CASE REPORT

Squamous cell carcinoma with rhabdoid phenotype and osteoclast-like giant cells in a renal–pancreas transplant recipient

K Aljerian, K O Alsaad, R Chetty, D Ghazarian

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Squamous cell carcinoma (SCC) is the commonest non-melanotic malignant skin tumour encountered after solid-organ transplantation. In this setting it is associated with a worse prognosis than sun-damage-induced SCC. Rhabdoid cells and osteoclastic giant cells are infrequently seen in SCC. This case highlights the unusual occurrence of rhabdoid cells and osteoclastic giant cells in a post-transplant SCC.

Squamous cell carcinoma (SCC) is very common, and is the second most common cutaneous neoplasm after basal cell carcinoma. It is more commonly seen in men, except for lesions on the lower legs where it is more common in women. Cutaneous SCC has a favourable prognosis, and distant metastasis is uncommon after complete surgical excision. Many risk factors are associated with SCC, including exposure to the sun, psoralen and ultraviolet A phototherapy, chronic exposure to ionising radiation, chemical carcinogens such as arsenic and coal tar products, longstanding burns, scars, ulcers or sinus tract, and genetic disorders such as xeroderma pigmentosa. Patients with HIV infection, and recipients of solid organ transplantation also have an increased risk of skin cancer, especially highly aggressive SCC.¹ Various histological types of SCC have been described, such as spindle, papillary and rhabdoid. To the best of our knowledge, only four cases of SCC with rhabdoid phenotype have been reported.^{2–5} This paper describes a cutaneous SCC with a unique combination of histological features in the form of rhabdoid and sarcomatoid differentiation, accompanied by osteoclast-like giant cells arising in a kidney and pancreas transplant recipient.

CASE HISTORY

A 42-year-old white man presented with a rapidly growing nodular, ulcerated lesion on the right cheek for 5 months. He showed no evidence of other cutaneous or mucosal lesions, and no evidence of regional lymphadenopathy at the time of presentation. Medical history included hypothyroidism, hypertension for 10 years and type 2 diabetes mellitus, complicated by retinopathy, peripheral neuropathy, peripheral vascular disease and end-stage renal disease, which led to kidney and pancreas transplantation 26 months before. Both grafts were functioning at the time of presentation. The patient was maintained on immunosuppressive drugs, FK506 (tacrolimus) and prednisone. The lesion was locally excised with clear surgical margins.

PATHOLOGICAL FINDINGS

Grossly, the specimen consisted of an ellipse of skin that measured 2.8×1.2×0.3 cm. The centrally located, well-circumscribed ulcerated lesion with raised edges measured

0.8 cm in maximum diameter. On cut section, the tumour was soft, had a uniform white–tan colour and was submitted entirely for histological examination. The tissue sections were fixed in 10% neutral buffered formalin, routinely processed, embedded in paraffin wax and stained with haematoxylin and eosin. Immunohistochemistry was carried out on the formalin-fixed, paraffin-wax-embedded tissue.

Light microscopic examination showed a moderately cellular, poorly differentiated neoplasm with infiltrating borders into the papillary and reticular dermis. The tumour consisted predominantly of monomorphic polygonal neoplastic cells, arranged in solid sheets (fig 1). The cells possessed a defined cell membrane, pleomorphic vesicular nuclei, prominent centrally located nucleoli and abundant eosinophilic cytoplasmic inclusions with peripheral displacement of the nuclei, giving rise to the characteristic rhabdoid phenotype (fig 2). Focally, the tumour showed sarcomatoid differentiation, in which the neoplastic cells showed spindle or oval vesicular nuclei, abundant eosinophilic cytoplasm and were arranged in fascicles. Numerous mitotic figures (17 per 10 high-power fields) and foci of necrosis were present. A large number of osteoclast-like giant cells containing multiple nuclei and abundant cytoplasm was distributed throughout the tumour (fig 1). Intracellular bridges and keratinisation were not evident. Destruction of skin adnexal structures by tumour cells was evident. Vascular invasion and lymphatic permeation were not seen. Intraepithelial SSC in the overlying epidermis was not identified, as the epidermis was extensively ulcerated.

Immunohistochemically, the rhabdoid and spindle-shaped tumour cells showed diffuse coexpression of high-molecular-weight cytokeratin (fig 3) and vimentin, and immunopositivity for cytokeratin 5/6, cytokeratin 14 and p63. In addition, the rhabdoid tumour cells were diffusely immunoreactive for CD117 (c-kit) and calponin, whereas the spindle cells showed focal immunopositivity for smooth-muscle actin and muscle-specific actin. The osteoclast-like giant cells were immunoreactive for CD68. All cell components show no staining for S100-protein, HMB45, microphthalmia transcription factor, Melan A, factor XIIIa, CD34, desmin, monoclonal carcino-embryonic antigen, low-molecular-weight cytokeratin, epithelial membrane antigen or BER-EP4.

DISCUSSION

Cutaneous neoplasms are more common in renal transplant recipients than in the general population, and are the most common malignancies in these patients.⁶ The incidence of skin cancer is estimated in 10–40% of patients 10–20 years after transplantation.⁷ In the transplant recipients, the most common cutaneous non-melanocytic malignancy is SCC,

Abbreviations: OGC, osteoclast-like giant cell; SCC, squamous cell carcinoma

Figure 1 The tumour is composed of mononuclear polygonal tumour cells and a large number of osteoclast-like giant cells. Haematoxylin and eosin staining, $\times 10$.

Figure 2 The rhabdoid phenotype. The tumour cells have vesicular nuclei, prominent nucleoli and abundant hyaline cytoplasmic inclusions with peripheral displacement of the nuclei. Haematoxylin and eosin staining, $\times 20$.

with an incidence of 40–250 times that in the general population, followed by basal cell carcinoma with an incidence of 10 times that in the general population.^{8–10} The duration of immunosuppression treatment using ciclosporin or tacrolimus-based regimens,^{11,12} older age at transplantation, presence of actinic keratosis and verrucae vulgaris, smoking and outdoor occupation are major risk factors associated with SCC.¹³ The development of SCC in transplant recipients is believed to be caused by the interaction of multiple factors: exposure to ultraviolet radiation, the direct effect of immunosuppressive agents, infection by oncogenic viruses such as human papillomavirus and genetic factors.¹⁴

SCCs in the setting of solid organ transplantation tend to evolve more rapidly than in the general population, can be multiple and behave more aggressively, with an increased tendency of recurrence and metastasis.¹⁰ Histologically, these SCCs are often poorly differentiated or undifferentiated, and may exhibit a spindle-cell morphology,¹⁵ mimicking other cutaneous spindle-cell lesions, such as spindle-cell melanoma, leiomyosarcoma, dermatofibrosarcoma protuberans, fibrosarcoma and atypical fibroxanthoma. The neoplastic spindle cells can sometimes be admixed with pleomorphic osteoclast-like giant cells (OGCs).¹⁶ The origin of the OGCs is not fully understood, as they may present in a wide spectrum of benign and malignant, epithelial and mesenchymal tumours. It is not clear whether they represent a non-neoplastic mesenchymal component reactively induced in the tumour stroma, or a neoplastic epithelial component. In the pancreas, Sakai *et al*¹⁷ showed the OGCs to be immunoreactive for CD68 and lacking *k-ras* mutations, supporting the fact that OGCs are of reactive and non-neoplastic origin.

The rhabdoid phenotype is characterised by large polygonal cells with eccentric nuclei, large nucleoli and abundant hyaline filamentous cytoplasmic inclusions. Extrarenal malignant neoplasms with a rhabdoid phenotype and coexpression of epithelial and mesenchymal markers were initially designated as “extrarenal malignant rhabdoid tumours”, and thought to represent a rhabdomyosarcomatous variant of Wilms’s tumour. Later, the rhabdoid phenotype was recognised in many tumours at various sites, such as melanoma,^{17,18} adenocarcinoma,¹⁹ neuroendocrine neoplasms,²⁰ plasmacytoma and diffuse large B cell lymphoma, and malignant peripheral nerve sheath tumour.²¹ It is currently believed that the rhabdoid phenotype represents a common clonal dedifferentiated end point in malignant tumours of varying histogenesis.²² More recently, it has been

Figure 3 The rhabdoid tumour cells are diffusely positive for high-molecular-weight cytokeratin, $\times 20$.

suggested that rhabdoid changes may be a type of degeneration, or a preliminary stage before apoptosis or cell necrosis.³ Cutaneous malignant rhabdoid non-melanocytic tumours are rare, especially cutaneous carcinomas with a rhabdoid phenotype, and tend to grow rapidly and have an early involvement of the regional lymph nodes.³ This report is the first case of cutaneous SCC with a rhabdoid and spindled phenotype with accompanying osteoclastic giant cells arising in a solid organ transplantation. Despite the rhabdoid morphology, the presence of perineural invasion and the

Take-home messages

- Squamous cell carcinoma (SCC) can exhibit a rhabdoid phenotype, uncommonly, in post-solid-organ transplantation.
- Osteoclastic giant cells can be seen in SCC.
- SCC with the rhabdoid phenotype may be considered to be a more aggressive form of SCC.
- Unusual morphological variants of SCC may be encountered in transplant patients.

immunocompromised status in the current case, no evidence of recurrent or metastatic SCC was seen after 10 months of follow-up. Whether the rhabdoid or sarcomatoid phenotype confers the aggressive behaviour or occurs because the patient is at a high risk is conjectural. However, it seems that the two rationales are not mutually exclusive.

Authors' affiliations

K Aljerian, K O Alsaad, R Chetty, D Ghazarian, Department of Laboratory Medicine and Pathobiology, University of Toronto, University Health Network, Toronto, Ontario, Canada

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Correspondence to: D Ghazarian, University Health Network, Princess Margaret Hospital, 610 University Avenue, Toronto, ON M5G 2M9, Canada; danny.ghazarian@uhn.on.ca

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REFERENCES

- Penn I. Skin disorders in organ transplant recipients. *Arch Dermatol* 1997;**133**:221–3.
- Pai SA, Vege DS, Borges AM, et al. Rhabdoid phenotype in squamous cell carcinoma. A report of two cases. *Indian J Cancer* 1996;**33**:161–4.
- Urdiales-Viedma M, Fernandez-Rodriguez A, De Haro-Munoz T, et al. Squamous cell carcinoma of the penis with rhabdoid features. *Ann Diagn Pathol* 2002;**6**:381–4.
- Urdiales-Viedma M, Fernandez-Rodriguez A, Romero Diaz JA, et al. Squamous carcinoma of the penis with a rhabdoid phenotype. *Arch Esp Urol* 2003;**56**:425–7.
- Mathers ME, O'Donnell M. Squamous cell carcinoma of skin with a rhabdoid phenotype: a case report. *J Clin Pathol* 2000;**53**:868–70.
- Rubel JR, Milford EL, Abdi R. Cutaneous neoplasms in renal transplant recipients. *Eur J Dermatol* 2002;**12**:532–5.
- Hartevelt MM, Bouwes Bavinck JN, Kootte AM, et al. Incidence of skin cancers after renal transplantation in the Netherlands. *Transplantation* 1990;**49**:506–9.
- Bouwes Bavinck JN, De Boer A, Vermeer BJ, et al. Sunlight, keratotic skin lesions and skin cancer in renal transplant recipients. *Br J Dermatol* 1993;**117**:429–40.
- Wu JJ, Orengo IF. Squamous cell carcinoma in solid-organ transplantation. *Dermatol Online J* 2002;**8**:4.
- Bordea C, Wojnarowska F, Millard PR, et al. Skin cancers in renal-transplant recipients occur more frequently than previously recognized in a temperate climate. *Transplantation* 2004;**77**:574–9.
- Hiesse C, Larue JR, Kriaa P, et al. Incidence and type of malignancies after renal transplantation in conventionally and in cyclosporin-treated recipients: single-center analysis of a 20-year period in 1600 patients. *Transplant Proc* 1995;**27**:2450–1.
- Carroll RP, Ramsay HM, Fryer AA, et al. Incidence and prediction of nonmelanoma skin cancer post-renal transplantation: a prospective study in Queensland, Australia. *Am J Kidney Dis* 2003;**41**:676–83.
- Ramsay HM, Fryer AA, Reece S, et al. Clinical risk factors associated with nonmelanoma skin cancer in renal transplant recipients. *Am J Kidney Dis* 2000;**36**:167–76.
- Dreno B. Skin cancers after transplantation. *Nephrol Dial Transplant* 2003;**18**:1052–8.
- Kurzen H, Zeier M, Zelger B, et al. Unusual spindle cell squamous cell carcinoma in a renal transplant patient. *Acta Dermatol Venereol* 2004;**84**:61–4.
- Velazquez EF, Melamed J, Barreto JE, et al. Sarcomatoid carcinoma of the penis: a clinicopathologic study of 15 cases. *Am J Surg Pathol* 2005;**29**:1152–8.
- Sakai Y, Kupelioglu AA, Yanagisawa A, et al. Origin of giant cells in osteoclast-like giant cell tumors of the pancreas. *Hum Pathol* 2000;**31**:1223–9.
- Abbott J, Amirkhan R, Hoang M. Malignant melanoma with rhabdoid phenotype. Histologic, immunohistochemical, and ultrastructural study of a case and review of the literature. *Arch Pathol Lab Med* 2004;**128**:686–88.
- Mogotlane L, Chetty R. Infiltrating ductal carcinoma of the breast with rhabdoid phenotype. *Int J Surg Pathol* 2001;**9**:237–9.
- Chetty R, Asa SL. Pancreatic endocrine tumour with cytoplasmic keratin whorls. Is the term "rhabdoid" appropriate? *J Clin Pathol* 2004;**57**:1106–10.
- Morgan MB, Stevens L, Patterson J, et al. Cutaneous epithelioid malignant nerve sheath tumor with rhabdoid features: a histologic, immunohistochemical and ultrastructural study of three cases. *J Cutan Pathol* 2000;**27**:529–34.
- Weeks DA, Beckwith JB, Mierau GW. Rhabdoid tumor: an entity or a phenotype? *Arch Pathol Lab Med* 1989;**113**:113–14.

ECHO

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Markers to distinguish between benign and malignant conjunctival lesions

The immunophenotypic marker S100A1 could be a possible candidate to differentiate conjunctival naevi from conjunctival melanoma, while S100B seems to differentiate between uveal melanoma and conjunctival melanoma, according to a new study. However the authors warn that the study size was small and that the data need to be confirmed by others.

Clinically, the distinction between the most common melanocytic lesions of the conjunctiva including conjunctival naevus, primary acquired melanosis (PAM), and conjunctival melanoma may be difficult. In case of doubt histological investigation is required.

Immunophenotypic markers such as calcium binding proteins like S100 have been implicated in establishing the malignant and metastatic phenotype of various tumours. The S100 protein family consists of over 20 members. The authors investigated the potential usefulness of S100A1, S100A6, S100B, MelanA, and CEA in assessing the pathological differential diagnosis of conjunctival naevi, PAM, conjunctival melanoma, and uveal melanoma.

Paraffin embedded sections of 18 conjunctival naevi, 14 PAM, 16 conjunctival melanomas, and 20 uveal melanomas were immunostained for S100A1, S100A6, S100B, MelanA, and CEA. The survey found that expression of S100A1 differed significantly between conjunctival naevi and conjunctival melanoma, with percentages of positive cells of 30.6% and 71.4%, respectively.

Conjunctival melanomas had high average scores for S100A1 and S100B (71.4%, 62.9% respectively), while uveal melanomas also had high S100A1 but low S100B scores (88.5% and 18.5% respectively). MelanA was highly variable; naevi and uveal melanoma had higher average scores than conjunctival melanoma. CEA was hardly detectable in all four groups.

▲ Keijser S, et al. *British Journal of Ophthalmology* 2006;**90**:213–217