)

and blood iPTH > 190 pg/ml, while thyroglobulin levels were 2.7 ng/ml in the fluid aspirate and blood samples as well.

In spite of the patient's advanced age and her progressively worsening state, a surgical resolution was proposed in order to reach an aetiological confirmation and to alleviate persistent symptoms. Surgery was finally approached through a cervicotomy. Intraoperatively, a hard mass infiltrating neighbouring structures, such as thyroid gland, carotid artery, oesophagus and trachea, was found. The procedure had to be terminated as any attempt to remove the mass produced substantial bleeding. The cyst-wall biopsy revealed parathyroid tissue. By correlating clinical, histological and intraoperative findings, a diagnosis of parathyroid carcinoma was established. To this day, the patient remains well with mild dysphagia and moderate dyspnoea upon exertion, and requires enteral feeding.

DISCUSSION

There are approximately 700 reports of parathyroid carcinomas.[1-3] Most of them have been diagnosed while evaluating a primary hyperparathyroidism or a cervical mass, but a few have been detected from mediastinal, usually solid and small-sized, tumours. The median age gathered from aetiological confirmation ranges from 44 to 54 years.[1,2] Its course varies; while one-third of the patients may remain tumour-free after a complete resection, another third may have a local recurrence or distant metastases mainly in lymph nodes, lungs, bones and liver. The remaining third may experience an aggressive behaviour which ultimately leads to death.[1,2] Hypercalcaemia secondary to tumour-cell PTH hyperproduction, accounts for the main cause of morbimortality in this group of patients. An elevation of PTH levels is usually reported as three to ten-fold above normal, while calcium levels may be found above 14 mg/dL.

In our case, the main problem arose from tumoral infiltration and compression of neighbouring structures. Calcium values were not as high as the average value, which might have been associated with a coexistent vitamin D insufficiency and only moderately increased values of iPTH by three-fold. The latter might have been related to the cystic features of the tumour with a lesser amount of functioning cells than a solid mass. On the other hand, macroscopic parathyroid cysts, defined as ≥ 1 cm in size, are well-known but infrequent entities. Cases reported so far show that most of them are cervical and only 94 were located within the mediastinum (i.e., wholly mediastinal or cervicomediastinal). This last group of mediastinally-located cysts was usually found in the anterosuperior compartment.[4,5,7,12]

Although cysts occur 2.5 times more frequently in women than in men, functioning cysts seem to occur 1.6 times more frequently in men.[5] Most cases are uniloculated, encapsulated and contain a transparent fluid, although they may occasionally be sanguineous. Mediastinal parathyroid cyst descriptions abound in literature, ranging from 0.5 to 12 cm in size. Most of them are small (< 4 cm) and giant cysts are the exception.[5,13] There are a myriad of theories proposed to explain the mechanisms for the formation of these cysts: gradual intraglandular fluid accumulation creating a retention cyst; microcyst coalescence; cystic degeneration of a parathyroid adenoma; productive vestiges of remnant Kursteiner canals; or cysts derived from embryologic pieces of the third and fourth branchial arches.[4,7,12]

Depending on whether they are located in the anterior, middle or posterior compartments in the mediastinum, cysts are classified into: (1) anterosuperior, i.e., pretracheal and retrosternal, which are the most frequently seen and usually originate in the inferior glands, although proliferation from supernumerary glands may also occur; (2) middle mediastinal, such as the case described here, located in the retrotracheal region; and (3) posterior mediastinal, which are rarely found.[5]

Patients with mediastinal parathyroid cysts may be free of symptoms, or may be symptomatic due to tracheal, oesophageal or superior vena cava compression, recurrent laryngeal nerve involvement or elevated PTH-induced hypercalcaemia.[4,9,11,12] Suspicions of a parathyroid origin, aroused from an increased tracer uptake after a Tc-99 sestamibi scan, may be confirmed by an elevated cystic fluid-serum-iPTH ratio after a fine-needle aspiration, or through a surgical biopsy. Small and asymptomatic cysts, especially nonfunctioning ones, may be treated with a minimally-invasive puncture and aspiration. Bigger and symptomatic cysts usually require surgery.[5] The treatment of choice for parathyroid carcinoma is surgical resection, and medical treatment is required for the management of hypercalcaemia. As for other treatment methods, chemotherapy has not yet been proven useful, and the role of radiotherapy is controversial.[14,15] This is the first known case report of giant functioning parathyroid carcinomas located in the middle mediastinum with cystic features.

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