

Spitz Nevi Difficult to Categorize, Manage

BY SHERRY BOSCHERT

SAN FRANCISCO — Follow-up on 219 patients with Spitz nevi found that 7 (3%) developed malignant melanoma, and in each case the original biopsy showed an atypical or desmoplastic Spitz nevus.

The patients who developed melanoma also were older (aged 34-66 years) at the time the Spitz nevi were diagnosed, compared with patients who did not develop melanoma (whose Spitz nevi appeared predominantly between ages 6 and 30 years), Dr. Lori Prok said at a meeting of the Society for Pediatric Dermatology.

Follow-up of the patients from three clinical sites in Colorado ranged from 1 month to more than 11 years. Many of the Spitz nevi were located on the extremities, especially the lower extremities, "which was a little bit surprising to me," said Dr. Prok, a pediatric dermatopathologist who also handles adult dermatopathology cases at the University of Colorado Hospital, Denver.

Six of the malignant melanomas appeared at different anatomic sites than the Spitz nevus location. One melanoma was re-excised and found to be malignant melanoma in situ. Two patients underwent sentinel node biopsy, with negative results. One patient died of causes unrelated to the tumors.

Dr. Prok and her associates have been studying Spitz nevi to try to better understand the lesion, which histologically shows features of malignant melanoma but is clinically associated with a favorable prognosis. They now are reviewing the charts of the 219 patients to see if the original diagnoses were correct or if melanomas were mistaken for atypical or desmoplastic Spitz nevi. They also will be following these patients for longer-term outcomes.

Dermatopathologists are easily confused by Spitz nevi, as illustrated in a study of 10 dermatopathologists who reviewed 30 melanocytic lesions (including 17 Spitzoid lesions) and were blinded to clinical data and patient outcomes. They were asked to choose a label for each lesion from five categories: Spitz nevus, atypical Spitz nevus, malignant melanoma, neoplasm of uncertain behavior, or other.

Only one case engendered agreement by six or more dermatopathologists. At least seven pathologists scored 13 normal lesions as melanomas, and some fatal lesions were categorized by most of the pathologists as Spitz nevi or atypical Spitz nevi (*Hum. Pathol.* 1999;30:513-20).

"The take-home message is that the pathologists were just not very good," Dr. Prok said. "It's not that pathologists are stupid, it's that it's really difficult" to categorize Spitzoid lesions.

Physicians also are confused by Spitz nevi because they raise unanswered questions in management. If Spitz nevi really are benign, why did a meta-analysis of 716 Spitz nevi conclude that all Spitz nevi should be completely excised, with re-excision of positive margins (*J. Am. Acad. Dermatol.* 1993;29:667-8)? How wide should those margins be? One paper suggests 1-cm margins, Dr. Prok noted.

Separate, unpublished data analyzed by two of her associates—a dermatopathologist and a cutaneous oncologist at the university—found that 100% of patients who were treated for Spitzoid melanomas or melanomas with Spitzoid features or atypical melanoma tumors were disease-free 7 years later. In comparison, around 75% of patients who were treated for classical, unequivocal melanoma were disease-free 7 years later.

Sentinel lymph node biopsies in 57 patients with atypical Spitz tumors were positive in 27 (47%), a separate study found. The patients with positive nodes were younger (an average 18 years old versus 29 years old in node-negative patients) and had good outcomes at a median follow-up of 44 months. All 27 node-positive patients were alive and disease-free at follow-up (*Cancer* 2009;115:631-41).

The authors concluded that atypical Spitz tumors do not behave like conventional melanoma, and they questioned the role of sentinel lymph node biopsy in managing atypical Spitz nevi. ■

National Study: Acral Lentiginous Melanoma Incidence Remains Steady

BY BRUCE JANCIN

SAN FRANCISCO — Acral lentiginous is the rarest of the major histologic subtypes of melanoma, but is the most common subtype in blacks, according to a national study.

The study showed that the age-adjusted incidence of acral lentiginous melanoma (ALM) is similar in black and non-Hispanic white patients at about 1.8 cases per 1 million person-years. But ALM accounted for close to 40% of all cutaneous melanomas in blacks, whereas two-thirds of melanomas in non-Hispanic whites were of the superficial spreading subtype and ALM accounted for less than 2%, Dr. Porcia Bradford reported at the annual meeting of the American Academy of Dermatology.

Her analysis of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database for 1986-2005 turned up 1,413 cases of histologically-confirmed ALM in 16 participating cancer registries. This was the first population-based study focusing on ALM, according to Dr. Bradford of the division of cancer and epidemiology, National Cancer Institute, Bethesda, Md.

The incidence of ALM was greatest in Hispanic whites, at 2.5 cases per 1 million person-years. The rate was lowest in Asian/Pacific Islanders at 1.1 cases per 1 million person-years. ALM comprised about 20% of all melanomas in Asian/Pacific Islanders and 10% of those in Hispanic whites.

The prognosis for individuals with ALM was significantly worse than for cutaneous melanoma as a whole. Five- and 10-

year melanoma-specific survival rates for cutaneous melanomas overall were 91% and 87%, respectively, compared with 80% and 68% for ALM.

This disparity in outcomes was related in part to the fact that ALMs tended to be thicker at diagnosis. For example, 70% of all cutaneous melanomas were 1 mm thick or less, and 10-year melanoma-specific survival for patients with such tumors was 95%, whereas only 41% of all ALMs were 1 mm thick or less, and their associated 10-year survival was 88%. Mortality in Asian/Pacific Islanders and Hispanic whites was worse than in blacks or non-Hispanic whites with ALM. This appeared to be a result of the greater tumor thickness and more advanced stage at presentation of ALM in Asian/Pacific Islanders and Hispanics; after controlling for these variables, there were no longer significant racial differences in 5- and 10-year melanoma-specific survival for ALM.

The analysis demonstrated that the incidence of ALM has remained steady during the last couple of decades, while rates of other forms of melanoma have increased steadily. ■



Acral lentiginous melanoma accounted for almost 40% of all cutaneous melanomas in black patients and 2% in non-Hispanic white patients.

PHOTOS COURTESY DR. GARY PECK/DR. CHERIE YOUNG

New Tests Help Diagnose Challenging Nevi

MAUI, HAWAII — Good old cost-effective hematoxylin and eosin staining remains perfectly adequate for diagnosis of most melanomas in the modern molecular era, but help is on the way for the toughest cases in the form of novel tests that assess chromosome copy alterations.

These new tests include a comparative genomic hybridization, which compares the DNA in the full genome of the tumor to that of normal control DNA, and fluorescence in situ hybridization (FISH).

"These tests are just starting to become available in routine clinical practice," Dr. Maxwell A. Fung said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

The FISH test (Abbott Laboratories), although marketed in Europe, isn't yet approved for use in the United States, but it has performed well on an investigational basis at the University of California, San Francisco, Dr. Fung said. The test probes four specific gene loci that are of particular interest because abnormalities at those sites are strongly associated with melanoma.

Three of the loci are on chromosome 6, and one is on chromosome 11. Although this combination doesn't include some of the mutations that figure

prominently in melanoma, it does offer a desirable blend of technical ease along with a reported sensitivity and specificity of about 80%, said Dr. Fung of the University of California, Davis.

Distinguishing nevi from melanomas by using conventional histologic criteria is often straightforward, but there are challenges, as illustrated by a recent report by Dr. Saurabh Lodha and colleagues at Columbia University, New York.

They presented a retrospective analysis of 6 years' worth of Columbia dermatopathology consultation reports. The investigators showed that in cases in which a dermatopathologist sought consultation with a colleague regarding a tumor, there was complete agreement as to whether the lesion was a nevus or melanoma only 55% of the time (*J. Cutan. Pathol.* 2008;35:349-52).

"It's hard enough to decide what lesions to biopsy, but then in a small percentage of the lesions that get biopsied we just don't know what to call them," Dr. Fung said.

Dr. Fung disclosed having no relevant relationships with industry. SDEF and this news organization are owned by Elsevier.

—Bruce Jancin