Other primary systemic cancers in patients with melanoma: Analysis of balanced acral and nonacral melanomas

Soo Hyeon Bae, MD,[a] Hyun Ju Seon, MD, PhD,[b] Yoo Duk Choi, MD, PhD,[c] Hyun-Jeong Shim, MD, PhD,[d] Jee-Bum Lee, MD, PhD,[a] and Sook Jung Yun, MD, PhD[a]
Gwangju, Korea

Background: Although other primary systemic cancers in patients with melanoma have been studied, there have been few focusing on acral melanomas.

Objectives: We assessed other primary systemic cancers in patients with acral and nonacral melanomas.

Methods: We analyzed other primary cancers in 452 patients with melanoma from 1994 to 2013. Metachronous cancers were defined as those given a diagnosis more than 2 months after diagnosis of melanoma. The others were considered prechronous or synchronous cancers.

Results: Among 51 cases of other primary cancers, gastrointestinal cancer (35.3%, n = 18/51) was the most common, followed by thyroid (17.6%), lung (11.8%), and breast (5.9%). Those were more prevalent in the acral melanoma group (12.8%, n = 31/243) compared with the nonacral melanoma group (9.6%, n = 20/209). Of 23 cases of metachronous cancer, the risk was the highest in bone marrow, followed by oral cavity, bladder, colon, lung, and thyroid. Among 28 cases of prechronous or synchronous cancers, gastrointestinal tract (35.7%, n = 10/28) was the most common site, followed by thyroid (17.9%), breast (10.7%), and lung (7.1%).

Limitations: The study is limited by a small number of patients.

Conclusion: Careful follow-up and imaging studies are necessary for early detection of other primary cancers and metastatic lesions in patients with melanoma. (J Am Acad Dermatol 2016;74:333-40.)

Key words: acral melanoma; metachronous cancer; nonacral melanoma; other primary systemic cancer; prechronous or synchronous.

Melanoma is associated with the highest fatality rate among skin cancers. Unfortunately, several studies have shown an extra susceptibility for other primary systemic cancers in patients with melanoma, which also increase mortality and reduces the overall life quality of patients.[1-3] Crocetti and Carli[4] showed an increased

Abbreviations used:

ALM:	acral lentiginous melanoma
CI:	confidence interval
NMSC:	nonmelanoma skin cancer
SIR:	standardized incidence ratio
SSM:	superficial spreading melanoma

From the Departments of Dermatology,[a] Radiology,[b] Pathology,[c] and Oncology,[d] Chonnam National University Medical School.
Drs Soo Hyeon Bae and Hyun Ju Seon contributed equally to all aspects of this article.
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Reprint requests: Sook Jung Yun, MD, PhD, Department of Dermatology, Chonnam National University Medical School, 160 Baekseo-ro, Dong-gu, Gwangju 501-746, Korea (South). E-mail: sjyun@chonnam.ac.kr.
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risk of second primary cancers in patients with melanoma, especially in those aged 60 years or younger. Several studies have reported the prevalence of specific cancers in patients with melanoma: non-Hodgkin lymphoma,[1] chronic lymphocytic leukemia,[5] female breast,[1,6] ovary,[6] endometrium,[7] testis,[8] prostate,[1] kidney,[9] bladder,[10] brain,[11] and colon.[7]

Acral melanomas, which involve the acral sites such as palm, sole, and subungual areas, are common in Asian countries, comprising up to 71.4% of all patients with melanoma.[12-14] In Caucasians, on the other hand, nonacral melanoma—primarily, superficial spreading melanoma (SSM)—is the prevalent type.[15] Interestingly, Asian Americans who share the same environmental background with non-Hispanic white Americans nevertheless showed different anatomical sites, subtypes, and stages of melanoma.[16] Also, it was suggested that the development of cancer can differ among each subtype of melanoma. Nagore et al[17] revealed a strong relation between acral lentiginous melanoma (ALM) and personal/familial nonskin cancer history, as compared with other subtypes, which suggests a different genetic and/or environmental cause relative to different melanoma subtypes.

CAPSULE SUMMARY

- Other primary systemic cancers occurred in patients with acral and nonacral melanomas.
- Gastrointestinal cancer was the most frequent other primary systemic cancer combined with melanoma, followed by thyroid, lung, and breast. Those cancers were more prevalent in the acral melanoma group than in the nonacral melanoma group.
- Careful follow-up examinations and imaging studies are necessary for early detection of other primary systemic cancers and metastatic lesions to improve survival in patients with melanomas.

The first aim of this study was to evaluate an association of melanoma with other primary systemic cancers, diagnosed both before and after melanoma, in patients with melanoma. Although previous reports only focused on the risk of second primary cancers (diagnosed after melanoma) in patients with melanoma,[1,2,4,7] we analyzed the whole history of other primary cancers in patients with melanoma. We reasoned that the genetic and/or environmental cause shared in both melanoma and nonmelanoma cancers should be emphasized. Also, the temporal ordering between melanoma and nonmelanoma cancer can be questionable because delayed diagnosis of melanoma in clinical fields is frequent, especially in the case of acral melanomas.[18,19] Secondly, we sought to examine the pattern of other primary cancers between patients with acral and nonacral melanoma. Most previous studies focused on nonacral melanoma rather than acral melanoma.[15] In this study, however, the prevalence of both acral and nonacral melanoma was similar (53.8% and 46.3%, respectively). We think that comparing both types of melanoma with a balanced number of patients within the same ethnicity allows for a more precise analysis of clinicopathologic and etiologic features. This study not only represents the overall risk of other primary cancers in patients with melanoma, but also a balanced analysis between acral and nonacral melanoma.

METHODS

Patients

A total of 468 patients with melanoma were identified from Chonnam National University Hospital, Gwangju and Chonnam National University Hwasun Hospital, Hwasun, in Korea (between January 1, 1994, and December 31, 2013). The medical records and histopathological reports, including demographics, clinical presentation, histologic features, and follow-up data, were systematically reviewed. The histologic subtypes of melanoma are as follows: ALM, SSM, nodular melanoma, lentigo maligna melanoma, and mucosal melanoma. Otherwise, 13 patients with unclassified melanomas or less frequent variants (eg, desmoplastic) and 3 non-Korean patients were excluded. The patients were divided into acral and nonacral groups, to evaluate the influence of melanoma location on the development of nonmelanoma primary cancers. The institutional review boards of the hospitals approved this retrospective study.

Other primary systemic cancer

The data for other primary systemic cancers were obtained from Gwangju-Jeonnam Cancer Registry and clinicohistopathological diagnoses made in the pathology department of above hospitals (until December 31, 2013). Histopathological diagnosis of primary cancer was confirmed by excluding the probability that one is a metastatic lesion originating from the other. To avoid potential selection bias, metachronous (second or tertiary) primary cancer was defined as those cancers diagnosed more than 2 months apart after diagnosis of melanoma.[4] In our study, second primary melanomas[4] and nonmelanoma skin cancer (NMSC) were excluded. The others were considered prechronous or