Parathyroid carcinoma

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Parathyroid carcinoma is rare, comprising less than 1% of all cases of primary hyperparathyroidism. Parathyroid carcinoma occurs in patients of all ages, and there is no predilection for either sex. Its clinical features are primarily attributable to the effects of hypercalcemia and excessive secretion of parathyroid hormone (PTH). Most of its symptoms—weakness, fatigue, anorexia, weight loss, and nausea—are nonspecific, but an excessively high serum calcium level (>16 mg/dl) can be associated with nephrolithiasis, renal insufficiency, and bone "brown tumors." A palpable neck mass suggests a parathyroid carcinoma. Parathyroid carcinoma is a suggested component of hyperparathyroidism-jaw tumor syndrome.

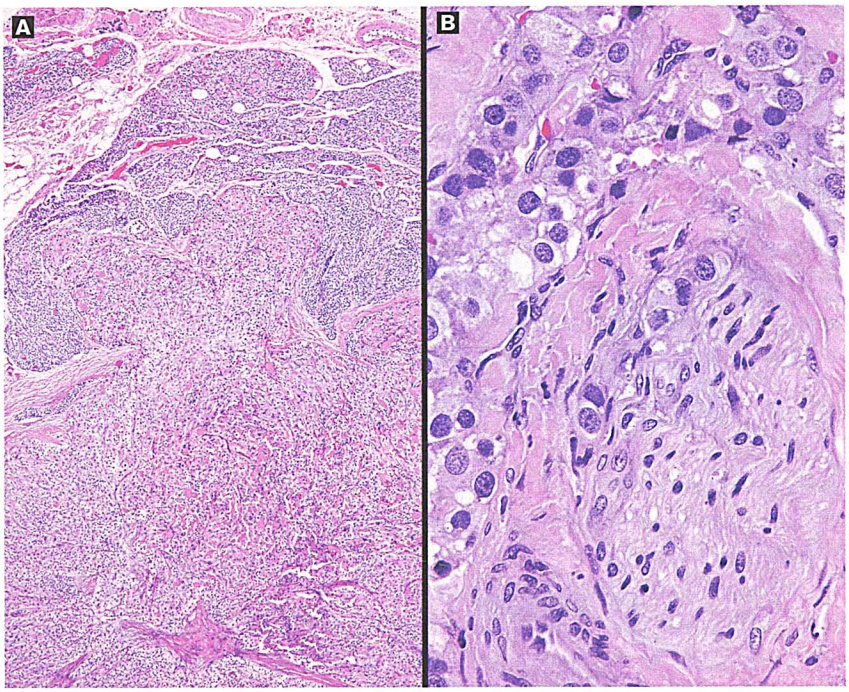

Figure 1. ***A:*** *Invasion is seen through the tumor capsule into the adjacent uninvolved parathyroid gland tissue.* ***B:*** *Neoplastic tumor cells are located immediately adjacent to and within a nerve.*

Parathyroid carcinoma usually manifests as a large tumor that is adherent to surrounding soft tissues, nerves, and the thyroid gland; the adherence often makes the tumor difficult to remove at surgery. In patients who have previously undergone surgery, signs of scarring and hemorrhage may simulate invasion. The cut surface is firm, white-tan, and may exhibit areas of necrosis.

No single histologic feature is considered diagnostic for parathyroid carcinoma; a constellation of features can usually be used to support the diagnosis. The features of malignancy are definitive vascular invasion, capsular invasion with extension into the uninvolved periparathyroid adipose tissue (figure 1, A), and/or attachment to the thyroid parenchyma. Perineural invasion is almost always diagnostic of parathyroid carcinoma (figure 1, B). The tumor is separated into small compartments by thick, band-forming, acellular, dense fibrosis (figure 2, A). True tumor comedo-type necrosis suggests malignancy.

The tumor cells are arranged in a variety of patterns; the trabecular pattern is quite common (figure 2, A). Chief cell neoplasms are more common than oncocytic neoplasms. The cells exhibit an increased nucleus-to-cytoplasm ratio, cellular enlargement, profound pleomorphism, and prominent, irregular, brightly eosinophilic macronucleoli (figure 2, B). Remarkably increased mitotic activity, including atypical forms, is more likely in parathyroid carcinoma than in

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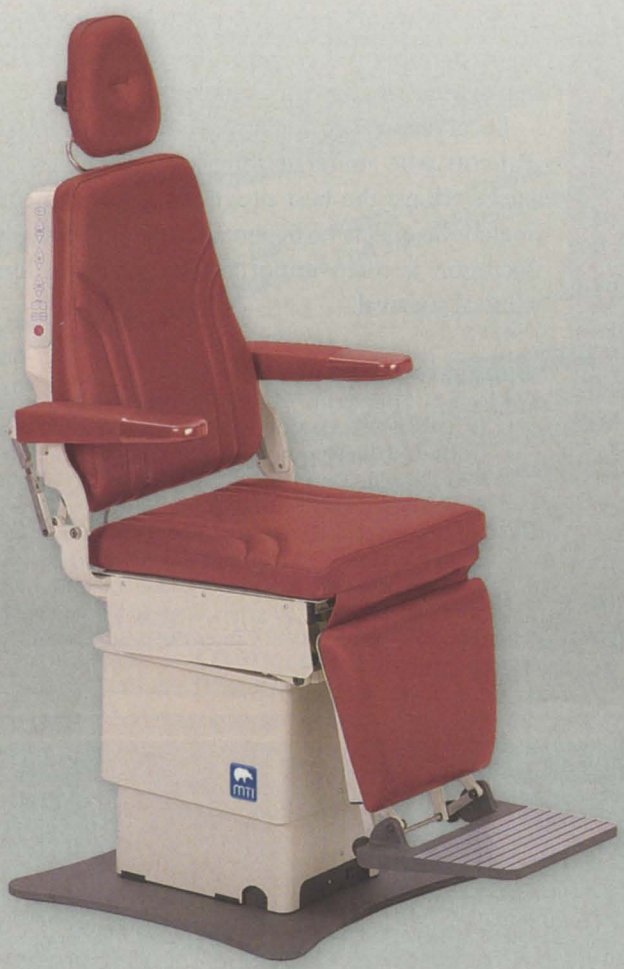

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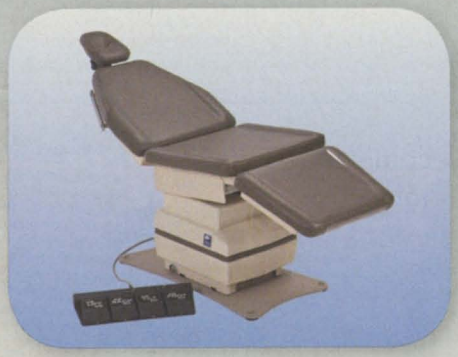

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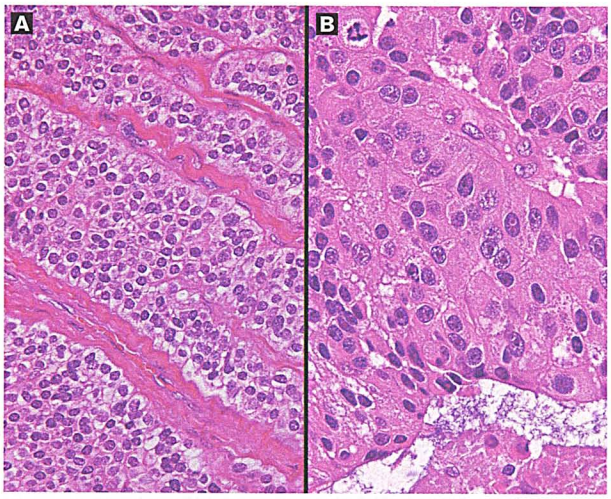

Figure 2. ***A:*** *A trabecular arrangement is separated by fibrosis.* ***B:*** *Pleomorphic tumor cells with prominent nucleoli are seen. An atypical mitotic figure is present in the upper left and necrosis seen in the lower part of the field.*

parathyroid adenoma, but mitotic figures alone cannot differentiate between the two (figure 2, B). Parathyroid carcinoma must be differentiated not only from parathyroid adenoma, but also from thyroid tumors and metastatic disease. Frozen-section analysis is discouraged, especially if it involves an incisional biopsy, because it results in tumor cell seeding with recurrent hyperparathyroidism, regardless of whether the original disease was benign or malignant.

Local recurrence is common (up to 70% of patients). Patients who undergo complete resection at the first surgery have the best prognosis. Management of the metabolic effects of hypercalcemia and excessive PTH secretion is often important to achieving long-term clinical survival.

Suggested reading

Bondeson L, Grimelius L, DeLellis RA, et al. Parathyroid carcinoma. In: DeLellis RA, Lloyd R, LiVolsi VA, Eng C, eds. Pathology and Genetics of Tumours of the Endocrine Organs and Paraganglia. World Health Organization Classification of Tumours. Lyon, France: IARC Press; 2004:124-7.

Hundahl SA, Fleming ID, Fremgen AM, Menck HR. Two hundred eighty-six cases of parathyroid carcinoma treated in the U.S. between 1985-1995: A National Cancer Data Base Report. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 1999;86(3):538-44.