Case Report

Parathyroid carcinoma with multiple lung metastases

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Introduction

Parathyroid carcinoma is a rare complication of secondary hyperparathyroidism in chronically uremic patients. Nodular hyperplasia in patients with renal (secondary) hyperparathyroidism is associated with monoclonal growth\cite{1} and numerous deletions. One would, therefore, anticipate that parathyroid carcinoma should occur, however, the number of reported cases is low\cite{2,3}.

In the following, we describe a case of intractable tertiary hyperparathyroidism persisting after two attempts at parathyroid surgery, in a patient who had pulmonary metastases and died with persistent hyperparathyroidism and hypercalcaemia.

Case

A 20-year-old female patient had suffered since childhood from intermittent haematuria and progressive deterioration of renal function. Haemodialysis therapy was started at age 15 years. Over the next 5 years she complained of bone and joint pain. Intravenous vitamin D\textsubscript{3} (Calcijex, 1–2 µg three times a week) was administered for 5 months. In August 1995, she was referred for management of refractory hyperparathyroidism. She had the following findings: S-calcium 12.7 mg/dl, phosphate 6.0 mg/dl, alkaline phosphatase 586 U/l and intact parathyroid hormone (iPTH) 1143 pg/ml. At that time, X-ray of the skull and hands showed a salt and pepper appearance, subperiosteal resorption at the medial aspect of middle phalanges and tunneling of cortical bone respectively. Parathyroid sonography showed bilateral parathyroid nodules with calcification. A TI-201 and Tc-99m subtraction parathyroid scan revealed hot spots in the upper poles of both thyroid lobes. Serum aluminum concentrations were within the normal range (pre-DFO 6.9 µg/dl, post-DFO 9.4 µg/dl). Based on these results, a first operation was performed on 29 September 1995. Parathyroid glands were not adherent to the adjacent tissue. The frozen section showed Parathyroid carcinoma should occur, however, the number of reported cases is low\cite{2,3}.

In the following, we describe a case of intractable tertiary hyperparathyroidism persisting after two attempts at parathyroid surgery, in a patient who had pulmonary metastases and died with persistent hyperparathyroidism and hypercalcaemia.

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Fig. 2. Serial serum levels of i-PTH and calcium and clinical events.

Fig. 3. Chest CT scan revealed multiple lung nodules indicative of multiple lung metastases.

Fig. 4. Histological findings of lung tumor showed a well-defined mass composed of uniform and tall columnar cells in trabecular or organoid patterns (hematoxylin and eosin, 224 ×).

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serum iPTh (2429 pg/ml) persisted after second operation (Figure 2) without evidence of ectopic parathyroid tissue. Repeated Tl-201/Tc-99m subtraction scan and a computed tomography (CT) scan of the neck and upper mediastinum were negative.

She then developed chronic cough and intermittent haemoptysis. Thoracic X-ray revealed lung lesions which were diagnosed as pulmonary microlithiasis. They increased in size and number. The chest X-ray and CT scan then showed multiple lung nodules (Figure 3). The Tl-201 whole-body scan revealed diffuse uptake of radiotracer in both lungs. The abdominal sonography, gastrointestinal series, pelvic sonography and tumor markers all were negative. The bone scan showed severe bone lesions and diffuse soft-tissue-tracer uptake, including lung and heart. On 25 July 1996, a diagnostic wedge resection of nodules in the right lung (third operation) showed a well-defined mass composed of uniform and tall columnar cells in a trabecular and organoid pattern (Figure 4). Neither mitoses nor necrosis within the tumor were seen. Nevertheless, in the context of the histological findings, persistent hypercalcaemia and elevation of iPTH, the diagnosis of parathyroid carcinoma was made.

Calcium-free haemodialysis therapy and administration of clodronate and calcitonin were tried, but hypercalcaemia was refractory. Operation (en bloc resection of tumour) and chemotherapy were suggested, but the patient’s family refused. Eventually, she expired due to respiratory failure caused by diffuse calcification and multiple metastases of the lung on 7 September 1996.

Discussion

Parathyroid carcinoma in patients on haemodialysis therapy is very rare. Berland et al. reported the first case in 1982 [4]. Recently, there was a total of 13 cases reported in the English-language literature [2,3]. In these cases, only three had lung metastases. Among these, there was no patient in whom parathyroid carcinoma was diagnosed before operation. Five patients were diagnosed because local invasion was found during the initial operation. In three patients, the diagnosis could not be made until the detection of
distant metastases. Because the symptoms and signs of parathyroid carcinoma are non-specific, it may be very difficult to make a diagnosis of parathyroid carcinoma. Scantz and Castleman [5] distinguished parathyroid carcinoma from adenoma histologically by the trabecular pattern, mitotic figures, thick fibrous bands, and capsular and vascular invasion. However, consideration of the histological criteria only may lead to overdiagnosis [6]. McKeown et al. [6] re-analysed seven cases of parathyroid carcinoma and insisted that mitotic activity must be distinguished from that in endothelial cells, capsular invasion should be beyond the capsule and blood-vessel invasion should be true tumor embolus in the vessels. Only three cases were confirmed as malignant: one had metastasis to the regional lymph node, two had invasion of adjacent tissue. Therefore, they concluded that considering histological criteria only may lead to overdiagnosis. Definite evidence of parathyroid carcinoma are: (i) local invasion of the thyroid and other tissues, (ii) metastasis to the regional lymph nodes, and (iii) distant metastases [6]. In our case the diagnosis was made based on the distant metastases to both lungs.

In Schantz and Castleman’s series (including 70 cases), three features are more common with parathyroid carcinoma than with benign hyperparathyroidism; they are bone disease, a palpable neck mass and a high serum-calcium level [5]. In this series, the initial serum-calcium level averaged 15.2 mg/dl; in 62% of the patients, the value was above 14 mg and only 22% had a value below 13 mg/100 ml. In Wang and Gaz’s series (including 28 cases), the average greatest dimension of parathyroid carcinoma was 3.0 cm, and the average weight was 6.7 g [7]. Our case had severe bone disease and the average serum-calcium level was about 14 mg/dl (Figure 2). The greatest dimensions of the right and left upper parathyroid nodules of our case were 3.5 and 3.5 cm and the weights were 6.22 and 4.8 g respectively. The above findings in our case implicate parathyroid carcinoma.

The pathological findings of parathyroid nodules of our case showed diffuse hyperplasia with focal adenomatous change (nodular hyperplasia). In fact, most of the parathyroid carcinoma in patients on haemodialysis therapy coexisted with hyperplasia and adenoma. Frequent recurrence of renal hyperparathyroidism and DNA analysis of autografted parathyroid tissue clearly indicated that nodular hyperplastic parathyroid tissue has a higher growth potential [8]. Clonal analysis of nodular parathyroid hyperplasia in renal hyperparathyroidism concluded that nodular hyperplasia represents monoclonal parathyroid neoplasia [9]. According to the multistep hypothesis of carcinoma development all transitions from diffuse hyperplasia, nodular hyperplasia and parathyrosis (sherrad) to carcinoma are conceivable. With prolonged survival of dialysis patients, the above sequence of events and the occurrence of parathyroid carcinoma may become more frequent.

The management of parathyroid carcinoma in 13 patients with chronic renal failure has been reviewed [2,3]. Five patients underwent parathyroidectomy only; parathyroidectomy and neck lymphadenectomy were performed in two patients (but there was no evidence of lymph node metastasis); parathyroidectomy with partial thyroidectomy because of local invasion of parathyroid carcinoma was performed in five patients [2]. One patient underwent parathyroidectomy, lymphadenectomy, radical neck dissection and wedge resection of some lung nodules [4]. Our patient also received parathyroidectomy and wedge resection of some lung nodules. The recurrent rate of parathyroid carcinoma in 13 patients on haemodialysis therapy was 45%, and only two cases died of the disease itself; 55% are alive without disease. In contrast, the recurrent rate of primary parathyroid carcinoma has been reported to range from 41 to 67% [10]; the rate of death from primary parathyroid carcinoma is 31%; only 29% are alive without disease (59 cases, 5-year follow-up) [5]. Whether the prognosis of parathyroid carcinoma in haemodialysis patients is better than in those with primary parathyroid carcinoma is difficult to state at present, since the in haemodialysis patients is small. It is, however, postulated that parathyroid carcinoma in haemodialysis patients runs a more benign course and has a good prognosis.

References


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