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Introduction

Altered T-cell immunity, oncogenic viruses and immunosuppression are known to cause an increased risk of cancers in organ transplant recipients, leading to the rise in morbidity and mortality among these patients. Recent studies have observed that thyroid lesions are more frequently encountered in kidney transplant recipients.

A 45-year-old woman with history of chronic hypertension, kidney transplant and graft failure, was admitted for assessment for a second renal transplant and detected to have a thyroid nodule by ultrasound (US). A fine needle aspirate (FNA) on the nodule was reported as Hurthle cell neoplasm. Histopathology revealed a Hurthle cell adenoma with an incidental micro papillary carcinoma. On follow up a year later, US investigation revealed another nodule in the inferior pole of the remnant lobe of thyroid. FNA showed sheets of uniform small round cells arranged in micro follicles, intermixed with Hurthle—like cells with absence of colloid, raising the possibility of a parathyroid lesion. Biochemical tests, clinical history, cytomorphological, immunocytochemical and biochemical tests supported a parathyroid adenoma.

Advancements in diagnostic techniques and management strategies have not only improved survival rates in patients with chronic renal disease but have also identified an increasing number of multiple primary tumors in these patients. Thyroid lesions have cytomorphological similarities and may masquerade parathyroid neoplasms. Regular thyroid screening in post— transplant patients, meticulous pathological examination and parathormone assay are crucial in the early diagnosis, management and prevention of morbidity and mortality in these patients.

Keywords: Fine needle aspiration, kidney transplant, Hurthle cell neoplasm, parathyroid adenoma, micropapillary carcinoma.

Abstract

Chronic immunosuppression is known to cause an increased risk of cancers in organ transplant recipients leading to the rise in morbidity and mortality among these patients. Recent studies have observed that thyroid lesions are more frequently encountered in kidney transplant recipients.

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Case Report


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Introduction

Altered T—cell immunity, oncogenic viruses and immunosuppression are known to cause an increased risk of cancers in organ transplant recipients, contributing to the second most common cause of morbidity and mortality next to cardiovascular disease among these patients.1 Moreover cancers caused due to oncogenic viruses such as lymphoproliferative disorders are more commonly observed in these patients than the cancers not related to oncogenic viruses (such as lung, breast, thyroid). Few studies conducted in kidney transplant recipients showed that thyroid disease was common among this population, with a significant number of patients exhibiting morphologic or functional alteration in the thyroid gland, and of which 13.9% of the cases necessitated fine needle aspiration.2

Various combinations of thyroid carcinoma variants have been reported, which include follicular carcinoma with papillary carcinoma, medullary carcinoma with follicular carcinoma and anaplastic carcinoma with follicular carcinoma. We report a patient with hypertension and kidney transplant seventeen years back, with recent onset graft failure, who was diagnosed to have a Hurthle cell adenoma with micro papillary carcinoma and later developed a parathyroid adenoma which proved to be a diagnostic challenge.

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Case Presentation

A 45-year-old woman with history of hypertension and kidney transplant done seventeen years back was admitted for graft failure and assessment for a second renal transplant. The only other major event she had in the post-transplant period was a surgery for uterine leiomyoma and recurrent lung infections. A PET/CT showed focal hyper metabolic lesion in the inferior pole of left lobe of thyroid lobe, while a complementary ultrasound (US) showed an isoechoic solitary nodule in the same region (Fig 1a).

US guided fine needle aspiration (FNA) showed a cellular aspirate comprising of sheets, micro and macro follicles and singly dispersed Hurthle cells with mild nuclear pleomorphism and conspicuous nucleoli in a background of colloid mixed with blood. Transgressing capillaries were seen in few of the clusters. Aspirate of the solitary thyroid nodule was reported as “suspicious of a follicular neoplasm (Hurthle cell type)” (Fig 2).

The patient underwent left partial thyroidectomy, which revealed a Hurthle cell adenoma, with an incidental papillary micro carcinoma. Immunohistochemistry (IHC) done on the tumor focus containing papillary micro carcinoma expressed cells to be positive for CK 19 positivity and negative for CD 56 (Fig 3).

On follow up, a year later, a MIBG scan showed increased uptake in the remnant lower pole of the remnant right of thyroid. A further US neck showed a well-defined hypoechoic nodule (app 1.3x1x0.7cm) in the posterior inferior aspect of the right lobe of thyroid. High-resolution gray scale and colour Doppler showed the lesion to be inseparable from the thyroid with an increased internal vascularity (Fig 1b). FNA of the lesion in the right lobe showed sheets of uniform round cells with scant cytoplasm arranged in micro follicles, intermixed with Hurthle–like cells and absence of colloid. A differential diagnosis of follicular lesion of undetermined significance (FLUS) or a parathyroid lesion was considered, based on the medical history and morphological findings. Immunocytochemistry (ICC) done on the cell block section showed the cells positivity for Chromogranin A and negative for TTF-1 and Thyroglobulin. (Fig 4)

Parathormone (PTH) antibody was unavailable in our laboratory and the needle rinses were not sent for parathormone assay as a parathyroid lesion was not suspected.

Review of medical files revealed that patient had rising blood urea and creatinine levels and was diagnosed to have a failed kidney graft. Biochemical tests showed mild hypocalcaemia, hyperphosphatemia and hyperparathyroidism (Table 1). The cytomorphological, immunocytochemical and biochemical tests supported a parathyroid adenoma at the level of the inferior pole of right thyroid lobe.

Discussion and Conclusion

This case report documents the rare occurrence of three endocrine tumors in a kidney transplant recipient with graft failure, evolving during a period of one year and discovered...
Figure 2. (a) Fine needle aspirate (FNA) of nodule left lobe of thyroid shows a cellular aspirate with follicular cells in macro and micro follicles; (b, c) Higher magnification showing cells with moderate to abundant granular cytoplasm—oncocyes/Hurthle cells; (d, e) The cells stain positive for Thyroid transcription factor–1 (TTF–1) and Thyroglobulin; and (f) negative for Chromogranin A.

Figure 3. (a) Resected left lobe of thyroid shows a follicular adenoma with intact capsule (b) in addition an adjacent incidental micropapillary carcinoma is seen, (c) Cells stain positive for CK19 and (d) negative for CD 56.

(a, b: Hematoxylin and eosin X200; c: CK–19 X200; d: CD56 X200).
Another noteworthy finding was that the patient had a graft failure demonstrated through serial biochemical tests that exhibited hypercalcemia and hyperparathyroidism, triggering the formation of a parathyroid adenoma.

Studies show that the parathyroid growth response in chronic renal failure progresses through several stages. An initial diffuse, polyclonal, secondary hyperplasia is initiated by hypocalcaemia and becomes more severe as a result of Calcitriol deficiency. The hyperplasia then becomes nodular and multiclonal over time accompanied by hypercalcemia. Increased turnover of parathyroid cells in secondary hyperparathyroidism renders the parathyroid glands more susceptible to mitotic nondisjunction leading to tumor formation and the emergence of an adenoma as a result of a mutation in one of the cells in a nodule. This sequence referred to as tertiary hyperparathyroidism, is a disorder that combines in its aetiology, the hyperplasia of

during routine follow up 17 years post transplantation. Another noteworthy finding was that the patient had a graft failure demonstrated through serial biochemical tests that exhibited hypercalcemia and hyperparathyroidism, triggering the formation of a parathyroid adenoma. Studies show that the parathyroid growth response in chronic renal failure progresses through several stages. An initial diffuse, polyclonal, secondary hyperplasia is initiated by hypocalcaemia and becomes more severe as a result of Calcitriol deficiency. The hyperplasia then becomes nodular and multiclonal over time accompanied by hypercalcemia. Increased turnover of parathyroid cells in secondary hyperparathyroidism renders the parathyroid glands more susceptible to mitotic nondisjunction leading to tumor formation and the emergence of an adenoma as a result of a mutation in one of the cells in a nodule. This sequence referred to as tertiary hyperparathyroidism, is a disorder that combines in its aetiology, the hyperplasia of

Figure 4. (a, b, c) FNA smears of the nodule in the postero inferior aspect of the right lobe of thyroid shows small round cells in macro and microfollicular pattern with few Hurthle–like cells and absence of colloid. (d) The cells stain negative for Thyroglobulin (e) negative for TTF−1 and (f) positive for Chromogranin A.

(a: Papanicolaou stain X 100; b: Papanicolaou stain X 400; c: May Grunwald Giemsa X 400; d: Thyroglobulin X400; e: TTF −1X400; f and inset: Chromogranin A X 400)

Table 1: Preoperative biochemical profile of the patient

Table 1 shows blood values of the patient depicting renal failure with mild electrolyte disturbance. The intact parathyroid hormone (iPTH) is very high compared to mild hypocalcemic level. (Note: i PTH is the greatest part of circulating PTH– like bioactivity. iPTH assay allows to distinguish between primary hyperthyroidism and non parathyroidal hypercalcemic patients.)
secondary hyperparathyroidism with the monoclonality of primary hyperparathyroidism.3

Studies have shown that chronic immunosuppression is related to the increased risk of thyroid cancers along with other cancers. Among thyroid cancers, papillary cancers were found to be more common and these tumors were found to be more aggressive compared to the general population. 2

Our case was found to be an incidental micropapillary carcinoma during the surgery done for a Hurthle cell neoplasm. Over a period of one year, a parathyroid adenoma was also diagnosed in the remnant lobe. Hurthle cells are seen in FNA from Hashimoto thyroiditis, Hurthle cell tumors and Hurthle cell nodules in adenomatous nodules as well as in parathyroid lesions. Since, Hurthle cells can be present in both non neoplastic and neoplastic thyroid lesions it can be diagnostically very challenging.4

This case highlights the fact that follicular neoplasms arising in a thyroid tissue may masquerade parathyroid adenomas and vice versa, not only due to its proximity, but also due to the cytomorphological (Hurthle cell like) similarities. Parathyroid scans may show increased uptake, but is unable to differentiate between suspicious thyroid nodule from an abnormal intra—thyroid parathyroid gland.5 Clinical information, meticulous examination aided with immunological studies, PTH assay and additional radiological tests are crucial to reach the correct diagnosis. Secondly, as thyroid diseases are shown to evolve years after transplantation, as a consequence of chronic immunosuppression; a regular screening of thyroid disease by biochemical tests and ultrasound is recommended in such patients. Thyroid nodules if found to increase in size to more than 1 cm necessitates FNAC, thereby rendering early diagnosis, appropriate treatment and a significant decrease in the morbidity and mortality in this patient population.6

References