

Distant subcutaneous recurrence of a parathyroid carcinoma: abnormal uptakes in the ^{99m}Tc -sestamibi scan and ^{18}F -FDG PET/CT imaging

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We report a rare case of distant subcutaneous parathyroid carcinoma recurrence. A 50-year-old woman was referred to our hospital because of sustained hypercalcemia despite surgical removal of a parathyroid carcinoma. A focal uptake in the upper mediastinal area was detected in a ^{99m}Tc -sestamibi scan, and ^{18}F -fluorodeoxyglucose (FDG) positron-emission tomography (PET)/computed tomography (CT) imaging demonstrated a subcutaneous mass. She underwent tumor resection, and the pathological findings were consistent with a parathyroid carcinoma. The postoperative serum parathyroid hormone (PTH) level remained within normal limits. However, a new palpable solitary mass was identified in the upper portion of the left breast 1 year postoperatively. Both a ^{99m}Tc -sestamibi scan and ^{18}F -FDG PET/CT imaging revealed an abnormal lesion in the upper breast, and subsequent pathology reports confirmed parathyroid carcinoma metastasis. Serum PTH and calcium levels fell within normal ranges after tumor resection. Two subcutaneous recurrent lesions appeared likely due to tumor seeding during the previous endoscopic operation at a local hospital.

Keywords: Positron-emission tomography; Hyperparathyroidism; Parathyroid neoplasms; Neoplasm recurrence

INTRODUCTION

Parathyroid carcinoma is a rare disease, responsible for less than 1% of hyperparathyroidism cases in most parts of the world. Although the apparent incidence of hyperparathyroidism has increased since the introduction of multichannel autoanalyzers, the incidence of parathyroid carcinoma still remains low [1]. Because of its rarity, the natural history, biology, and prognosis of parathyroid carcinoma are poorly understood. Regarding prognostic and therapeutic issues associated with this carcinoma, it has been difficult to establish an accurate preoperative diagnosis, local recurrence is

frequent and requires repeat operations, and metastatic disease may occur. Distant recurrences or metastases occur late in the course of the disease with spread via both hematogenous and lymphatic routes. The sites and frequencies of metastases include the lung (40%), cervical lymph nodes (30%), liver (10%), bone, pericardium, pancreas, brain, and other sites [2]. To our knowledge, this is the first reported case of distant subcutaneous recurrence in recurrent parathyroid carcinoma.

CASE REPORT

A 50-year-old woman was referred to our hospital because of persistent hypercalcemia after surgical removal of a parathyroid carcinoma. The patient had undergone an endoscopic parathyroidectomy using a bilateral axillo-breast approach for a right lower parathyroid adenoma 2 years earlier at a local hospital. The tumor was reported as having no histological features suggestive of malignancy. The serum calcium level was returned to normal after surgery. However, approximately 2 years after surgery, the patient's serum calcium level was found to be elevated again, and an enlargement of the left lower parathyroid gland was detected. The patient underwent conventional parathyroidectomy to remove a left lower parathyroid tumor, with a subsequent histological diagnosis consistent with parathyroid carcinoma. Despite the removal of the left lower parathyroid tumor, her serum calcium levels remained high for 2 months, prompting the referral.

Upon presentation, the patient complained of mild fatigue, anorexia, and constipation. Her family history

was unremarkable for cancers or endocrine neoplasias. Physical examination revealed no significant abnormality except her previous surgical neck scar. The patient's weight was 46.1 kg, her height 154 cm, and her body mass index 19.4 kg/m². On laboratory examination, her serum calcium level was 15.0 mg/dL (ionized calcium, 1.95 mmol/L) and serum phosphorus level 3.6 mg/dL. Serum alkaline phosphatase was elevated at 481 IU/L. Her serum parathyroid hormone (PTH) level was elevated markedly (540.2 pg/mL). Blood urea nitrogen on admission was 26.1 mg/dL with a serum creatinine of 1.7 mg/dL. Urine analysis showed low specific gravity, leukocyturia (24/HPF), and mild erythrocyturia (4 to 5/HPF).

A ^{99m}Tc-sestamibi scan was performed and demonstrated focal abnormal uptake in the upper mediastinal area in the 2-hour delayed image (Fig. 1A). A subsequent ¹⁸F-fluorodeoxyglucose (FDG) positron-emission tomography (PET)/computed tomography (CT) imaging study revealed a mass in the soft tissue at the anterior border of the sternum, with focally increased FDG uptake (maxSUV, 2.6) that correlated with the initial ^{99m}Tc-sestamibi scan (Fig. 1B). The patient displayed re-

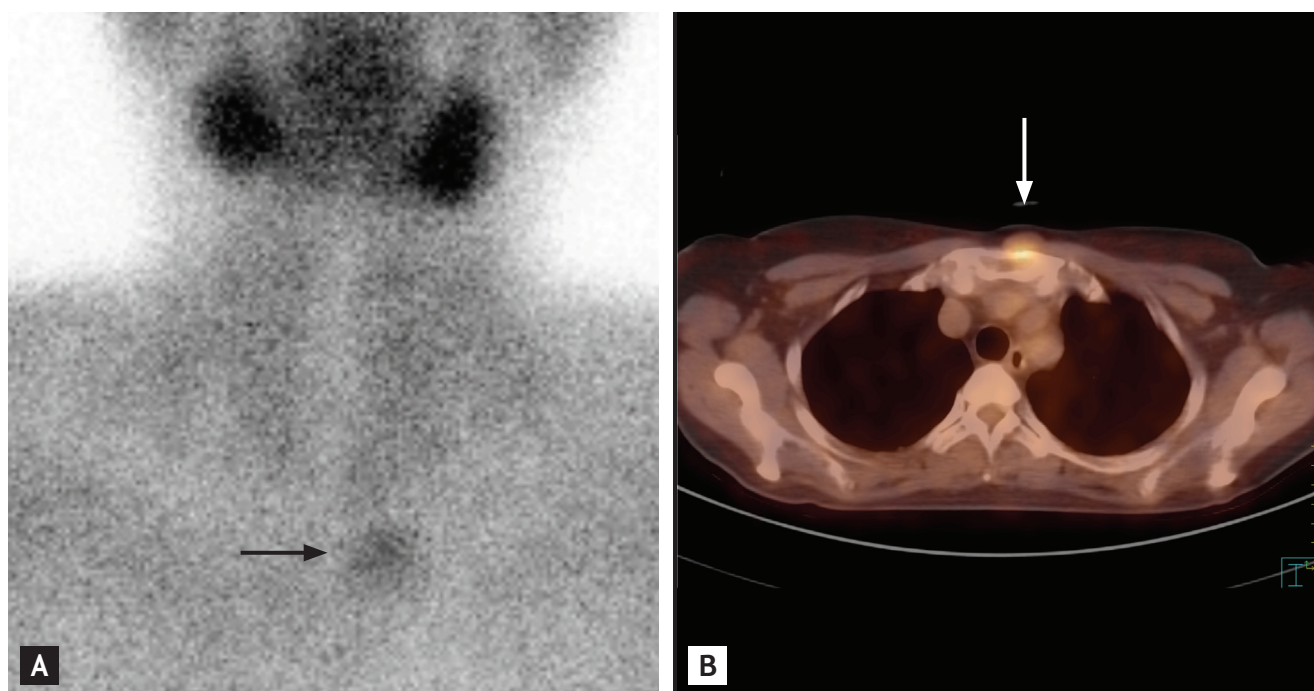


Figure 1. (A) ^{99m}Tc-sestamibi scan showing focal abnormal uptake (black arrow) in the upper mediastinal area in 2-hour delayed imaging. (B) ¹⁸F-fluorodeoxyglucose (FDG) positron-emission tomography/computed tomography image showing a mass (white arrow) in the soft tissue at the anterior border of the sternum with focally increased FDG uptake (maxSUV, 2.6).

duced bone mineral density at the lumbar spine (L_{1-4} , 0.889 g/cm^2 ; T-score, -1.9 SD) and at the proximal femur neck (0.695 g/cm^2 ; T-score, -1.7 SD). There were no definite radiographic findings or signs of trabecular bone resorption in the skull or other bones, apart from mild subperiosteal bone resorption in the third metacarpal bone. A whole-body bone scan with ^{99m}Tc MDP showed diffuse, subtle uptake in the skull and long bones. An abdominal CT scan showed bilateral medullary nephrocalcinosis. Preoperatively, we marked the outline of the mass on the skin, based on the imaging and manual palpation (Fig. 2).

Based on the preoperative findings, the patient underwent an anterior chest wall mass resection. A frozen section revealed pathological parathyroid tissue, and a wide local resection of the tumor with surrounding structures was performed. A final pathological examination revealed a 2.3-cm parathyroid carcinoma with fibrous bands, numerous mitoses, nuclear pleomorphisms, and foci of capsular invasion (Fig. 3). An intraoperative PTH test showed an 82% decline from the pre-excision level (540.1 pg/mL) to the postexcision level (97.5 pg/mL). The postoperative serum PTH and calcium levels dropped significantly to 57.6 pg/mL and 9.3 mg/dL , respectively. Both levels remained stable and within the normal ranges with temporary oral calcium

supplementation. Her hospital course was otherwise uncomplicated, and she was subsequently discharged.

During the patient's outpatient follow-up period, the serum PTH and calcium levels remained near the upper limits of normal. However, approximately 1 year later, her serum PTH level was elevated to 84.1 pg/mL , and a new mass was palpated in the upper portion of her left breast upon physical examination. A ^{99m}Tc -sestamibi scan and ^{18}F -FDG PET/CT imaging were performed, revealing an abnormal lesion in the upper area of her left breast (Fig. 4). Subsequently, tumor resection was performed, and the pathological report demonstrated parathyroid carcinoma metastasis. Her postoperative serum PTH and calcium levels dropped significantly to 38.9 pg/mL and 9.5 mg/dL , respectively. We are currently watching her cautiously, conducting serial blood examinations and, more specifically, serum PTH and calcium measurements.

DISCUSSION

Parathyroid carcinoma is a tumor with low malignant potential that tends to recur locally. Characteristically, it infiltrates into the surrounding thyroid, recurrent laryngeal nerve, trachea, esophagus, or muscle tissues. Parathyroid carcinoma spreads into the adjacent cervical lymph nodes via the lymphatic route, and distant metastases normally involve the hematogenous route [3]. Despite a possibly curative resection, parathyroid carcinoma has a recurrence rate of more than 50%. A significant number of patients will also have distant recurrence or metastasis after resection of the primary tumor [2]. A review of the literature revealed only one previous case of subcutaneous parathyroid carcinoma recurrence [4]. That case described a local subcutaneous neck lump recurrence at the prior operative site, suggesting that the subcutaneous deposit was due to tumor seeding during the operation.

Differentiating carcinoma from a benign disorder is difficult during the preoperative and intraoperative stages and, sometimes, even after a histological evaluation. A carcinoma cannot be reliably distinguished from an adenoma by histopathology alone. Several subtle pathological findings may overlap with those of benign adenomas, and they can easily be misinterpreted



Figure 2. The subcutaneous mass beneath the skin.

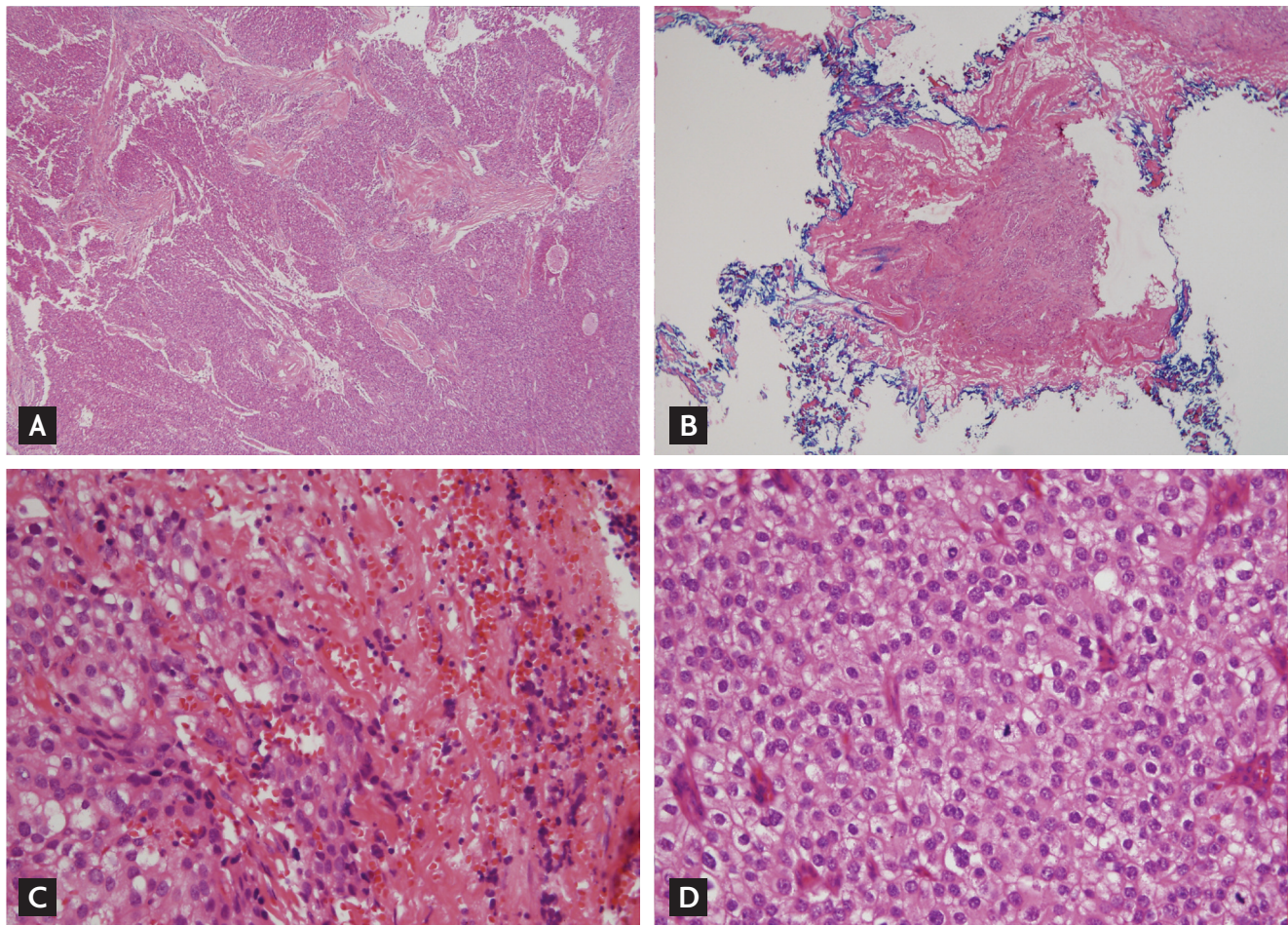


Figure 3. Histological findings. (A) Lobules of parathyroid tissue are separated by fibrous bands (H&E, $\times 40$). (B) The cancer cells invading the capsule are stained blue (H&E, $\times 40$). (C) Capsular invasion of malignant cells (H&E, $\times 400$). (D) Several highly mitotic cells in a high-power field (H&E, $\times 400$).

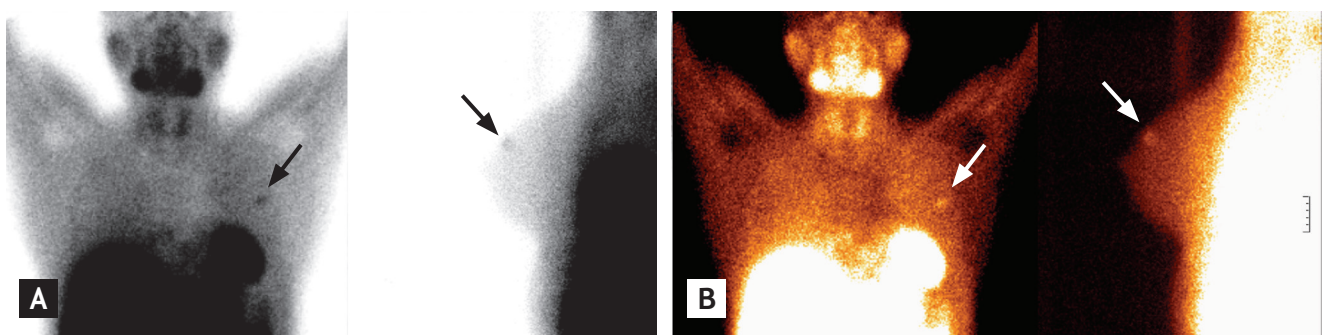


Figure 4. (A) ^{99m}Tc -sestamibi scan of the breast demonstrating abnormal uptake (black arrows) in the upper area of the left breast. (B) ^{18}F -fluorodeoxyglucose positron-emission tomography/computed tomography image revealing abnormal uptake (white arrows) in the corresponding areas of the ^{99m}Tc -sestamibi scan.

[1]. As a result, the most definitive method for parathyroid carcinoma diagnosis is the identification of secondary deposits. The right lower parathyroid tumor in our patient was initially diagnosed as an adenoma at a

local hospital. However, it may be more likely that it was a parathyroid carcinoma misdiagnosed as an adenoma, because the recurrent subcutaneous tumors were located in an access route of the first endoscopic

parathyroidectomy. Given our patient's clinical history and presentation, the recurrent tumors in subcutaneous tissue may have been due to tumor seeding during the endoscopic operation rather than hematogenous distant metastasis or tumor development from ectopic parathyroid glands. If the adenoma of the right lower gland had been misdiagnosed in our patient, the final diagnosis would have been multiglandular parathyroid carcinoma in the right and left lower parathyroid glands. Several case reports have shown an associated pathology in other parathyroid glands [1]. A review of the literature demonstrates that multiglandular (double) parathyroid carcinoma is rare [5].

Several surgeons have introduced endoscopic techniques to the field of parathyroid surgery for primary hyperparathyroidism in appropriately selected patients [6]. Although this endoscopic surgery can improve overall outcomes with smaller incisions and reduced trauma to the muscles, it should only be performed if there is proper indication for endoscopic parathyroidectomy, precise preoperative localization, the availability of intraoperative PTH monitoring, and the absence of evidence of malignancy [6].

Preoperatively, a noninvasive investigation using a ^{99m}Tc -sestamibi scan may help to localize recurrences and metastases. Although parathyroid scintigraphy with sestamibi is now a standard imaging procedure worldwide for localization of hyperactive parathyroid glands, significant accumulation of FDG can be seen in parathyroid carcinomas, as demonstrated by PET scanning [7]. One report showed superior sensitivity of FDG PET scans, compared with ^{99m}Tc -sestamibi scans, for localization of tumors during recurrence [8]. Currently, there is a general consensus that PET scanning is useful in cases where ultrasound and sestamibi scans have failed in tumor localization, especially in patients with recurrent hyperparathyroidism [9]. We were able to localize our patient's distant recurrent tumor site using both ^{99m}Tc -sestamibi and FDG PET scans.

Parathyroid carcinoma reportedly has a significant rate of recurrence (up to 70%), seen within observation periods of several months to over 20 years. Mortality is usually secondary to the metabolic consequences of hypercalcemia, rather than malignant spread itself. Thus, regular medical check-up visits are recommended after surgery for long-term survival [10]. Although

this carcinoma has a relatively indolent disease course, localizing recurrences using ^{99m}Tc -sestamibi and ^{18}F -FDG PET/CT scanning in cases of elevated PTH levels after primary surgery may provide significant insight into not only the common recurrence sites but also unusual recurrence sites, such as with this patient. When an endoscopic procedure is planned as a surgical treatment for primary hyperparathyroidism, it should be performed in selected patients based on the information learned from our case.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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