# How to deal with parathyroid carcinoma: case report, histological difficulties and literature review

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**Abstract**

The histological diagnosis of parathyroid carcinoma is often difficult due to the existence of many potentially misleading similarities, between this malignant entity and its main differential diagnosis: parathyroid adenoma.

Several histological criteria of malignancy have been proposed in order to solve this diagnosis problem: the presence of fibrous bands emerging from a thick capsule dividing the tumor proliferation into lobules, tumor cells arranged in clusters and trabeculae, moderate to clear cytonuclear atypia and low mitotic activity. Unfortunately, these criteria are not exclusive to carcinomas and can also be seen in cases of adenomas.

The more relevant histological criteria of malignancy are proposed, such as atypical mitosis, capsular invasion, vascular invasion or the exceptional perineural invasion. But these criteria are rarely found. Infiltration of the thyroid gland, adjacent soft tissue and the occurrence of metastases remain the only indisputable signs of malignancy.

Immunohistochemistry can contribute to the differential diagnosis, especially with the loss of expression of Parafibromin, commonly found in carcinomas unlike adenomas, or the expression of parathormone, allowing the elimination of a thyroid tumor.

Keywords
Parathyroid carcinoma; Parathyroid adenoma; Histological difficulties; Comparative table

## Introduction

Parathyroid carcinoma (PC) is a rare endocrine malignancy that remains enigmatic. Commonly a sporadic disease, it may occur in familial PHPT, namely the hyperparathyroidism-jaw tumor syndrome (HPT-JT), and very rarely, in the multiple endocrine neoplasia type1 (MEN1) [1]. Usual clinical features are mainly due to the excessive secretion of Parathormone (PTH) causing hypercalcemia, hypophosphatemia, and hypercalciuria. Thus, the clinical phenotype is characterized by symptoms of hypercalcemia and end-organ damage, including renal failure, bone disease, cardiac arrhythmia and neurocognitive dysfunction [2].

The disease commonly has an indolent and slow progressive course, and most patients ultimately succumb to complications of relentless hypercalcaemia rather than tumour invasion or metastatic spread. None of these, however, are strict rules. Indeed, the very first documented case of parathyroid carcinoma was a non-functioning carcinoma reported by Fritz De Quervain, in 1904. It wasn't until 1933 that Sainton and Millot were first to report a patient with a functioning parathyroid carcinoma. The main differential diagnosis is the parathyroid adenoma, which shares with parathyroid carcinoma a lot of clinical, biological and histological features that can make the diagnosis challenging.

Given the lack of specific clinical and biological features, the distinction between benign and malignant parathyroid tumor is often difficult preoperatively and very often it is diagnosed postoperatively at histological examination. However, even histology of PC can be equivocal or frankly misleading. Thus, it is common that the diagnosis of PC is made a posteriori, when local recurrence or distant metastases occur. Although no breakthrough have been made regarding curative options, the greater expansion of the parathyroid carcinoma's molecular pathogenesis knowledge, has led to the development of diagnostic markers that can be helpful in making the diagnosis more certain, particularly when the histological presentation is ambiguous.

Surgical resection is the accepted 'gold standard'. There is now a growing consensus on the use of adjuvant radiotherapy as it has been shown to provide a survival benefit [6]. The understanding of the natural history and prognostic factors of the parathyroid carcinoma was for a long time restrained by the rarity of this kind of neoplasia on the one hand, and on the another hand by the paucity of series and case reports in the literature, preventing a clear consensus about its surgical and adjuvant treatment. The aim of this article is to discuss histological criteria's of this tumor, and to make a review of the literature in order to clarify it pathogenesis, clinical features, or pathology diagnosis, and on the basis of this, to shed the light on the management of this condition, for practitioners generally, and for pathologists specifically.

## Case Report

We report the case of a 54-year-old man, who consulted in January 2019 and for whom the laboratory work-up revealed hypercalcemia and elevated serum parathormone. CT scan revealed a mass of the right inferior parathyroid gland, with images of liver metastasis. Right parathyroidectomy was performed. Macroscopically, the parathyroid mass was badly limited, of firm consistency, measuring 3 x 2 x 1.5 cm with a weight of 6.9 grams. On section, it comprised multiple whitish color nodules, of variable sizes, with fibrous and hemorrhagic features. Histological examination revealed a badly limited tumor proliferation, made of uniform cells arranged in lobules, trabeculae and clusters that are separated by dense fibrous bands. A vast network of finewalled vessels was insinuated between the tumoral trabeculae.

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