Parathyroid Carcinoma Visualized by Gallium-67 Citrate Scintigraphy

Mitsunori Iwase, Yoshirou Shimizu, Hidemi Kitahara, Norihiko Tobioka, Kensuke Takatsuki

Toyota Hospital, Toyota-cho, Toyota-shi; and First Department of Internal Medicine, Nagoya University School of Medicine, Tsurumai-cho, Showa-ku, Nagoya, Japan

An abnormal uptake of [^{67}Ga]citrate by a palpable neck tumor was observed in a patient with primary hyperparathyroidism. The pathological diagnosis of the surgically resected specimen was parathyroid carcinoma invading the thyroid. The uptake was negative in nine patients with parathyroid adenoma. These results suggest that ^{67}Ga scintigraphy may be useful to differentiate parathyroid carcinoma from benign parathyroid tumor.

J Nucl Med 27:63–65, 1986

Parathyroid carcinoma is responsible for 0.5–4% of the cases of primary hyperparathyroidism (*1,2*). Although the adequate resection at the initial operation is most important for the prevention of recurrence or metastasis, the preoperative differentiation of carcinoma from benign parathyroid neoplasia is extremely difficult (*3*). In this report we will describe a case of parathyroid carcinoma which showed an abnormal accumulation of gallium-67 (^{67}Ga) citrate, an uncommon finding in parathyroid adenomas.

CASE REPORT

A 54-yr-old woman was admitted to our hospital with severe constipation, polyuria, nausea, and pain in the cranium. She had a history of duodenal ulcer 10 yr previously. Upon physical examination, a firm, thumb-tip-sized nodule was felt in the left thyroid region. Cervical lymphadenopathy was not evident. Laboratory values included serum calcium of 17.7 mg/dl (normal 8.4–10.0), serum phosphate of 2.5 mg/dl (normal 2.5–4.7), and serum alkaline phosphatase of 20.8 K-A unit (normal 2.0–10.0). The carboxyl terminal immunoassay of parathyroid hormone in the peripheral blood gave 16.0 ng/ml (normal <0.5). Renal tubular reabsorption of phosphorus was 59.8% (normal 85–95). The elevation of serum carcinoembriogenic antigen (CEA) with 5.5 ng/ml (normal <5.0) and ferritin with 408 ng/ml (normal 100–200) was also noted. A radiographic skeletal survey illustrated generalized demineralization, being seen most prominently in the skull, and cystic changes in the humeri and the femurs. Typical subperiosteal resorption in the phalanges and pathologic fractures of the costae were observed.

A thyroid scan, done 30 min after the administration of 5 mCi of technetium-99m (^{99m}Tc) showed a lesion with reduced uptake in the lateral portion of the left lobe. The corresponding lesion was shown by computed tomography to be an irregularly shaped mass with a lower attenuation than the rest of the thyroid.

Since parathyroid carcinoma was suspected from the above findings as well as the severity of the symptoms, ^{67}Ga scintigraphy was performed. Three millicuries of [^{67}Ga]citrate were administered intravenously, and the patient was scanned 72 hr later on a scintillation camera with a 20 × 14.5-in. detector. A 300-keV collimator was used. The scan revealed intense accumulation of the radionuclide in the left side of the neck corresponding to the palpable nodule (Fig. 1). The actual size of the hot area was estimated to be 3.9 × 2.5 cm by measuring the major and the minor diameters of the hot spot in the scintigram and multiplying each number with the ratio of the width of the patient's head to the width of the contour of the head in the scintigram. In addition, increased uptake of ^{67}Ga was observed diffusely in the cranial bones where pain and radiographic demineralization were unusually severe.

During surgery, a tumor 1.5 cm in diameter tightly attached to the upper pole of the left thyroid lobe was found. The tumor was removed together with the left thyroid lobe (Fig. 2a), followed by an extended resection of the regional lymph hodes, none of which appeared enlarged. The other parathyroid glands were not detected. A cross-section of the removed specimen (Fig. 2a) revealed a lesion in the thyroid, which was broadly connected to the tumor. The size of the whole abnormal tissue (the tumor and the thyroid lesion) was 3.7 × 2.3 cm at the frontal cross section. Microscopically, the tumor was composed of atypical acidophilic cells (Fig. 2b).

Received Jan. 14, 1985; revision accepted Sept. 18, 1985.

For reprints contact: Kensuke Takatsuki, MD, First Dept. of Internal Medicine, Nagoya University School of Medicine, 65, Tsurumai-cho, Showa-ku, Nagoya, Japan 466.

FIGURE 1
Gallium-67 scintigraphy of patient, demonstrating abnormal uptake in lower left neck

The capsule was thick, and broad fibrous trabeculae traversed the tumor. Moderately increased mitosis within the parenchymal cells and intravascular cell proliferation was observed. More than half of the left thyroid lobe was displaced by atypical cells that were indistinguishable from those in the adjacent tumor. There was no appreciable infiltration of lymphocytes in the tumor and the thyroid gland. The pathological diagnosis was parathyroid adenocarcinoma invading the thyroid gland.

The patient became asymptomatic postoperatively and serum levels of calcium, phosphate, parathyroid hormone, CEA, and ferritin returned to normal within a few days. A ^{67}Ga scan performed 4 wk after the operation showed no accumulation of activity in the neck, although the uptake was still high in the cranial bones.

DISCUSSION

Reliable criteria for preoperative differentiation of a parathyroid carcinoma from a benign parathyroid tumor has not yet been established (*3,4*). The differentiation is difficult to make even during operation, since gross appearance and the frozen-section histopathology of carcinomas are often similar to those of adenomas (*2,4,5*). Because operations of relapsed parathyroid carcinomas bring about no definite healing in most cases, and since there is no effective chemotherapy or radiotherapy, the complete removal of the lesion at the initial surgery is crucial. In order to make confident decisions regarding extending the dissection, a need for techniques to diagnose carcinoma is evident.

Gallium-67 citrate scintigraphy has been successfully employed for the detection of many varieties of malignant tumors, but the use of this technique to visualize

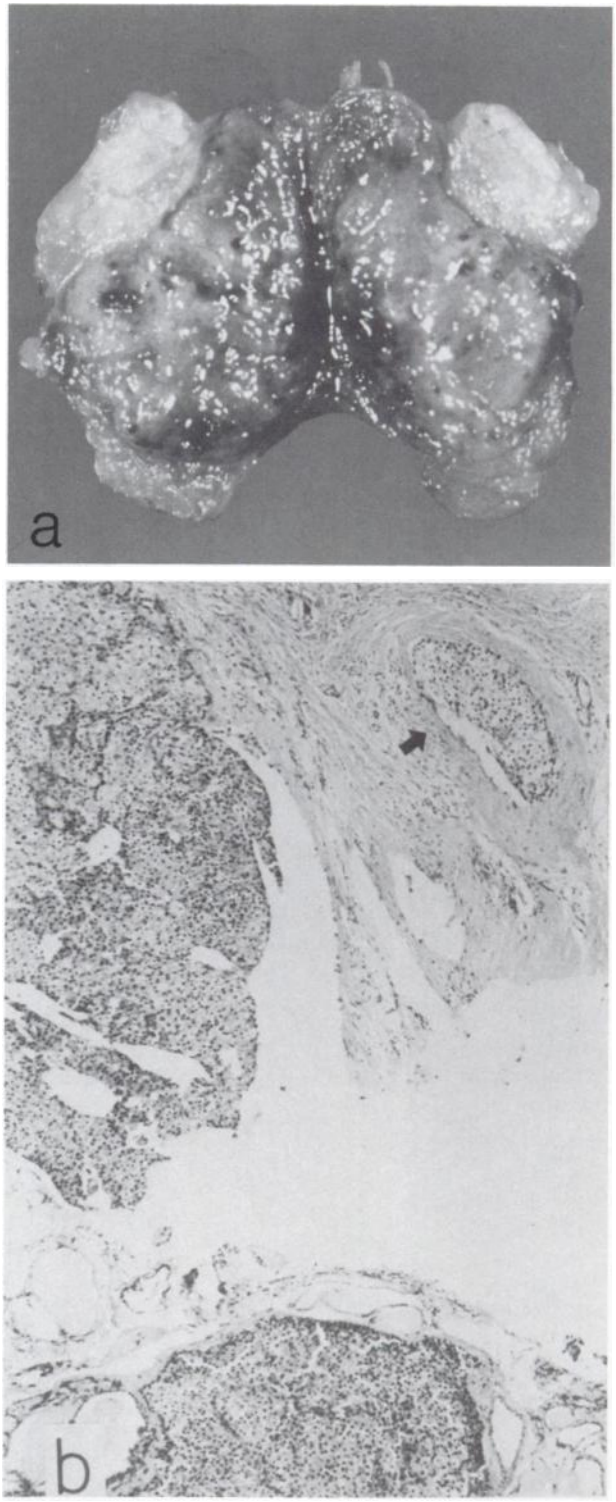

FIGURE 2
a: Cross section of parathyroid tumor and left thyroid lobe. b: Light microscopy showing portion of parathyroid tumor (upper ⅔) and invasion of tumor cells into thyroid tissue (lower ⅓). (Hematoxylin-Eosin, original × 100). Arrow indicates intravascular proliferation of tumor cells

parathyroid carcinoma has not been reported as far as we can determine. In the present case, the abnormal accumulation of ^{67}Ga suggested the possibility of a

malignant tumor. Although a ^{67}Ga image of the resected specimen was not made, it is obvious that both parathyroid carcinoma and its invasion in the thyroid were responsible for the accumulation. This is indicated by the fact that the size of the whole abnormal tissue (parathyroid plus thyroid), which was 3.7 × 2.3 cm at a frontal cross section, was consistent with the estimated size of the hot area in the neck (3.9 × 2.5 cm).

In contrast to the patient with parathyroid carcinoma, ^{67}Ga uptake was negative in subsequent testing of nine patients with parathyroid adenoma which weighed from 0.2 to 3.0 g (unpublished observation). In previous literature, the only adenoma so far detected by ^{67}Ga scintigraphy was extraordinarily large, weighing over 15 g (*6*). In view of these findings, ^{67}Ga scintigraphy might be an effective procedure for preoperative diagnosis of a parathyroid carcinoma. Further studies are necessary, therefore, to investigate whether parathyroid carcinomas can be generally visualized by [^{67}Ga]citrate scintigraphy, particularly before invasion of surrounding tissues.

REFERENCES

1. Pyrah LN, Hodgkinson A, Anderson CK: Primary hyperparathyroidism. *Br J Surg* 53:295–316, 1966
2. Schantz A, Castleman B: Parathyroid carcinoma: A study of 70 cases. *Cancer* 31:600–605, 1973
3. Anderson BJ, Samaan NA, Vassilopoulou-Sellin R, et al: Parathyroid carcinoma: Features and difficulties in diagnosis and management. *Surgery* 94:906–915, 1983
4. Altenähr E, Saeger W: Light and electron microscopy of parathyroid carcinoma: Report of three cases. *Virchows Arch (Pathol Anat)* 360:107–122, 1973
5. Bichel P, Thomsen OF, Askjaer SAA, et al: Light and electron microscopic investigation of parathyroid carcinoma during dedifferentiation, Survey and study of a case. *Vichows Arch (A)* 386:363–370, 1980
6. Beckerman C, Shululak JA, Kaplan EL, et al: Parathyroid adenoma imaged by Ga-67 citrate scintigraphy: Case report. *J Nucl Med* 18:1096–1098, 1977