Dear Sir,

Hyperparathyroidism and parathyroid hyperplasia invariably accompany chronic renal failure [1]. However, parathyroid carcinoma rarely occurs in this setting. Indeed, our survey of the English language literature revealed only one patient developing this lesion during chronic renal failure [2]. We report a second patient manifesting such an association.

A 64-year-old white female developed end-stage renal disease in 1976 secondary to idiopathic chronic interstitial nephritis. Her serum calcium at that time was 9 mg/dl (1.97 mmol/l), phosphorus 7.9 mg/dl (2.55 mmol/l) with a normal albumin concentration. Despite therapy with phosphate-binding agents, serum phosphate levels remained greater than 6 mg/dl (1.94 mmol/l). Over the next several years she developed multiple bone fractures (ribs, ankle and hip) from severe secondary hyperparathyroidism. Beginning in September 1983, serum calcium levels ranged from 10 to 11 mg/dl (2.50–2.74 mmol/l). Parathyroid hormone (PTH) levels (C-terminal assay) in February 1985 were greater than 10,000 pg/ml (normal 0–340 pg/ml). At parathyroidectomy in May 1985, the two inferior glands were hyperplastic while both superior glands revealed malignant changes with infiltration of adjacent thyroid tissue (fig. 1). Immunoperoxidase studies using monoclonal antibodies, positive for PTH and negative for thyroglobulin, confirmed that the tumor indeed originated from parathyroid tissue. No metastatic foci were identified in the seven paratracheal lymph nodes resected. As of June 1988 the patient is in a stable condition with no clinical evidence of metastatic disease. Parathyroid carcinoma is a rare cause of hyperparathyroidism, accounting for only 1–3% of patients with hypercalcemia and elevated PTH-levels [3–5]. Since adenomas have repeatedly been demonstrated in hyperplastic glands, many have suggested that hyperplastic cells may undergo neoplastic transformation, which ultimately could lead to malignant changes in the parathyroid.

20. b Neoplastic cells infiltrating dense connective tissue, from the parathyroid carcinoma. ×200.

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glands [4]. Should this sequence develop, even rarely, one would think that patients with chronic renal failure would be a common source of these lesions, since parathyroid hyperplasia is a constant feature of the disease. Indeed, adenomatous transformation of such hyperplastic glands is a well-recognized complication of chronic renal failure. There are various precedents for neoplastic transformation in chronically overstimulated endocrine glands or in target tissues chronically overexposed to hormones. Such examples include: endometrial cancer in women with estrogen-producing ovarian tumors, ACTH-producing pituitary tumors following total adrenalectomy for Cushing’s syndrome and development of thyroid neoplasms in patients chronically exposed to excessive endogenous thyroid-stimulating hormone [6].

The discovery of malignant changes in two of our patient’s four hyperplastic parathyroid glands suggests that cytologic changes in uremic patients may range from hyperplasia to benign neoplasia and eventually to malignant neoplasia. Simultaneous involvement of more than one gland is an extremely rare occurrence in patients with spontaneous primary hyperparathyroidism due to a parathyroid malignancy [3, 5]. It is surprising, however, that despite the large numbers of patients with chronic renal failure and secondary or tertiary hyperparathyroidism, to our knowledge, there has been only one previous report in the English literature of parathyroid cancer diagnosed in a patient with chronic renal failure [2]. The apparent rarity of parathyroid carcinoma may relate to the duration of renal failure. With improved survival on dialysis, parathyroid carcinoma may be encountered with greater frequency.

References