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CASE REPORT

A kidney transplant recipient with recurrent trichilemmal carcinoma and multiple other primary malignancies

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ABSTRACT

Kidney transplant recipients are at increased risk of developing malignancy, with prolonged immunosuppressive therapy being a strong risk factor. Non-melanoma skin cancers are most commonly reported and multiple primary malignancies are also described. This is the first report of a recurrent trichilemmal carcinoma, a rare cutaneous tumour, in a kidney transplant recipient. This case, and the associated literature, indicate that regular screening, thorough examination, and tailored immunosuppressive regimens are critical in managing these patients.

Keywords: recurrent trichilemmal carcinoma; kidney transplant recipient; multiple primary malignancies.

INTRODUCTION

Malignancies occur relatively more frequently in transplant recipients and are associated with an aggressive course and increased morbidity and mortality [1]. The prevalence in this group ranges from 4–18%, which is 2 to 3 times greater than the general population [1,2]. Malignancy can develop de novo, as a recurrence or be transmitted from the organ donor. Risk is associated with the duration of pre-transplant dialysis, type and duration of immuno-suppression, and infection with oncogenic viruses [3].

Skin cancers are the most frequent. Non-melanoma skin cancers (NMSC) account for over 90% of post-transplant skin malignancies. In contrast to the general population, squamous cell carcinomas are more common than basal cell carcinomas, with a frequency of 65 to 250 times greater in transplant recipients [4]. The incidence rises with increased exposure to ultraviolet radiation [5].

Trichilemmal carcinoma is a rare adnexal neoplasm. It develops from the hair follicle's external sheath [6]. It is usually indolent with a low metastatic potential although there have been reports of metastatic disease [6,7]. There have been two prior cases of trichilemmal carcinomas documented in kidney transplant recipient (KTR)s [7,8].

This case reports multiple primary malignancies in a KTR in the form of recurrent trichilemmal carcinoma, recurrent basal cell carcinomas and an oesophageal squamous cell carcinoma.

CASE PRESENTATION

A 48-year-old white male received two renal transplants in the course of his treatment for end-stage renal disease (ESRD). At age six years, he developed ESRD secondary to atypical haemolytic-uraemic syndrome and received a kidney transplant from a living donor. At age 20 years, he was re-transplanted with a deceased-donor kidney.

For his initial transplant, he received methylprednisolone as induction therapy, and prednisone and azathioprine for maintenance therapy. For the second transplant, methylprednisolone and anti-thymocyte globulin were

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used for induction. The maintenance immunosuppressive agents were initially cyclosporine, prednisone and azathioprine. Mycophenolate later replaced the azathioprine.

Comorbidities included tophaceous gout, hypertension and dyslipidaemia. His medication included colchicine, allopurinol, atenolol, perindopril, amlodipine, simvastatin and aspirin. He reported occasional ethanol use. There was no history of tobacco usage, trauma or family history of malignancy.

Sunburn and sun damage were documented. He developed multiple skin lesions, which were managed with topical fluorouracil and surgical excision. Histology of the skin biopsies revealed multiple invasive basal cell carcinomas and underlying hypertrophic solar keratosis.

At age 47 years, he presented with a fungating right shoulder mass. Magnetic resonance imaging (MRI) showed a subcutaneous mass with no local extension that involved muscle or bone (Figure 1, arrow). There was no evidence of metastases. Primary surgical resection was performed with 1 cm clear margins. The nodular, exophytic tumour measured 115 mm x 115 mm x 48 mm. Histology revealed an ulcerated, invasive trichilemmal carcinoma (Figure 2). The dosages of immunosuppressive agents were reduced upon making this diagnosis.

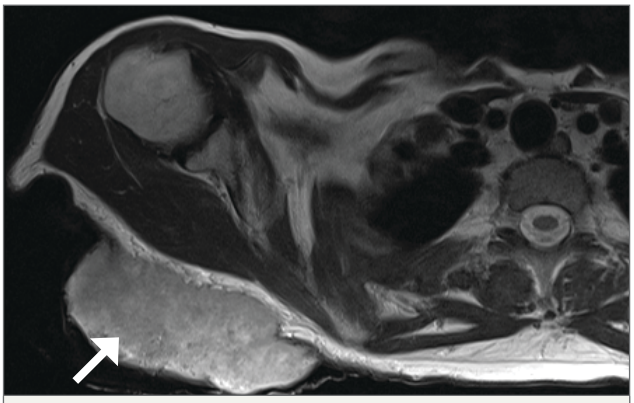

Figure 1. Magnetic resonance imaging of the right shoulder demonstrating a subcutaneous mass (arrow) without local extension to muscle or bone.

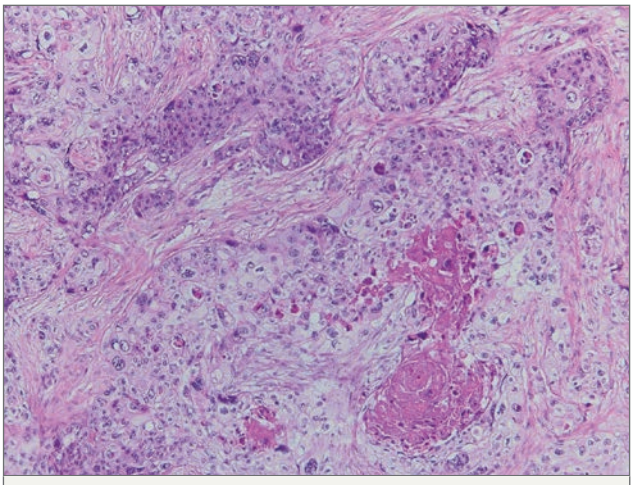

Figure 2. Histology of the trichilemmal carcinoma. There are nests of malignant epithelial cells with abrupt keratinization. There is marked nuclear pleomorphism with clearing of occasional cells (haematoxylin and eosin stain, original magnification x100).

After six months, he presented with significant weight loss, dysphagia, and a right axillary mass. He was severely wasted. Gastro-duodenoscopy revealed a suspected malignant stricture in the distal third of his oesophagus and biopsy confirmed a poorly differentiated invasive oesophageal squamous cell carcinoma. Computed tomography of the chest and abdomen showed a locally aggressive oesophageal tumour with pulmonary metastases and a right axillary mass (Figure 3, arrow). Biopsy of the axillary mass demonstrated recurrent trichilemmal carcinoma. Viral studies for human immunodeficiency virus and BK virus were negative, whereas those for cytomegalovirus, Epstein–Barr virus and parvovirus B19 IgG were positive.

His allograft function had declined over time and this was attributed to the combination of an ageing graft, possible rejection secondary to the reduction of immunosuppression, vesicoureteral reflux and recurrent urinary tract infections.

Given his poor overall functional state, failing renal allograft and metastatic disease, the decision was made with the patient and his family to follow a palliative course. A stent was placed to relieve the dysphagia. The patient was discharged on prednisone and cyclosporine as immunosuppression. He died a month later.

DISCUSSION

This is the first case report of recurrent trichilemmal carcinoma in a KTR. The other primary malignancies were oesophageal squamous cell and recurrent basal cell carcinomas.

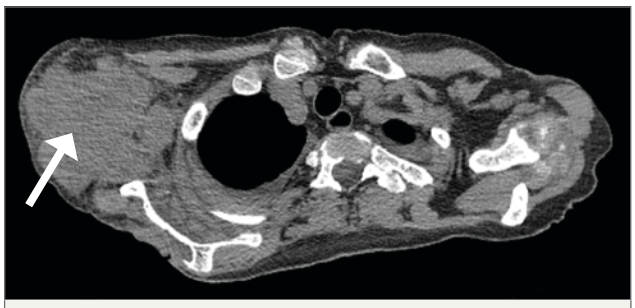

Figure 3. Computed tomography scan of the chest, demonstrating a right axillary mass (arrow).

Malignancy risk in immunosuppressed patients is well documented, as immunosurveillance plays a protective role against tumour development [9]. This case highlights the risk of developing a malignancy post-transplantation as well as the further risk of developing multiple primary malignancies. In a local study by Moosa [10], the incidence of malignancies was similar in different ethnic groups. Squamous and basal cell carcinomas were common in white patients whereas there were no cases of skin cancer in nonwhites and Kaposi sarcoma was the most common malignancy, accounting for almost 80% of all cancers.

Data regarding the occurrence of second malignancies in solid organ transplant recipients is limited. A single-centre study showed an increased incidence of multiple primary malignancies in KTRs as compared to the general population [11]. An Italian multicentre study of KTRs reported a standardized incidence ratio (SIR) of 8.3 for developing a subsequent NMSC in patients with a primary NMSC. Those with a primary non-cutaneous cancer had an SIR of 1.8 for developing a second non-cutaneous malignancy [12].

The incidence of multiple primary malignancies is increasing due to advances in screening, diagnostic testing and anti-cancer treatment regimens allowing for prolonged survival. The pathogenesis of multiple primary malignancies also involves genetic susceptibility, lifestyle, environmental factors, as well as chemotherapy and radiation exposure [13].

Trichilemmal carcinoma is a rare cutaneous malignancy that develops from the hair follicle's external sheath. The exact pathogenesis has not been established. The risk factors for its development are immunosuppression, solid organ transplantation, radiation, previous burns or scars, and certain genetic disorders (xeroderma pigmentosa and Cowden's disease). Trichilemmal carcinomas usually follow a benign course, but metastatic disease has been reported [6,7].

There are two prior reports of a trichilemmal carcinoma in KTRs. The first described a hyperkeratotic papulonodular lesion on the chest, which was treated with Mohs micrographic surgery, with no recurrence after 6 years [8]. The second case described a more aggressive tumour with metastases to lymph nodes, liver, and lung. The patient died despite optimal surgical management of the primary lesion and radiotherapy [7].

The risk of esophageal cancer following transplantation is not well-defined. Oesophageal squamous cell carcinoma is associated with tobacco use, alcohol, achalasia, prior radiation exposure, poor economic status and nutritional deficiency [14]. A nationwide cohort study showed a threefold increased risk following solid organ transplantation [15]. Grulich et al. confirmed an increased risk of developing oesophageal cancer post-transplantation with an SIR of 3.05 [16].

According to the 2009 KDIGO Clinical Practice Guidelines for Care of Kidney Transplant Recipients [17], KTRs are at increased risk of skin malignancies. Risk factors include fair skin, a sunny climate, and employment which involves sun exposure. Precautions include the use of ultraviolet-light-blocking agents, minimizing sun exposure, undergoing regular skin examinations and individualized screening for non-skin malignancies. There should be reduction of immunosuppressive therapies in KTRs who develop malignancies with a high or moderately increased SIR. Clinicians must weigh the potential benefit of prolonged survival against the consequence of potential graft loss [17].

There is no evidence of any direct aetiological link between trichilemmal, basal cell and oesophageal squamous cell carcinoma. However, all occur more frequently in immunosuppressed individuals. Our patient's potential risk factors included prolonged exposure to immunosuppressive agents, recurrent sun exposure and ethanol use.

Definitive management of the initial trichilemmal carcinoma was primary excision of the tumour with 1 cm margins. Mohs micrographic surgery is another option and allows for greater preservation of surrounding healthy tissue with possibly higher recurrence-free rates [18]. The use of radiation and chemotherapy has been described for metastases but there is no standardized treatment regimen [6].

NMSC and oesophageal squamous cell carcinomas are associated with high or moderately increased SIR. The patient's immunosuppression was reduced in line with the KDIGO transplantation guideline recommendations [17]. Azathioprine was switched to mycophenolate, which may be associated with decreased risk of developing a malignancy [19]. Due to the patient's metastatic disease, significant graft dysfunction and overall poor functional status and prognosis, no definitive oncological management was instituted for the oesophageal carcinoma.

CONCLUSIONS

This is a first report of a recurrent trichilemmal carcinoma in a KTR. Our case also provides another example of the risk of multiple malignancies in patients exposed to long-term immunosuppressive therapy. Regular screening, thorough examinations and individualized immunosuppressive regimens are critical in managing these patients.

Ethical considerations

Ethical clearance was granted by the University of the Witwatersrand's Human Research Ethics Committee (reference number M180390).

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