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Case Report
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Venous Thrombosis Revealing Metastatic Intrathyroid Parathyroidal Carcinoma

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Abstract

Intrathyroid Parathyroidal Carcinoma (PC) is an extremely rare entity. Preoperative diagnosis can be difficult, particularly, in case of thyroidal nodule without clinical or biological signs of hyperparathyroidism. We share our experience with a case of metastatic intrathyroidal PC, in a 53 year-old female, mistaken for a thyroidal tumor. Histopathological examination with immunohistochemical staining confirmed the diagnosis of PC. Signs of hyperparathyroidism should be routinely searched in the presence of thyroidal nodule. Surgery is the mainstay of the management of this pathology with close surveillance.

Introduction

Parathyroid Carcinoma (PC) is an uncommon malignant endocrine neoplasm which accounts for less than 1% of all cases of primary hyperparathyroidism [1]. PC arising from thyroid gland is an extremely rare entity [2]. To our knowledge, 25 cases have been reported in English Medical Literature. The preoperative diagnosis of intrathyroid PC can be difficult and made at later stages, especially in the absence of hypercalcemia. We share our experience on an unusual case of metastatic intrathyroid PC, with normal serum calcium level, revealed during venous thrombosis investigation.

Case Presentation

A 53 year-old female, with no medical history, presented to the emergency room with 5 days of painful swelling of the right limb. A deep venous thrombosis was confirmed by color Doppler ultrasonography and the patient was referred to the cardiology department. During investigation, the patient reported bone pain and progressive deterioration of general status. A chest-abdomen-pelvis Computed Tomography (CT) scan was performed revealing left thyroid nodule and multiple osteolytic lesions suggesting bone metastasis.

Neck examination showed firm left thyroid nodule. Neck ultrasonography demonstrated a 3 cm mildly hypoechoic left thyroid nodule with an oval shape and regular margins, classified EU-TIRADS 4 (Figure 1). Laboratory examination revealed normal levels of thyroid hormones. Serum calcium was at the high limit of normal range (2.5 mmol/l) with normal serum phosphorus and normal renal function. There were no signs or symptoms of hypercalcemic crisis such as nausea, vomiting or confusion.

The patient underwent surgery. During neck exploration, a firm mass was distinctly part of the left thyroid without a plane between the tumor and the thyroid lobe. Three normal-sized parathyroid glands were identified. En-bloc resection of the left thyroid lobe was performed. The intraoperative rapid pathology demonstrated malignancy features suggesting follicular thyroid carcinoma; a total thyroidectomy was then performed. There were no lymph nodes during exploration.

Final histopathological examination showed neoplastic epithelial cells, predominantly chief cells associated to oxyhil ones in solid arrangement with mitotic figures (<5 mitoses/10 high-power fields) (Figure 2A). Capsular invasion was observed. Immunohistological staining of tumoral cells showed strong positive chromogranin expression (Figure 2B), while thyroglobulin (Figure 2C) and calcitonin (Figure 2D) were negative; thus confirming that the tumor cells were parathyroid in origin. Osteolytic lesions on CT scan were thought to be related to bone metastasis and initial venous thrombosis to paraneoplastic syndrome.

Postoperatively, the patient presented hypocalcemia. A supplementation with intravenous and oral calcium as well as calcitriol and levothyroxine was started. The patient was discharged on the 7th postoperative day with an appointment for 99mT sestamibi scintigraphy. Unfortunately, the

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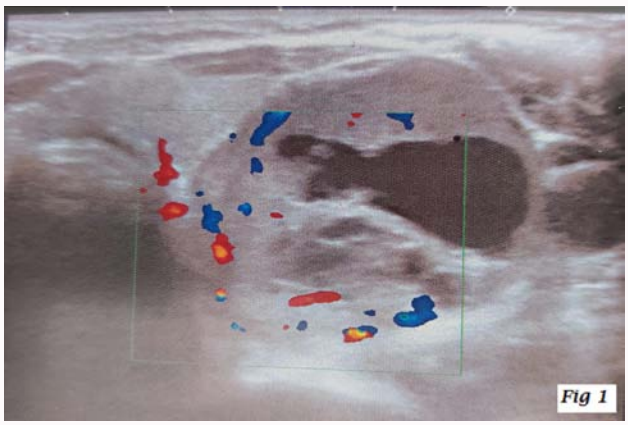

Figure 1: Ultrasonography showing a 3 cm mildly hypoechoic left thyroid nodule with an oval shape and regular margins, classified EU-TIRADS 4.

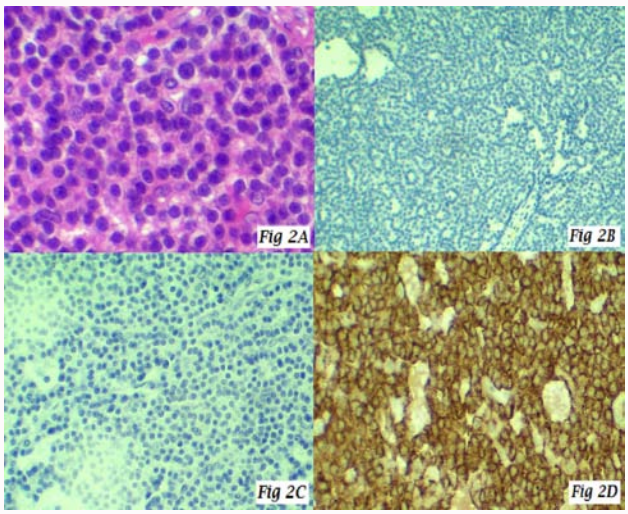

Figure 2: A) Histopathological examination showing neoplastic epithelial cells in solid arrangement with few mitotic figures. B) Strong positive chromogranin staining. C) Negative expression of thyroglobulin. D) Negative expression of calcitonin.

patient was not compliant and she refused any further exploration or treatment.

Discussion

PC is a rare malignant endocrine neoplasm. Less than 1000 cases of PC have been reported in the English Medical Literature [3] and only 25 cases with intrathyroidal localization. To the best of our knowledge, our patient is the first reported intrathyroidal PC revealed by paraneoplastic syndrome and the second reported one with normal serum calcium [2].

Parathyroid glands can be located in ectopic sites in some individuals. This event is due to faulty migration from the third and fourth branchial pouches, during embryogenesis, leading to the formation of mediastinal, pharyngeal or intrathyroidal parathyroid glands [3]. The latter is considered the most uncommon site of ectopic gland (0.2%) [2].

Patients with PC are usually severely symptomatic at the time of presentation with severe hypercalcemia, while patients with normal level of serum calcium are extremely rare (2%) [2,4]. This may lead to diagnosis at later stages and thus a poorer prognosis. In our case, there were no symptoms related to hyperparathyroidism; serum calcium was at the high limit of normal range and venous thrombosis, related to paraneoplastic syndrome, revealed metastatic disease. A palpable mass can be found, as in our case, in 30% to 75% of patients with PC [1]. Most cases of intrathyroidal PC reported palpable thyroidal nodule at presentation, making confusion with a thyroidal tumor, especially in the absence of clinical or biological signs of hyperparathyroidism [1-3].

The diagnosis of PC is suspected in the presence of biological and imaging criteria. However, the final diagnosis is based on histological analysis. Preoperative localization of parathyroid lesions is mainly based on neck ultrasound and especially 99mT sestamibi scintigraphy. The combined use of ultrasonography with sestamibi scintigraphy has a sensitivity of 95% *vs.* 80% for sonography alone and 87% for scintigraphy alone [5]. Recently, 11C-methionine PET/CT or 18F-fluorocholine PET/CT have been shown as useful second-line imaging tools in patients with negative or discordant conventional imaging modalities [6,7].

Unfortunately, to distinguish PC from adenomas is still challenging. Architecturally, the PC shows a solid to trabecular growth pattern. Histopathologically, it can show islands of tumor cells separated by thick fibrous bands, tumor cell necrosis, capsular, vascular and perineural invasions. Moreover, increased mitotic activity, high nuclear-to-cytoplasmic ratio, irregular nucleoli and perinuclear halos indicate malignancy [4,8]. Furthermore, adjacent tissues invasion, lymph or distal metastases are suggestive of carcinoma [2,4,8].

The other challenge for the pathologist is to distinguish thyroid (follicular and medullary thyroid carcinomas) from parathyroid malignancies. As in our case, immunostaining for PTH, chromogranin, thyroglobulin and calcitonin can be successfully used. Indeed, PC malignancies are immunoreactive for PTH and chromogranin and not for thyroglobulin and calcitonin [9].

Surgery is currently the only effective treatment modality of PC. It requires an "en-bloc" resection of the tumor and an ipsilateral thyroid lobectomy with gross clear margins as well as remove of involved structures or local metastatic lymph nodes [1,3,10]. PC is usually radio-resistant [1]. In the absence of effective chemotherapy regimen, adjuvant chemo-radiation is useless [1].

After surgery, long term surveillance is required to detect persistent or recurrent PC. Besides, PTH and calcium levels monitoring, imaging follow-up is based mainly on 99mTc-sestamibi SPECT/CT. Recently, the role of 18F-fluorocholine PET/CT has been demonstrated, particularly in early stages [11].

Conclusion

Intrathyroidal parathyroid carcinoma is an extremely rare entity. In the presence of thyroidal nodule, clinical and biological signs of hyperparathyroidism should be routinely assessed. Localization of ectopic parathyroid gland is mainly based on ultrasonography and 99mTc-sestamibi scintigraphy. Surgery is the mainstay of the management of this pathology. Close clinical, biological and radiological follow-up is mandatory because of the high risk of recurrence.

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