With Dysplastic Nevi, Pause Before You Biopsy

BY BETSY BATES
Los Angeles Bureau

PORTLAND, ORE. — Dysplastic nevi, also known as nevi with architectural disorder, are "overbiopsied and overtreated" in what has become a money-making "nevi-melanocytic industrial complex," Dr. Terry Barrett asserted at the annual meeting of the Pacific Northwest Dermatological Society.

Nevi with architectural disorder do not generally need to be excised unless severe cytologic atypia is present in a lesion that has been incompletely excised or if severe atypia extends to the margins, said Dr. Barrett, clinical professor of pathology and dermatology at the University of Texas Southwestern Medical Center in Dallas.

Confusion has reigned since 1978 when Dr. Wallace Clark first described what has become known as the dysplastic nevus, an entity clearly distinct from melanoma at one end of the spectrum and common acquired nevus at the other, he said. By 1992, a National Institutes of Health Consensus Statement tried to banish the term "atypical nevus," preferring that clinicians and pathologists use the term "nevus with architectural disorder," followed by a statement about the degree of cytologic atypia present.

Today, both terms are used, often with little agreement on their definitions or even what constitutes atypia, said Dr. Barrett, who is also director for the dermatopathology division of Dallas-based ProPath pathology services. "It has been a quagmire." Physicians were confused. The general pathologist had difficulty, and "even the dermatopathologists fought with one another. The histology became an incredible mess."

Because the clinical significance of the lesions was unclear, patients were overtreated with biopsies, excisions, and reexcisions of numerous nevi as they evolved.

Dr. Barrett said he believes there is room for moderation in managing nevi with architectural disorder, based on increasing evidence that the lesions represent markers for the development of melanoma, rather than precursors leading to the disease. In other words, they share the same risk factors, such as intermittent sun exposure.

"A marker tells us that this patient has received the same assault that they need to develop melanoma. It's absolutely clear that these patients need to be followed," he said, adding that it is unclear whether melanoma arises from nevi, but it is doubtful.

The degree of atypia must be spelled out in a straightforward way and labeled as either 'mild' or 'severe.'

DR. BARRETT

About 40% of patients who develop melanoma have a history of dysplastic nevi, but 70%-80% of melanomas arise on normal-appearing skin. About 10% of the U.S. population has dysplastic nevi.

Further complicating the biopsy issue is the dynamic nature of nevi with architectural disorder.

The lesions change histologically as well as clinically, displaying cellular activity (atypia) if biopsied at a particular point in time, but looking quiescent at another, raising serious questions about whether any important information can be gained by the knowledge that they show atypical features.

If they are biopsied, Dr. Barrett said, he believes that the degree of their atypia must be spelled out in a straightforward way and characterized as either "mild" or "severe" with an explanation of their significance attached.

His laboratory currently uses a modified version of Dr. Arthur R. Rhodes' atypia grading system from Massachusetts General Hospital (Mod. Pathol. 1989;2:306-19), using the following definitions:

► **Mild atypia.** The nucleus is 1.5-2 times the diameter of the nucleus of the basilar keratinocyte. The nucleolus is not visible, or if visible, there is only one per cell.

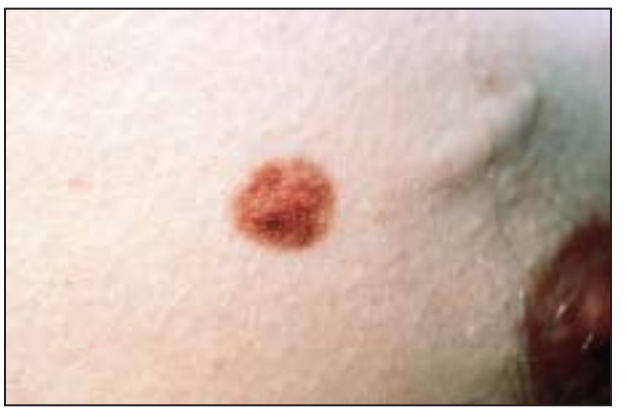
► **Severe atypia.** The nucleus is more than twice the size of the nucleus of the basilar keratinocyte; there are multiple nucleoli per cell; or there is chromatin clumping or nuclear membrane notching. "It's very simple. It's reproducible," Dr. Barrett said.

Excision is rarely necessary, and not justified in patients with absent or mild atypia, he asserted.

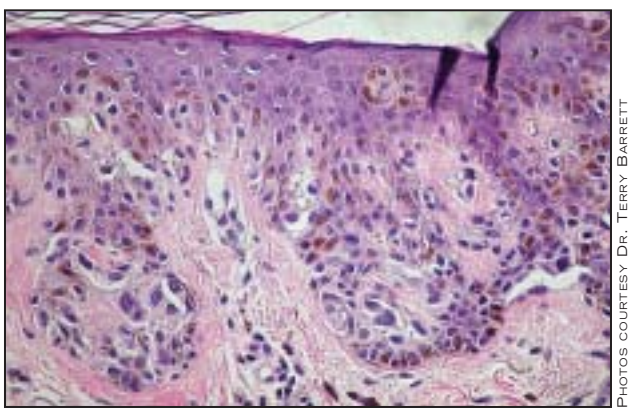
Patients should be followed up according to their degree of risk at 3- to 12-month intervals.

They should be taught how to perform skin self-examination and sun protection strategies, and their blood relatives should be screened.

As always, any lesion suspected to be melanoma should be excised, and reexcision should be considered when a lesion appears to be becoming more atypical, he said. ■



Dysplastic nevi seem to represent a marker for melanoma risk, rather than precursors to the disease.



PHOTOS COURTESY DR. TERRY BARRETT

Lack of clarity in describing the histology of dysplastic nevi, shown here, has resulted in overtreatment.

What to Look Out for, Clinically and Histologically

In clinical appearance, nevi with architectural disorder tend to be macules, with or without a papule. If a papule is present, it is usually in the center of the macule. These nevi are generally symmetrical with regular, but fuzzy borders. Sharp angulations and prominent notching should not be present. Color includes variations of tans and browns, but rarely black. Grey suggests regression and should not be present. Erythema may be present. Histologically, the cellular components include lentiginous junctional melanocytic proliferation, with lateral fusion of nests and shouldering, and epidermal hyperplasia with elongation of the rete ridges. The stromal reaction involves fibrosis (concentric eosinophilic, lamellar) and inflammation. The cytologic atypia has large nuclei with variation of nuclear size, irregular nuclear membrane, variably stained chromatin, large eosinophilic nucleoli, and fine dusty melanin pigment in cytoplasm.

Source: Dr. Barrett

First Nonmelanoma Skin Cancer May Flag Risk for Second

BY SHERRY BOSCHERT
San Francisco Bureau

WINNIPEG, MAN. — People who developed their first basal cell carcinoma or squamous cell carcinoma had a higher risk of developing and dying of a second primary cancer, data from a retrospective study of 43,275 patients showed.

A first basal cell carcinoma quadrupled the relative risk for melanoma in men, tripled the risk for melanoma in women, and raised women's risk for lip cancer fivefold. Men with a first primary squamous cell cancer had nine times the risk for salivary gland cancer, compared with men without the first cancer, Dr. Marni C. Wiseman said.

Death from esophageal cancer was seven times more likely in men and five times more likely in women if they'd had a first primary nonmelanoma skin cancer. A first squamous cell cancer increased the risk of death from Hodgkin's lymphoma 14-fold in men. Death from genitourinary cancer was three to four times more common in women after a first primary basal or squamous cell carcinoma, she said at the annual conference of the Canadian Dermatology Association.

The study looked at cancer-free people who developed a first primary nonmelanoma skin cancer between 1956 and 2000. These cancers seldom are treated with systemic therapy or chemotherapy that might alter a patient's chances of getting unrelated second primary cancers, said Dr. Wiseman of the department of dermatology at the University of Manitoba, Winnipeg, and director of cutaneous oncology at CancerCare Manitoba. Patients in the Manitoba Cancer Registry, which recorded other cancers but excluded second nonmelanoma skin cancers, were tracked.

Of the first primary nonmelanoma skin cancers, 21% were squamous cell carcinoma, 74% were basal cell carcinoma, and 5% were other nonmelanoma skin cancers. Of patients in the squamous cell cancer group, 16% developed a second primary nonmelanoma skin cancer, as did 17% of patients in the basal cell carcinoma group.

Compared with people who had no history of nonmelanoma skin cancer, men diagnosed between the ages of 40 and 79 years and women diagnosed between the ages of 40 and 74 years with basal or squamous cell carcinoma had a higher risk for a second primary cancer.

Overall, the risk remained elevated for only 4 years following diagnosis of the primary nonmelanoma skin cancer, except in women originally diagnosed with squamous cell carcinoma, whose risk stayed elevated. For patients diagnosed with a first primary basal or squamous cell carcinoma at a young age (under 60 years), however, the risk of a second primary cancer was permanently elevated, ranging from a relative risk of 1.07 to 1.51 depending on sex and type of first cancer. In general, the lifetime risk of developing a first primary basal cell or squamous cell cancer is common—14% in men and 16% in women.

Dr. Wiseman said it is not known why the risk for a second primary cancer and death is increased, but it is reasonable to think that in some patients, a nonmelanoma skin cancer may be a "first glimpse" of overall cancer-prone status. ■