



An 8-mm raised, blue-black nodule on an 11-year-old raised uncertainty among Stanford University specialists.

STANFORD UNIVERSITY DEPARTMENTS OF DERMATOLOGY AND PATHOLOGY AND THE MELANOMA CARE COALITION, PHARMADURA, LLC

## MELTUMP Lesions Often Perplexing

BY BETSY BATES  
Los Angeles Bureau

MONTEREY, CALIF. — Melanocytic tumors of unknown malignant potential represent some of the most difficult cases in pediatric dermatology, since little agreement exists about their diagnostic criteria, management, or outcome.

“They cause everyone, including pathologists, referring der-

matologists, and surgeons, to lose sleep,” said Dr. Susan Swetter, director of Stanford (Calif.) University’s pigmented lesion and cutaneous melanoma clinic, at the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

Dr. Swetter described the management of an 8-mm raised, blue-black nodule that appeared behind the right ear of an 11-year-old girl. Satellite blue-

black macules appeared on the periphery of the lesion.

A partial 5-mm punch biopsy was reviewed by pathologists at Stanford; the University of California, San Francisco; and Massachusetts General Hospital, Boston. The conclusion was that the lesion was a melanocytic tumor of unknown malignant potential (MELTUMP) with decidedly mixed signals: no ulceration but a relatively high mitotic rate (4/mm<sup>2</sup>) and probable angiolymphatic invasion.

Differential diagnoses included a pigmented epithelioid melanocytoma, an agminated Spitz nevus, or a “low-grade” melanoma. The patient underwent a “fairly intuitive” comprehensive work-up, including a thorough personal and family history, a review of the timing and speed of growth of the lesion, and a total body skin examination and physical examination, including palpation of regional lymph node basins to assess for metastasis.

Melanoma experts agree that MELTUMP lesions should be completely excised, but the specifics about recommended margins remain hazy, Dr. Swetter explained. Some experts would decide to perform a wide excision in such a case, perhaps including sentinel lymph node biopsy, as if they were treating a melanoma.

At Stanford, where the patient was seen, the decision was made to take a 1-cm margin, narrower than the 2-cm margin that would be appropriate for a 3.7-mm melanoma, and to await the pathology results before deciding whether to perform a sentinel lymph node biopsy or lymph node dissection.

The histology on the wide excision specimen showed that the lesion was symmetrical and well circumscribed with a polypoid proliferation of darkly pigmented melanocytes and a mitotic rate “well below 1/mm<sup>2</sup>.”

Dr. Swetter described the applicable histology images as revealing “deeply pigmented epithelial spindle cells and unmistakable angiolymphatic invasion.”

“Our pathologists thought this was most consistent with a melanocytoma diagnosis,” and noted its rarity as well as its “uncertain biological behavior,” said Dr. Swetter.

A comparative genomic hybridization study was ordered from the UCSF laboratory, but results were estimated to take 6-8 weeks, a period of time that could compromise afferent lymphatic drainage from a scalp lesion and reduce the accuracy of the sentinel node biopsy.

After extensive discussions with the child’s parents, the Stanford team elected to perform a sentinel lymph node biopsy but to await the outcome of the comparative genomic hybridization studies prior to performing complete lymph node dissection in the event that the sentinel node specimen was positive. A metastatic work-up with PET/CT scanning was performed “in part ... to allay some of the parental concern about metastatic disease.” Parenthetically, Dr. Swetter noted that such a scan would not generally be indicated in an asymptomatic patient with no signs of metastatic disease and would not preclude

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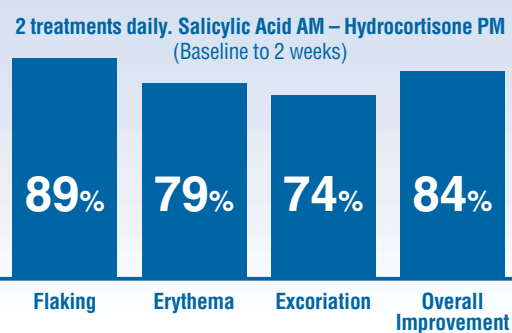
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## 'Rule of Threes' Guide Proposed

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risk for carrying the mutation, said Dr. Swetter.

Dermatologists already should be counseling a patient like this on prevention and the importance of early detection and should be in an active surveillance program for detection of a new or recurrent melanoma.

Recommendations currently being developed in part through GenoMEL (the Melanoma Genetics Consortium) and the Melanoma/Skin Cancer Committee of the American Academy of Dermatology suggest that patients with a melanoma history may be appropriate candidates for p16 genetic testing if they have multiple primary melanomas, family members with melanoma, or family members with pancreatic cancer or melanoma.

Researchers from Massachusetts General Hospital and the University of Utah

will soon present a proposal to the AAD's Melanoma/Skin Cancer Committee to establish even more specific criteria, based on the "Rule of Threes."

If that proposal is approved, dermatologists and other physicians would be advised to order screening in interested and appropriately counseled and consented patients only if they have had three confirmed melanomas in a family (any degree relative), three primary melanomas in an individual, or a two plus one pattern of

melanoma and pancreatic cancer in the family (two melanomas and one pancreatic cancer or two pancreatic cancers and one melanoma).

In her clinic, the most common question from patients is whether they should be tested based on their history of atypical moles or dysplastic nevi, said Dr. Swetter. "The reality is that the presence of clinically atypical or dysplastic nevi is not a marker for p16 mutation status."

Dr. Randall K. Roenigk, chair of the department of dermatology at the Mayo Clinic in Rochester, Minn., said that Dr. Swetter makes a worthwhile point. "We need to make intelligent decisions about

genetic testing, not just screen everyone because we're curious."

When patients do fit the personal or family history profile that suggests a p16 test may be justified, four clinical U.S. laboratories are available to perform the test. Some even will help patients obtain insurance approval.

These Clinical Laboratory Improvement Amendment-certified laboratories, listed at [www.genetests.org](http://www.genetests.org), include GeneDx Inc. in Gaithersburg, Md.; Myriad Genetic Laboratories Inc. in Salt Lake City; Yale University, New Haven, Conn.; and Creighton University Medical Center in Omaha, Neb. ■

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the possibility of a positive sentinel node biopsy. The scans were negative.

Two sentinel lymph nodes were identified and removed in the right cervical neck. One was positive for subcapsular and parenchymal metastatic foci of pigmented epithelioid melanocytoma and stained strongly positive for S100, MelanA, and HMB45.

Ironically, MELTUMP lesions have been associated with a very high rate of sentinel lymph node positivity in the two largest retrospective studies to date (44%-50%, compared with approximately 20% for typical melanomas with Breslow thickness greater than 1 mm).

However, the picture is confusing, because studies also associate atypical Spitz tumors with a very high survival rate despite apparent micrometastases.

In the case of Dr. Swetter's patient, a comparative genomic hybridization offered what appeared to be optimistic information, since the lesion contained aberrations on chromosome 11, a finding that has been exclusively associated with Spitz nevi in comparative studies with other benign nevi and melanomas. No complete lymph node dissection was performed and the patient has been followed for more than a year without evidence of recurrent disease.

Fatal outcomes have resulted in cases where several pathologists concurred with a diagnosis of Spitz nevus or atypical Spitzoid tumors, suggesting that these cases represented unrecognized melanoma, although this scenario does not appear to be the norm. The lesions should be completely excised, and treated similarly to melanomas when they are characterized by frank atypia or uncertain biologic behavior.

Until more information can be gathered from the national pediatric melanoma and melanocytic neoplasms database organized by Dr. Bruce Overbook at Case Western Reserve University in Cleveland, Dr. Swetter urged open and frank discussions among medical professionals and families about the diagnostic uncertainty regarding these lesions. ■



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