

Parathyroid Carcinoma

A Rare Yet Important Cause of Primary Hyperparathyroidism

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QUESTIONS:

1. Do preoperative biochemical parameters predict parathyroid carcinoma?
2. What is the characteristic long-term course of these patients?
3. Is adjuvant treatment indicated? If so, which treatment?

CLINICAL ASPECTS

A 46-year-old female presented to her primary physician with severe lassitude, diffuse muscle aching, and mild mental confusion. Pertinent physical examination revealed a firm left thyroid nodule, which was confirmed ultrasonographically (Figure 1)

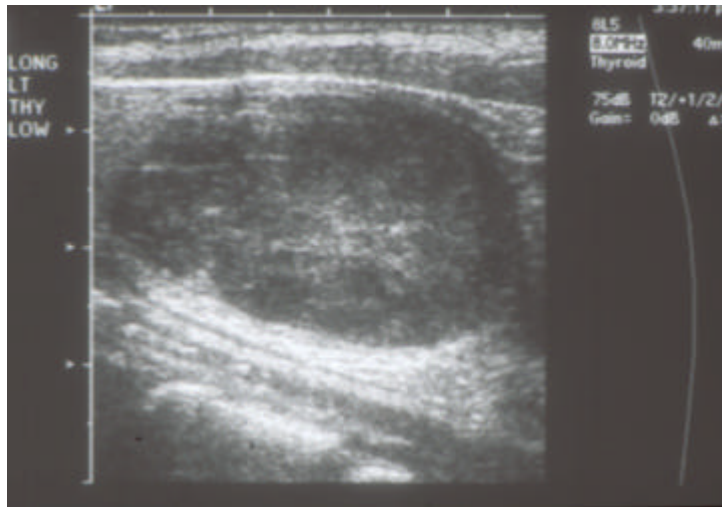


Fig. 1: Small-part ultrasound (10 MHz) showing a 3.5 cm hypodense mass in the lower pole of the thyroid gland on longitudinal scan.

Biochemical analysis demonstrated a serum calcium level of 14.8 mg/dL (nl=8.9-10.1) with a concomitant parathyroid hormone (PTH) level of 190 pmol/L (nl=<5.0) and a serum phosphorous of 3.2 mg/dL (nl=2.5-4.5). At cervical exploration, a left total thyroidectomy was performed. Regional node sampling was negative. Histology revealed that the “thyroid nodule”

was in fact a typical parathyroid carcinoma with cellular pleomorphism, bands of fibrosis, and vascular invasion (Fig.2A, B, C).

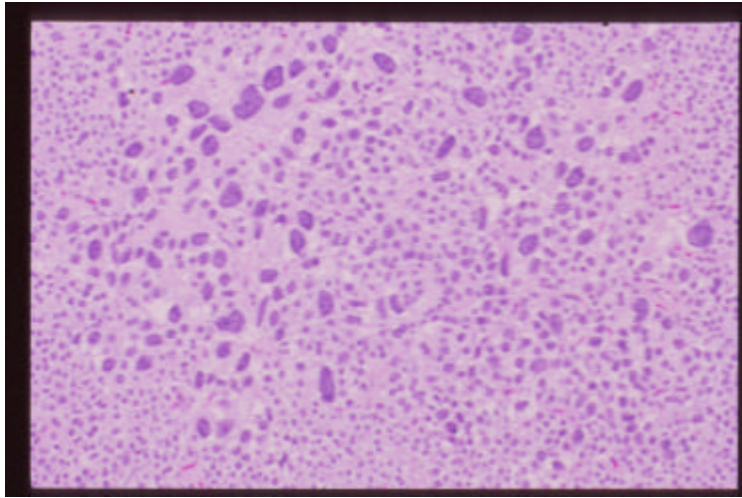


Fig. 2A: Diffuse nuclear pleomorphism.

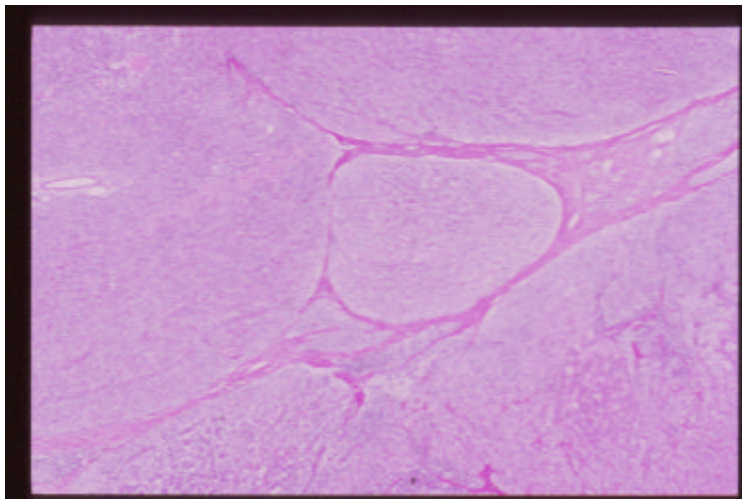


Fig. 2B: Broad bands of fibrosis commonly seen in parathyroid carcinoma.

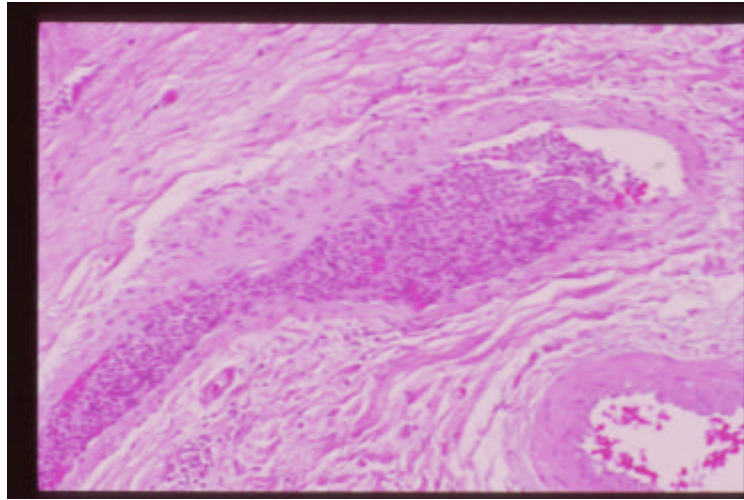


Fig 2C: Vascular invasion with tongue of tumor within a vessel.

Postoperatively, the patient's serum calcium dropped to 7.5 mg/dL with a PTH level of <0.6 pmol/L. She was started on both supplemental calcium and vitamin D for suspected osteopenic "bone hunger." At two months, her serum calcium was 8.2 mg/dL with a PTH level of 19 pmol/L compatible with continued bone hunger. Three months postoperatively, now off all supplemental therapy, her calcium and PTH levels were 9.2 mg/dL and 1.4 pmol/L, respectively.

She received 6600 cGy of external beam radiotherapy to the neck and is currently disease-free, with normal calcium levels two years after her operation.

DATA SUMMARY

Parathyroid carcinoma is rare and accounts for ~ 1% of patients with primary hyperparathyroidism (which in most series is due to an adenoma in 90% or multiglandular hyperplasia in 9%). Unfortunately, due to the propensity for vascular invasion in these patients, there is a high recurrence rate coupled with high long-term mortality, due mostly to uncontrollable severe hypercalcemia. In our experience, the one-, five-, and ten-year recurrence rates have been 27, 64, and 91%, respectively, with a five-year survival of only 69%. In light of this behavior pattern, adjuvant radiotherapy to the neck has been advised and has become our standard practice. This approach was initially pioneered by the group from the Princess

Margaret Hospital in Toronto, Canada who reported a 0% recurrence rate in a group of 7 patients followed for a mean period of 60 months.

The physiological response of the patient's iPTH levels were educational. The initial extremely high levels of 190 pmol/L were typical of most patients with parathyroid carcinoma. Postoperatively, the undetectable level of < 0.2 pmol/L was indicative of suppression of the remaining parathyroid glands. At two months, the level had increased to 19 pmol/L. Although this may suggest recurrent parathyroid carcinoma, the time-line is too short for recurrence and is compatible with severe "bone hunger" and "hard work" by the remaining normal parathyroid glands. This was substantiated by the return to a normal level of 1.4 pmol/L three months later indicating no residual or metastatic disease and stabilization of her osseous remineralization.

ANSWERS

1. The diagnosis of parathyroid carcinoma should be entertained preoperatively if any or a combination of the following are present:
 - A. High serum calcium levels. The mean calcium levels in these patients is ~ 14.5 mg/dL. In contrast, corresponding levels in patients with benign disease is ~ 10.8 mg/dL
 - B. Very high PTH levels. Our index patient had a level of 190 pmol/L (nl<5.0). In patients with benign disease, the level is rarely > 10 pmol/L.
 - C. A palpable cervical mass occurs. Approximately 40% of patients with parathyroid carcinoma will have a palpable mass, which is in contrast to ~ 0% in patients with either an adenoma or hyperplasia.
2. High recurrence rate and high long-term disease-specific mortality.
3. Adjuvant cervical radiotherapy. No chemotherapy.

SUGGESED READING

Chow E, Tsang RW, Brierley JD, Filice S. Parathyroid carcinoma—the Princess Margaret

Hospital experience. *Int J Radiation Oncol Biol Phys* 1998; 41:569-572

Obara T, Okamoto T, Kanbe M, Iibara M. Functioning parathyroid carcinoma:

Clinicopathologic features and rational treatment. *Semin Surg Oncol* 1997; 13:134-141.

Wynne AG, van Heerden JA, Carney JA, Fitzpatrick LA: Parathyroid carcinoma: Clinical and

pathologic features in 43 patients. *Medicine* 1992; 71(4):197-205.

“To know that even one life has
breathed easier because you have lived.

This is to have succeeded.”

Ralph Waldo Emerson