

Mucoepidermoid parotid carcinoma after renal transplantation

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The incidence of *de novo* post-transplant malignancy (PTM) increases three to five times after renal transplantation [1] with an average figure of 6% [2]. Compared to malignancies in the general population, PTM is considered to be more aggressive and carries poor prognosis [1]. Large registry data [3] suggests that skin cancers and lymphomas are the most common malignancies post-transplantation. Common malignancies in general population such as colon, lung and stomach cancers, occur twice more frequently in the transplant population, while rare tumours such as Kaposi's sarcoma (KS) occur 40 times more commonly [3]. Factors implicated in PTM include [1] genetic background, increasing recipient age, environmental factors (sunlight, smoking), infection by carcinogenic viruses and the general intensity of immunosuppression rather than specific agents.

We present a case of Mr RK, 34-year-old man, live related renal allograft recipient (basic disease: Chronic Glomerulonephritis), who presented to us 6 years after transplantation with a history of painless swelling on right side of the face in the parotid region since last 6 months. The patient had been on cyclosporine (CsA) + azathioprine (Aza) + prednisolone (P) initially, which was changed to tacrolimus (Tac) 1.5 mg BD + mycophenolate (MMF) 750 mg BD + prednisolone 5 mg OD after 3 years in view of the progressive rise in S. creatinine (S.cr) to 2.1 mg/dl (185.64 $\mu\text{M/L}$), which had stabilized to 1.2–1.3 mg/dl (106.08–114.92 $\mu\text{M/L}$) at the time of presentation. A 1.5 × 2 × 2 cm nontender mass, firm to hard in consistency, was noted in the right parotid region which became prominent on clenching of teeth.

Fine needle Aspiration Cytology of the lump was noncontributory. Contrast-enhanced CT Head and Neck revealed an ill-defined mass in the right parotid gland in the superficial lobe. In view of the possibility of malignancy, a right superficial parotidectomy with facial nerve sparing was performed. Detailed histopathological study revealed low grade mucoepidermoid carcinoma (Fig. 1), with no metastatic deposits in the retrofacial lymph nodes. Postoperative course was uneventful. We did not change the immunosuppression protocol. Graft function at 13 months postoperative period was stable

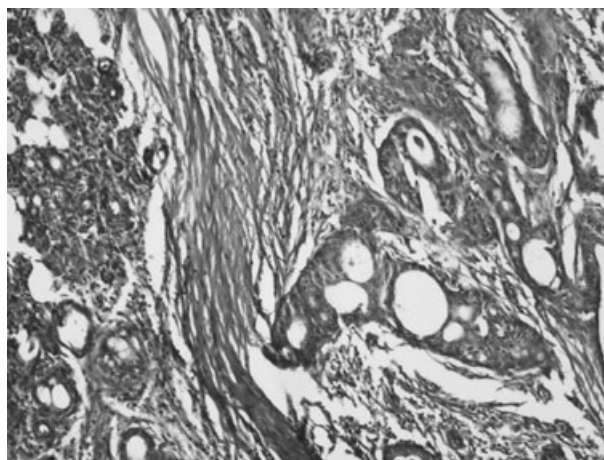


Figure 1 Microscopy of resected parotid gland (40×) showing an infiltrating tumour composed of epidermoid cells mixed with mucin-secreting cells with few scattered intermediate cells. The cells show high nuclear–cytoplasmic ratio, vesicular nuclear chromatin and moderate amount of cytoplasm. Areas of fibrosis, foamy macrophages, lymphomononuclear cell infiltrate and giant cell reaction. Surrounding salivary gland shows focal lymphomononuclear cell infiltrate.

with S.Cr = 1.4 mg/dl (123.76 $\mu\text{M/L}$). Clinical assessment till 13 months postparotidectomy showed that there was no recurrence of the tumour clinically and radiologically.

Increased graft survival after transplantation means longer exposure to immunosuppressives (IS) and hence an increased risk for malignancies. In a recent US study [4] on post-renal transplant patients, the cumulative incidence of nonmelanoma skin cancer was 19% and 17% for other cancers. Malignancies commonly noted in renal transplant recipient (RTR) were skin (40%), gastrointestinal (13%), urologic (11%) cancers and lymphomas (9%). Contrary to Western data [2–4], Indian data [5] suggests a very low incidence of PTM of 2% at 6 months and 3.8% at 2 years after transplantation with the average time to develop PTM being 24–169 months. The authors also noted that compared to Western data there was a paucity of cutaneous malignancy and a predominance of NonHodgkin's lymphoma [5]. While head and neck

malignancies (HNM) have been frequently reported in renal transplant recipients (RTR) from large cancer registry data [6], 80% are cutaneous cancers such as basal cell carcinoma, followed by noncutaneous squamous cell carcinomas. Overall incidence of noncutaneous, nonlymphomatous, head and neck cancer during a mean follow-up of 10 years after transplantation was 0.8% [6], which was 4 times that of the general population. Interestingly, Indian data [7] suggest a 20% incidence of oropharyngeal cancer after an average follow-up of 106 months.

Despite the common occurrence of HNM, salivary gland tumours and specifically parotid mucoepidermoid carcinoma (MEC) have rarely been reported in RTR. Makietie *et al.* [6] reported a single case of salivary gland tumour out of 113 nonlymphomatous head and neck malignancies in RTR, although the histological details were not available. Horta *et al.* [8] reported a 74-year-old male RTR who developed myoepithelial carcinoma of the parotid gland after 14 years of renal transplantation. Singh *et al.* [7] reported a 34-year-old female RTR with adenoid cystic carcinoma of the parotid. In a large registry data of bone marrow transplant recipients [9], three cases of parotid MEC were found out of 137 *de novo* malignancies.

Mucoepidermoid cancer (MEC) is the most common malignancy of the parotid gland [10]. Although there are no specific aetiological agents, ionizing radiation has been implicated. As an initial diagnostic work-up, FNAC has an accuracy of 77–95% [11]. Histopathological grading is the most important prognostic factor [12], with 5-year survival rates of 92–100% in low grade, 62–92% in intermediate and 0–43% in high grade lesions. Treatment of MEC is total surgical resection. Superficial parotidectomy is preferred for tumours which are lateral to the facial nerve and total parotidectomy is recommended in cases of deep lobe involvement and/or positive intraparotid nodes. Overall incidence of local recurrence is 7–26%, while distant metastasis occurs in 6–15% of cases [12].

IS promotes PTM [1] and is a well-realized aetiological factor in viral-mediated cancers such as post-transplant lympho-proliferative disorders (PTLD). Ironically, clinical data suggest that Tac may reduce the overall incidence of malignancy [13] while MMF may be neutral or even lower the incidence of PTLD [1]. There is a consensus that sirolimus may reduce the incidence of PTM [1] given its anti-proliferative and pro-apoptotic properties. In our case, sirolimus was avoided as the patient had significant baseline proteinuria. Overall, the rationale of reducing IS in lymphomatous malignancies is proven, while any such attempt in solid organ tumours invariably leads to graft loss [2]. There is no standard therapy for parotid malignancy in RTR. Singh *et al.* [7], while continuing with the same dose of IS in a single case of parotid (adenoid

cystic) carcinoma, noted stable graft function with one local recurrence after 23 months, which was treated with conservative radical parotidectomy.

Our index case showed good clinical outcome during a relatively short observation period of 13 months. In view of the absence of registry data, we were unable to compare this case with other malignancies in the RTR. This case was presented primarily to highlight a common malignancy of the general population with surprisingly rare occurrence in the transplant population.

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References

- Dantal J, Pohanka E. Malignancies in renal transplantation: an unmet medical need. *Nephrol Dial Transplant* 2007; **22**(Suppl 1): 4.
- Penn I. Tumors after renal and cardiac transplantation. *Hematol Oncol Clin North Am* 1993; **7**: 431.
- ANZDATA. Australia and New Zealand Dialysis and Transplant Registry, 2006. Available at: <http://www.anzdata.org.au/>. Accessed October 2008.
- Agraharkar M, Cinclair RD, Kuo YF, Daller JA, Shahinian VB. Risk of malignancy with long-term immunosuppression in renal transplant recipients. *Kidney Int* 2004; **66**: 383.
- Sakhuja V, Jha V, Ghosh AK, Singh SK, Chugh KS. Low incidence of malignancies following renal transplantation in India. *Nephrology* 1995; **1**: 301.
- Makietie AA, Lundberg M, Salmela K, Kyllonen L, Pukkala E. Head and neck cancer in renal transplant patients in Finland. *Acta Otolaryngol* 2008; **128**: 1255.
- Singh SK, Gupta AK, Jha V, *et al.* Treatment of oropharyngeal cancer in renal transplant recipients without cessation of immunosuppressive therapy. *Transplant Proc* 2006; **38**: 2088.
- Horta R, Barreto F, Marques M, *et al.* Epithelial-myoepithelial parotid carcinoma after kidney transplantation. Available at: <http://www.ecancermedicalscience.com/view-article.asp?doi=10.3332/ecancer2008.92&type=abstract>. Accessed 4 January 2009.

9. Scott Baker K, De For Todd E, Burns Linda J, *et al.* New malignancies after blood or marrow stem-cell transplantation in children and adults: incidence and risk factors. *J Clin Oncol* 2003; **21**: 1352.
10. Boahene Derek Kofi O, Olsen Kerry D, Lewis Jean E, Daniel Pinheiro A, Pankratz VernonShane, Bagniewski StephanieM. Mucoepidermoid carcinoma of the parotid gland – The Mayo Clinic experience. *Arch Otolaryngol Head Neck Surg* 2004; **130**: 849.
11. Kamal SA, Othman EO. Diagnosis and treatment of parotid tumors. *J Laryngol Otol* 1997; **3**: 316.
12. Pires FR, Paes de Almeida O, Cavalcanti de Araujo V, zKowalski LP. Prognostic factors in head and neck mucoepidermoid carcinoma. *Arch Otolaryngol Head Neck Surg* 2004; **130**: 174.
13. Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. *Am J Transplant* 2004; **4**: 905.