Clinicopathologic features and survival in Spitzoid malignant melanoma and conventional malignant melanoma

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Background: Although recent advances in genetics have revealed distinct mutational profiles and molecular signaling pathways associated with Spitzoid malignant melanoma (SMM), less is known about the clinicopathologic characteristics and behavior of SMM compared with conventional melanoma.

Objective: We sought to determine the clinicopathologic characteristics and mortality risk associated with SMM and conventional malignant melanoma.

Methods: We conducted a retrospective study of 30 patients with SMM and 30 patients with conventional melanoma. The two groups were matched by age, gender, and depth of tumor invasion. Additional patient- and tumor-level characteristics were compared between groups and regression modeling was used to assess relative mortality risk.

Results: Unadjusted analyses of SMM and conventional malignant melanoma revealed no significant differences in clinical impression, anatomic location, mitotic rate, and presence of ulceration. Sentinel lymph node biopsy, completion lymphadenectomy, and visceral metastases did not differ between groups. Cox proportional hazards regression showed no differences in mortality between Spitzoid and conventional melanoma.

Limitations: Small sample size, short follow-up duration, and residual confounding may limit the accuracy and generalizability of our results.

Conclusions: SMM and conventional malignant melanoma differ in some clinicopathologic features. We did not find a statistically significant difference in mortality between the two. (J Am Acad Dermatol 2014;71:516-20.)

Key words: conventional melanoma; melanoma; metastasis; prognosis; sentinel lymph node; sentinel lymph node biopsy; Spitzoid malignant melanoma; survival.

Recent molecular discoveries in the field of malignant melanocytic neoplasms provide growing evidence that the various types of cutaneous melanomas comprise biologically distinct subtypes, which may arise via different causal pathways. Understanding melanoma heterogeneity and the respective biologic behavior of each subtype is indispensable

Abbreviations used:

BRAF:	v-raf murine sarcoma viral oncogene homolog B
CMM:	conventional malignant melanoma
HRAS:	Harvey rat sarcoma viral oncogene homolog
NRAS:	neuroblastoma RAS viral (v-ras) oncogene homolog
SMM:	Spitzoid malignant melanoma

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in establishing precise diagnostic criteria and prognostic guidance.

Spitzoid malignant melanoma (SMM) is a bona-fide malignant tumor that bears histologic resemblance to Spitz nevus. SMM is seen in both children and adults, although it is more common after puberty, and its prognosis is dependent on age.[1] Recent studies have revealed genotypic differences between SMM and conventional malignant melanoma (CMM) resulting in distinct signaling pathways involved in the development of these tumors.[1] Few studies of the characteristics and behavior of SMM have been performed, mostly in small cohorts of patients, because of the rarity of this neoplasm.[2-4] Although SMM may be associated with lower mortality compared with CMM among pediatric patients,[2] less is known about the biologic behavior of SMM in adults.

CAPSULE SUMMARY

- Spitzoid malignant melanoma is a type of melanoma that resembles Spitz nevus histologically.
- This study compares the clinicopathologic characteristics and mortality risk associated with Spitzoid and conventional melanoma.
- Our study raised the possibility (without, however, firm confirmation), that Spitzoid melanoma may be less aggressive than conventional malignant melanoma.

We sought to compare the clinicopathologic characteristics and mortality associated with SMM and CMM in adults. Given known genetic differences distinguishing these tumors, we hypothesized that patients with SMM would be associated with a greater proportion of sentinel lymph node metastases compared with CMM, and that SMM would be associated with improved survival.

METHODS

We conducted a retrospective study of 30 patients diagnosed with SMM and 30 patients with CMM matched by age (±3 years), gender, and Breslow thickness (±0.3 mm). We compared clinicopathologic characteristics and survival between these groups. Cases of SMM were retrieved from the Yale Spitzoid Neoplasm Repository and reviewed by a consensus group (up to 8 dermatopathologists) at Yale Dermatopathology Laboratory. Only cases with an unequivocal consensus diagnosis of SMM were included in the study. SMM was defined as a melanoma, which resembles Spitz nevus and is composed of large epithelioid melanocytes. Most cases in the current study were also analyzed by mass spectrometry, a recently described method of proteomic analysis of melanocytic lesions, and all of these cases classified as Spitzoid melanomas.[5] CMM and SMM involving acral sites, mucous membranes, or the nail apparatus were excluded.

Patient-level characteristics of interest included personal history of melanoma, personal history of other malignancies, number of years of clinical follow-up, and mortality outcome (categorized as "alive with no evidence of disease," "alive with evidence of disease," or "dead of disease"). Tumor-level characteristics of interest included anatomic location of tumor (categorized as "head and neck," "trunk," "upper extremity," and "lower extremity"), clinical impression, number of mitoses per square millimeter, presence or absence of ulceration, presence or absence of solar elastosis, presence or absence of visceral metastases (categorized as "none," "1 organ," or ">1 organ"), sentinel lymph node biopsy status (categorized as "negative," "positive," or "not performed"), and completion lymphadenectomy status (categorized as "negative," "positive," or "not performed").

We performed unadjusted, bivariate comparisons of each patient- and tumor-level characteristic between SMM and CMM groups using the Student *t* test, Fisher exact test, or the binomial test for proportions as appropriate. We assessed unadjusted differences in mortality risk by calculating Kaplan-Meier survival curves stratified by SMM versus CMM and unadjusted estimated median survival time across select covariates of interest for all patients. We then performed Cox proportional hazards regression to obtain risk-adjusted estimates of survival by tumor type. Recognizing our small sample size, we chose a priori to examine the adjusted risk of mortality associated with the following covariates of interest: (1) anatomic location of interest (defined as above), and (2) evidence of any metastatic spread. We defined the latter categorical variable as "positive" for any patient with positive sentinel lymph node biopsy (when performed), positive completion lymphadenectomy (when performed), or positive visceral organ involvement. Likewise, any patient with negative visceral organ involvement, negative sentinel lymph node biopsy (when performed), and negative completion lymphadenectomy (when performed) was considered "negative" for evidence of metastatic spread. Those patients with negative visceral organ involvement who did not undergo