SHORT COMMUNICATION

Dermoscopic Features of Melanomas in Organ Transplant Recipients

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Melanomas are highly immunogenic tumours, and a well-orchestrated immune response is important for melanoma control (1). In order to avoid the rejection of a transplanted organ, lifelong immunosuppressive treatment is instrumental for organ transplant recipients (OTRs). In a systematic meta-analysis including 12 studies, a 2.4-fold (95% confidence interval (95% CI) 2.0–2.9) risk increase for melanoma in OTRs was observed compared with the general population (2).

Although OTRs have an enhanced relative risk of melanoma, their occurrence in absolute terms is remarkably rare. To exemplify this, in a Swedish nationwide retrospective cohort study, including 10,476 OTRs in the time period 1970–2008, only 52 malignant melanomas were diagnosed in 51 patients, standardized incidence ratio (SIR) 2.2 (95% CI 1.7–2.9) (3). In a retrospective Norwegian investigation, including 2,561 heart and kidney transplant recipients (15,123 person-years), 12 cases of melanoma were observed when only 3.56 were expected (SIR 3.4; 95% CI 1.7–5.9) (4). In another retrospective Swedish investigation, no more than 49 cases among OTRs were observed in the time period 1984–2008. Importantly, the melanomas in the OTR group had more advanced disease at diagnosis and an increased melanoma-specific mortality (5). Thus, diagnosing melanomas in OTR at an early stage is essential.

Dermoscopy is a valuable tool for assessing pigmented skin lesions and can improve the early detection of melanomas compared with the naked eye (6). Little is known about the dermoscopic criteria of melanomas arising in OTRs. The following retrospective study was performed as an exploratory investigation, in order to evaluate whether melanomas in this patient group demonstrate a different set of dermoscopic characteristics compared with melanomas in age- and sex-matched individuals.

METHODS

At our department, all OTRs are followed regularly or have open access to contact the clinic for a new scheduled visit. From January 2007 to June 2018, all individuals with an ICD-10 code of C43* (melanoma) and/or D03* (*in situ* melanoma) and/or Z08.9C (follow-up after melanoma) were sought out. The list was matched to a corresponding register of individuals with a post-transplantation ICD-10 code (Z94*) and non-transplanted individuals. The regional ethics review board in Gothenburg approved the study (approval number 283-18).

Eligible patient medical records were inspected and only patients with an available dermoscopic image were selected. Data on which organ(s) were transplanted, as well as the year of the first organ transplant, were noted. When available, clinical images were obtained and were cropped in order not to unblind the observer for a transplant surgery procedure. All cutaneous lesions sent for analysis from our clinic are examined exclusively by dermatopathologists, and all pathological reports, including subtype and characteristics of the melanomas, were obtained. Dermoscopic and clinical images were presented to 2 dermatologists for review. The clinicians were blinded and worked independently. In order to minimize errors in reliability between the 2 observers, the same computer set-up was used with standardized monitor and light settings. They were provided with a worksheet on which they could report the presence of features according to the most recent dermoscopic model presented by the International Dermoscopy Society (7). All dermoscopic images evaluated in this study, including the histopathological diagnosis, are available in Appendix S1[1]. Moreover, all individual responses for each case are presented in Table SI[1]).

All data were analysed using R version 3.0.3 (The R foundation for Statistical Computing, Vienna, Austria). Fisher's exact test was used for 2-sample tests. Cohen's kappa (κ) was used for interobserver agreement regarding the assessment of each dermoscopic feature. When comparing groups of features, for example melanoma-specific structures (11 in total), all the observations of all the different features were treated as a single list of observations and compared between the observers. The interobserver agreement was interpreted as poor (≤0), slight (>0 to 0.20), fair (>0.2 to 0.4), moderate (>0.4 to 0.6), substantial (>0.6 to 0.8) and almost perfect (>0.8). All tests were 2-sided and $p < 0.05$ was considered as statistically significant.

RESULTS

In the OTR group, 3 invasive melanomas and 6 *in situ* melanomas were identified in 8 male patients (age range at melanoma diagnosis: 47–74 years). The median time from first organ transplant to melanoma diagnosis was 11 years (range: 1–40 years). Seven OTRs had received kidney transplants, including one who had also received a pancreas transplant, and one patient was a lung transplant recipient. The control group included 24 invasive melanomas and 16 *in situ* melanomas in 34 male patients (age range at melanoma diagnosis: 46–75 years). In the OTR group, 33% (3/9) of melanomas were invasive and, in the control group, the corresponding number was 60% (24/40) ($p = 0.27$). Among all cases, 43% were on the trunk, 15% on the head and neck, 15% on the upper extremities and 8% on the lower extremities. There was no significant difference in the distribution of localization between the

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OTR group and the controls. Among the OTRs, 5 out of 9 melanomas were histologically associated with a melanocytic naevus. The corresponding number among the controls were 13 out of 40 ($p = 0.27$).

For the first observer, the presence of atypical blotches was more prevalent in OTRs compared with controls ($p = 0.029$). Nevertheless, no melanoma-specific structures were more prevalent in the OTR group than in the control group for any of the features when using Bonferroni correction for multiple comparisons. This also applied to regression structures and atypical vascular patterns. Moreover, facial melanomas in both groups displayed the same features. The 3 most common dermoscopic criteria detected among both observers were atypical network, atypical dots and globules and blue-white structureless area (Table SII[1]).

Among melanoma-specific structures there was a moderate interobserver agreement; κ=0.54 (95% CI 0.44–0.63). Regression structures and atypical vascular patterns had fair to moderate interobserver agreement; κ=0.44 (95% CI 0.24–0.64) and κ=0.45 (95% CI 0.28–0.62), respectively. Interestingly, although facial lesions only represented a few cases, there was substantial interobserver agreement (Table SIII[1]).

DISCUSSION

To the best of our knowledge, this is the first publication that specifically addresses the dermoscopic criteria for melanomas arising in OTRs. Differences in dermoscopic features between OTRs and controls could hypothetically be explained by an ineffective immuno-surveillance against melanocytic naevi and melanomas, which potentially might influence findings such as regression or inflammation. Alaibac et al. (8) presented a case-series of 10 renal transplant patients (age 19.4 ± 7.4 years at transplantation) who all developed eruptive melanocytic naevi shortly after transplantation and onset of systemic immunosuppression. Interestingly, most of these new naevi had a presence of a peripheral rim of globules, while this feature was not observed in pre-existing naevi. Koseoglu et al. (9) performed a case-control investigation comparing a cohort of patients with systemic immunosuppressive treatment (266 melanocytic naevi in 103 patients) with healthy controls (180 lesions in 60 patients). Interestingly, naevi among the immunosuppressed patients displayed statistically significant dermoscopic changes compared with controls. Notably, the 2 publications above only presented small selections of the dermoscopic images analysed.

Needless to say, in order to draw more generalizable conclusions in this patient group, we welcome further research with larger data-sets.

This investigation has limitations, including a small data-set and the retrospective design. Even though all lesions were analysed by a dermatopathologist, a re-examination of all pathological reports by an expert panel of dermatopathologists could perhaps have improved the validity of the results. Only melanomas with an available dermoscopic image were included, possibly precluding subtler and clinically difficult-to-assess melanomas. Although more *in situ* melanomas could have been detected in the OTR group due to surveillance bias brought on by access to regular follow-up visits, this was not observed. Moreover, as this investigation included patients over a time period of over 10 years, different camera set-ups were used and the image quality varied. The present retrospective study exclusively included patients with Caucasian skin types. Therefore, it is not excluded that melanomas in OTRs with other skin types might display a different set of dermoscopic features. One important strength of this investigation is that all data analysed are shared and available to all readers. To increase scientific transparency, we encourage researchers to share their dermoscopic images and, ideally, present them as e-supplements. Whenever an image is properly anonymized and demonstrates an unequivocal and validated diagnosis, we promote image sharing, as it can be used conveniently for machine learning and development of artificial intelligence.

In this retrospective investigation, there was no indication of a different distribution of dermoscopic features in melanomas in OTRs compared with non-OTRs. These results can be reassuring for physicians, in particular dermatologists monitoring OTRs.

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