Melanomas in renal transplant recipients: the London experience, and invitation to participate in a European study*

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SIR, In response to the report of Le Mire *et al.*[1] on the incidence of malignant melanoma in Oxford renal transplant recipients (RTRs), we detail our experience of melanoma in a series of RTRs at Bart's and the London NHS Trust. Although incidence rates in our population were similar to those documented in the Oxford study, metastatic disease was more common, and we suspect that RTRs with melanoma may have a worse prognosis than their immunocompetent counterparts, although larger, multicentre studies are now required to confirm this.

A retrospective clinical and histological review of melanomas diagnosed in patients attending a dedicated RTR dermatology clinic between 1990 and 2005 was performed. All specimens were resectioned and were assessed by an experienced dermatopathologist (R.C.). In a total population of 861 RTRs with a follow-up period of 8557 patient-years, there were seven cases of *de novo* melanoma (five invasive and two *in situ*) in three men and four women. All diagnoses were made in the RTR dermatology clinic. Clinicopathological data are presented in Table 1 and are illustrated in Figure 1. All patients were on prednisolone and azathioprine, with or without ciclosporin. The mean age at diagnosis was older than in Oxford [57·7 years (range 44–68) vs. 41] and the mean time from transplantation was shorter [102 months (range 10–247) vs. 132]. All patients had skin types I–III (although 20% of our RTR cohort have skin type V or VI). None had a family history of melanoma or fulfilled criteria for atypical mole syndrome, although two patients had several atypical naevi. A high proportion of patients had a history of other invasive skin tumours (five of seven vs. four of 10 in Oxford); in all but one patient (patient 1) these tumours arose prior to the diagnosis of melanoma. Melanomas were more commonly located on the head and neck in our series, with four of seven tumours occurring at this site, in contrast to the Oxford tumours which all occurred at extracephalic sites. Ten of 12 tumours in the Oxford series were superficial spreading melanomas, whereas this subtype accounted for two of our seven cases. As in the Oxford series, Breslow thickness in the majority of cases (five of seven) was < 1 mm, and an inflammatory response was either minimal or absent in all melanomas, as has previously been documented.[2] A contiguous pre-existing naevus was present in only one case, and, similarly, was detected in only a minority (three of 12) of the Oxford cases, in contrast to a previous proposal that over half of all transplant melanomas arise in pre-existing naevi.[2] All melanomas in our series were treated by complete surgical excision; sentinel lymph node biopsy was not

Table 1 Clinicopathological data

Patient no., sex/age at diagnosis (years)	Time since transplant (months)	IS drugs	Other invasive skin cancers	Skin phototype/ atypical naevi	Histological type	Site	Breslow thickness (mm)/Clark level	Ulceration	AJCC stage	Inflammatory infiltrate	Origin in naevus (on histology)	Duration of follow up (months)	Outcome
1. F/44	94	P, A	BCC × 1	N/A	SSM	Leg	0·25/II	No	IA	None	No	144	No recurrence
2. F/68	10	P, A, C	BCC × 2	I/no	LM	Cheek	*In situ*/I	No	0	None	No	24	No recurrence; died of IHD
3. M/60	180	P, A	SCC × 4 BCC × 7	III/no	NM	Back	4·7/IV	No	IIB	Minimal	No	25	Died of metastatic melanoma
4. M/58	114	P, A	No	III/yes	NM	Jaw	2·2/IV	Yes	IIB	Minimal	No	23	Died of metastatic melanoma
5. M/65	48	P, A, C	SCC × 13	II/no	SSM	Cheek	0·4/II	No	IA	Minimal	Yes	69	No recurrence; died of NHL
6. F/52	23	P, A, C	No	I/no	LMM	Nose	0·4/II	No	IA	Minimal	No	54	Died of metastatic melanoma
7. F/57	247	P, A, C	SCC × 4 CIS × 7 BCC × 2	III/yes	LM	Chest	*In situ*/I	No	0	Minimal	No	29	No recurrence

A, azathioprine; AJCC, American Joint Committee on Cancer; BCC, basal cell carcinoma; C, ciclosporin; CIS, squamous cell carcinoma *in situ* (Bowen's disease); IHD, ischaemic heart disease; IS, immunosuppressive; LM, lentigo maligna; LMM, lentigo maligna melanoma; N/A, not available; NHL, Non-Hodgkin lymphoma; NM, nodular melanoma; P, prednisolone; SCC, squamous cell carcinoma; SSM, superficial spreading malignant melanoma.

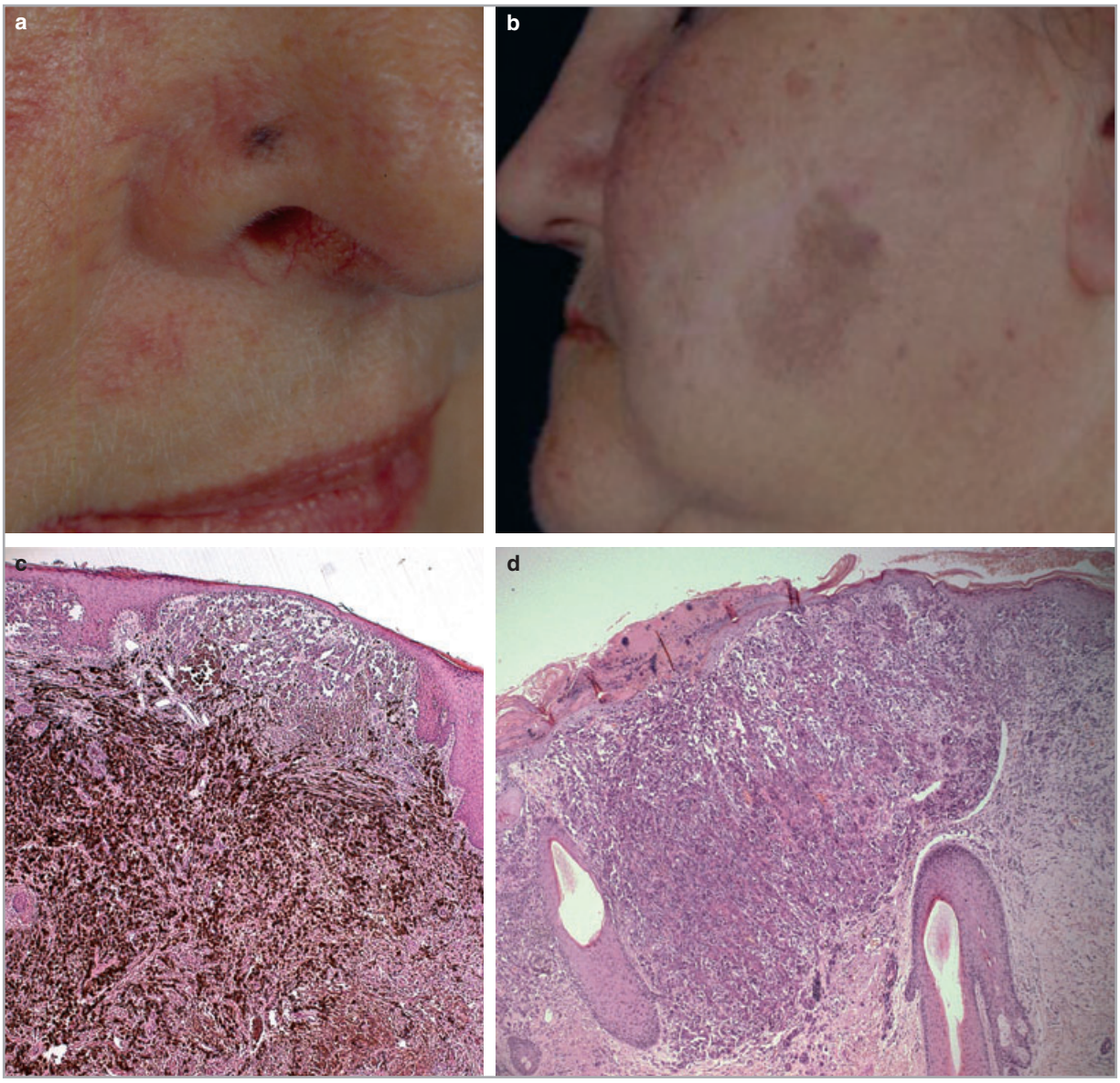

Fig 1. Clinical and histological examples of melanoma in renal transplant recipients. (a) Patient 6: lentigo maligna melanoma on right side of nose, Breslow thickness 0·4 mm. (b) Patient 2: lentigo maligna on cheek. (c) Photomicrograph of histology, patient 3: nodular melanoma in vertical growth phase, Breslow thickness 4·7 mm. (d) Photomicrograph of histology, patient 4: ulcerated nodular melanoma in vertical growth phase, Breslow thickness 2·2 mm.

available at the time these tumours were diagnosed. In most cases immunosuppression was reduced, but not stopped.

This series represents an elevated incidence of melanoma in our London RTR cohort: the rate in 2003 for the general population in North East Thames was 6·5 and 8·1 per 100 000 population for men and women, respectively, and we would therefore have expected approximately 0·9 cases of melanoma to have arisen in our cohort (in which 64% are male). If *in situ* tumours are included, these 7 cases represent an approximately 7·8-fold increased incidence compared with the general population. This is remarkably similar to the eight-fold increased rate found in Oxford, and is of the same order as that reported by Moloney *et al.*[3] who reported a 6·6-fold increase in males with melanoma in an Irish transplant population. These more recent studies report rates higher than previous estimates.[4–6]

Three patients in our series, but only one patient in Oxford, died from metastatic melanoma. Two deaths occurred in RTRs with melanomas exceeding 2 mm Breslow thickness. In accordance with American Joint Committee on Cancer staging, the predicted 5-year survival for patient 3 was 67% and that for patient 4 was 63%,[7] yet both died within approximately 2 years. Even more unexpectedly, patient 6 developed metastases from a lentigo maligna melanoma of Breslow thickness 0·4 mm, for which the expected 5-year survival is 95% or greater. Our series of patients is

too small to give statistical confirmation of a poorer prognosis in RTRs and previous studies have also not had sufficient power to examine this, although a compromised outcome from melanoma has similarly been observed in individuals with human immunodeficiency virus infection or AIDS.[8]

The incidence of melanoma is rising faster than for any other major cancer and will continue to do so over at least the next 30 years.[9] In conjunction with the steadily improving long-term survival from organ transplantation, it is likely that post-transplant melanoma will emerge as an increasing clinical problem in coming years. Many important questions have yet to be answered in this respect: whether prognosis is, indeed, worse for post-transplant melanoma, whether more aggressive management strategies are therefore required, and how reduction in immunosuppression should be approached. Although consensus statements such as those recently reported in this Journal are a useful guideline to management of post-transplant skin cancer,[10] a firmer evidence base is now required. This is a particular priority for management of post-transplant melanoma, and sufficient power to reach meaningful conclusions is only likely to be achieved in the context of a multicentre study. Such a study is currently being coordinated within the SCOPE network (Skin Care in Organ transplant Patients, Europe: http://www.scopnetwork.org) by our centre, and we invite clinicians who are interested in participating to contact us.

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Conflicts of interest: none declared.

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Melanomas in renal transplant recipients: the London experience, and invitation to participate in a European study: reply from authors

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Sir, We are pleased that our previous results showing an eightfold increased risk of melanoma in renal transplant recipients (RTRs)[1] is supported and confirmed by the study from London. However, we have re-examined the incidence in our cohort because these two reports included melanoma *in situ*, which has a different prognosis and management from invasive melanoma and could give a higher incidence ratio compared with other centres that excluded *in situ* melanoma. Moreover, since 2002 we have had further new cases of melanoma in RTRs in Oxford, including recently a case of invasive melanoma in an Asian patient, indicating that immunosuppression may be an independent pathogenetic mechanism for melanoma.

All new cases of invasive melanoma that occurred after 2002 in organ transplant recipients at the Oxford Transplant Centre were added to our previous data and cases of *in situ* melanoma were excluded. Data were taken from the Oxford Transplant Centre Clinical Database, on which all information on organ transplant patients and graft outcome are entered prospectively. We estimated the incidence of melanoma among patients who underwent organ transplantation between May 1964 and March 2006. Standardized incidence ratios (SIRs) were calculated by dividing the observed

