Cutaneous malignant melanoma in the Swedish organ transplantation cohort: A study of clinicopathological characteristics and mortality

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Background: Risk of cutaneous melanoma is increased among organ transplant recipients (OTRs) but outcome has rarely been evaluated.

Objective: We sought to assess melanoma characteristics and prognosis among OTRs versus the general population.

Methods: Using Swedish health care registers, we identified melanomas in OTRs (n = 49) and in the general population (n = 22,496), given a diagnosis between 1984 and 2008 and followed up through December 31, 2012. Tumor slides of posttransplantation melanomas were reviewed. Odds ratios for comparison of histopathological characteristics and hazard ratios of melanoma-specific death were calculated.

Results: Among OTRs the trunk was the most common anatomic melanoma site (50% among female vs 51% among male) and 73% (n = 36) of all melanomas were histologically associated with a melanocytic nevus, 63% (n = 31) atypical/dysplastic. Compared with population melanomas, posttransplantation melanomas were more advanced at diagnosis (Clark level III-V: odds ratio 2.2 [95% confidence interval 1.01-4.7, P = .03], clinical stages III-IV: odds ratio 4.2 [1.6-10.8, P = .003]). Risk of melanoma-specific death was increased among OTRs: adjusted hazard ratio 3.0 (1.7-5.3, P = .0002).

Limitations: Only posttransplantation melanoma slides were reviewed.

Conclusions: Melanomas were more advanced at diagnosis and melanoma-specific survival was poorer in OTRs than in the general population. Prophylactic excision of truncal nevi among OTRs may be advised. (J Am Acad Dermatol 2015;73:106-13.)

Key words: histopathology; immunosuppression; melanocytic nevi; melanoma; melanoma-specific mortality; population-based study; posttransplantation; Swedish Melanoma Register.

Risk of posttransplantation cutaneous malignant melanoma is approximately 2- to 3-fold increased compared with the general population,[1] with a higher risk reported in male compared with female organ transplant recipients (OTRs).[2-4] A few studies have also indicated a worse outcome than for melanomas in the general population.[5-8]

Histologically, the superficial spreading melanoma (SSM) subtype and association with a preexisting melanocytic nevus, ie, atypical/dysplastic

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or ordinary/common, has been reported more frequently among OTRs.[9-11]

Poorer melanoma-specific survival was reported previously mainly in OTRs with thicker melanomas (2.01-4.0 mm[11] and 1.5-3.0 mm[12]), but recently also for pT1 melanomas.[7] Limitations of previous studies on melanoma-specific survival among OTRs include incompleteness of noncompulsory data registries,[6,12] a potential reporting bias because of voluntary reporting,[6,11,12] and comparison of survival/outcome data with a control population geographically different from the index cases.[11]

In this population-based study we assessed clinical and histopathological traits of all cutaneous posttransplantation melanomas diagnosed in Sweden between 1984 and 2008. Furthermore, we estimated melanoma-specific mortality among patients with posttransplantation melanomas compared with patients with melanoma in the general population between 1990 and 2008 using national register data.

CAPSULE SUMMARY

- Risk of posttransplantation melanoma is 2- to 3-fold increased versus the general population.
- Truncal localization and histologic association with a nevus were common among posttransplantation melanomas and risk of melanoma-specific death was increased.
- Transplant recipients should be monitored for melanoma incidence and recurrence. Prophylactic excision of truncal nevi should be considered.

METHODS

Organ transplant recipients

The index cohort comprised 51 OTRs with 52 invasive melanomas, who had undergone transplantation from 1970 to 2008 and given a diagnosis of melanoma from 1984 to 2008. They were extracted from a cohort of 10,476 OTRs recently analyzed for overall cancer risks.[3] In Sweden, the health care system, including organ transplantation care, is tax funded and open to all residents, regardless of socioeconomic background. Briefly, we used the Swedish National Patient Register to identify OTRs through surgical procedure codes for solid organ transplantation. The occurrence of cancer (primary cutaneous melanoma *International Statistical Classification of Diseases, Seventh Revision* code 190) was ascertained through linkage with the compulsory Swedish Cancer Register using the unique Swedish person identity number.[13] One patient developed 2 melanomas; only the first melanoma contracted by this patient was included in the study and follow-up was censored at the date of diagnosis of the second melanoma. Two melanomas were relapses and therefore excluded. In all, 49 patients with 49 melanomas remained for further analyses.

Swedish Melanoma Register and general population

Since 1990, clinical data (eg, date of diagnosis, tumor localization) and histopathological parameters (eg, millimeter thickness, Clark level, ulceration, tumor type) of invasive melanomas have been assembled nationally in the Swedish Melanoma Register[14] according to the 2001 guidelines of the American Joint Committee on Cancer (AJCC).[15] The completeness is about 97%.[14,16] The Swedish Melanoma Register is regularly updated against the National Cause-of-Death Register (*International Statistical Classification of Diseases, 10th Revision*).[17]

From the Swedish Melanoma Register, we identified all patients given a diagnosis of melanoma between 1990 and 2007 (n = 27,235). Individuals younger than 27 years and older than 79 years at melanoma diagnosis (n = 4584), which were the minimum and maximum ages at melanoma diagnosis among OTRs, were excluded, as were patients given a diagnosis at autopsy (n = 116). Thirty-nine OTRs were identified in the Swedish Melanoma Register and were excluded from the comparison group, resulting in a final population comparison cohort of 22,496 patients with melanoma.

Histopathologic re-examination

All slides of the 49 posttransplantation melanomas were reviewed according to the established criteria of the melanoma classification of the AJCC,[15,18] eg, Breslow thickness, Clark level, ulceration status, mitoses in the infiltrative component, and presence of marked regression. Melanomas that did not fit into any of the 4 main categories,[19] eg, SSM, lentigo maligna melanoma, nodular melanoma, or acral lentiginous melanoma, were named "other"; these were further subclassified either as lentiginous/nested subtype[20,21] or primary melanoma not otherwise specified. The presence or absence of an adjacent melanocytic nevus, either atypical/dysplastic or ordinary/common, was noted.[19] Tumor-infiltrating lymphocytes (TILs), ie, pattern of lymphocytes infiltrating among tumor cells, were semiquantitatively graded as absent, sparse, or abundant.[22]