Combined cutaneous tumors with a melanoma component: A clinical, histologic, and molecular study

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Background: The histogenesis and clinical behavior of combined cutaneous tumors (CCTs) in which the mesenchymal component consists of melanoma remain unclear.

Objective: We sought to characterize the clinical, histologic, and molecular findings in CCTs with an epithelial and a melanoma component.

Methods: We retrospectively reviewed the records from 2 institutions for CCTs. Fluorescence in situ hybridization was performed to assess chromosomal copy number alterations in both components.

Results: Sixteen CCTs were included. The most common subtype was the squamomelanocytic tumor (11), followed by the basomelanocytic tumor (3) and the trichoblastomelanoma (2). CCTs were more common in men (87%), on the head and neck (57%), and had extensive solar elastosis (81%). The median follow-up was 25 months (range, 8-167 months). One case had an adverse outcome. Fluorescence in situ hybridization revealed chromosomal alterations in approximately 55% of the cases. Five cases showed chromosomal gains only in the melanocytic component. One case showed 11q13 gains in both the epithelial and melanocytic components.

Limitations: Our study is retrospective and the sample is small.

Conclusions: The low incidence of adverse outcomes suggests that CCT may be more indolent than noncombined tumors. 11q13 amplification in both components supports the theory of dual differentiation from a common progenitor cell. (J Am Acad Dermatol 2015;73:451-60.)

Key words: basomelanocytic tumor; biphenotypia; combined tumor; fluorescence in situ hybridization; melanoma; squamomelanocytic tumor; trichoblastomelanoma.

The presence of epithelial and mesenchymal tumors in close proximity to one another on the skin has been referred to with a variety of terms, including combined, composite, collision, contiguous, biphenotypic, biphasic, and colonizing tumors.[1-5] Microscopically, one may observe the epithelial and mesenchymal tumors as 2 distinct tumors in close proximity to each other or with the 2 cell types intimately intermingled. Miteva et al[4] attempted to clarify the terminology by recommending

Abbreviations used:

BCC:	basal cell carcinoma
BMT:	basomelanocytic tumor
CCT:	combined cutaneous tumor
FISH:	fluorescence in situ hybridization
MART1:	melanoma antigen recognized by T cells 1
MITF:	microphthalmia transcription factor
PEH:	pseudoepitheliomatous hyperplasia
SCC:	squamous cell carcinoma
SMT:	squamomelanocytic tumor
TP53:	tumor protein 53

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the use of "combined tumors" for all tumors with biphasic or dual differentiation, and further subclassifying these tumors into 2 patterns: "collision" for those with obvious distinction of the 2 components and "intermingled" for those where the 2 components are intimately admixed.

Although overall a rare entity, dermal squamomelanocytic tumor (SMT), a term coined by Pool et al,[6] is among the most commonly occurring tumor in this category. A related entity, the basomelanocytic tumor (BMT), was first described in the 1980s[1,7-10]; as the name suggests, it is a tumor with basal cell and melanocytic phenotypes.[3,11] Trichoblastomelanoma is an even rarer entity and is composed of trichoblastoma intermingled with melanoma.[12,13]

In addition to questions of histogenesis, little is known regarding the biologic behavior of these entities, and some have proposed that the melanomas seen in these tumors have a better prognosis compared to similarly staged conventional melanomas.[14] To address these issues, we investigated a series of combined cutaneous tumors (CCTs) in which the epithelial and mesenchymal components were intimately intermingled and the mesenchymal component consists of a melanoma. In addition to morphologic and immunohistochemical assessment, fluorescence in situ hybridization (FISH) studies were conducted to assess for chromosomal copy number alterations in both tumor components, and long-term clinical follow-up was reviewed.

CAPSULE SUMMARY

- The histogenesis and clinical behavior of combined cutaneous tumors remain unclear.
- The epithelial and melanoma components of combined cutaneous tumors may arise from a common progenitor cell.
- Distant metastases are uncommon; therefore, combined cutaneous tumors may have a better prognosis when compared to similarly staged conventional melanomas.

METHODS

After obtaining approval from the institutional review board, we retrospectively reviewed the dermatopathology records from Northwestern University for cases of CCT in which the mesenchymal component consisted of melanoma. Between 2000 and 2014, 25 cases were retrieved. Eleven cases in which the epithelial and mesenchymal components were not intimately intermingled were excluded. For the remaining 14 cases, clinical information and follow-up data were obtained from the pathology reports and medical records, including sentinel lymph node biopsy (SLNB) results, the presence of metastatic disease, and any disease-related mortality. Two additional cases of trichoblastomelanoma were contributed from the files of the Département de Biopathologie at the Centre Léon Bérard. One of these cases (patient 16) has been previously published elsewhere.[13]

For each case, hematoxylin–eosin-stained sections and any available immunohistochemically stained slides were reviewed for diagnosis, histologic characteristics of the tumors, relationship between the lesions (intermingled tumor cells vs 2 adjacent tumors), and the presence of in situ components, pigmentation, or solar elastosis. Extensive solar elastosis was defined by broad brands of amorphous gray elastotic material in the dermis.

Immunohistochemical staining for p53 (clone DO-7, Ready-to-Use; Dako North America, Carpinteria, CA) was also performed (5 cases) on a Dako Autostainer Plus using a high pH retrieval and the EnVision Flex+ visualization system (Dako North America). The staining patterns were interpreted as follows: weak and patchy nuclear expression (wild-type TP53), strong and compact nuclear expression (mutant TP53), or absent (mutant [truncated] TP53).[15] When possible, FISH studies were performed (11/16 cases) as previously described.[16,17] Two separate hybridizations were performed: one using the 4-probe FISH assay targeting 6p25 (*RREB1*), 6q23 (*MYB*), Cep6, and 11q13 (*CCND1*), and a second using the 4-probe FISH assay targeting 6p25 (*RREB1*), 9p21 (*CDKN2A*), 11q13 (*CCND1*), and 8q24 (*MYC*). These 2 probe sets were selected because they have previously undergone validation studies and were found to have a high sensitivity and specificity in discriminating melanocytic nevi from melanomas (86.7% and 95.4% for the first assay; 94% and 98% for the second assay).[16,17] Criteria for FISH positivity were as previously published for each probe set.[16,17]

RESULTS

Sixteen cases of CCTs in which the mesenchymal component consisted of melanoma were included (Table I). The average patient age was 70.9 years (range, 46-87 years; Table II). The tumors were more common in men (87%), frequently involved the head and neck region (57%), and had extensive solar elastosis (81%). In 68.8% of cases, the epithelial component was squamous cell carcinoma (SCC; Fig 1), while basal cell carcinoma (BCC; Fig 2) was