'Ugly Duckling' Could Be Useful Melanoma Flag

BY BRUCE JANCIN
Denver Bureau

WAIKOLOA, HAWAII — The "ugly duckling" sign showed impressive sensitivity for melanoma when applied by physicians as well as nonmedically trained individuals for rating melanocytic lesions, according to Dr. Ashfaq A. Marghoob.

The results of this study suggest the ugly duckling sign may be a valuable melanoma screening tool readily teachable to primary care physicians, nurse practitioners, and patients performing periodic skin self-examination, Dr. Marghoob reported at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

The ugly duckling sign was first described in 1998 by Dr. Jean-Jacques Grob of the Hôpital Sainte Marguerite, Marseille, France. It holds that nevi on a given individual tend to resemble each other. The ugly duckling—the outlier, the exceptional nevus, the one that looks different from the others—is more likely to be a melanoma, even if it does not exhibit the classic features ascribed to melanoma in the longstanding ABCD [assymetry, border, color, and diameter] rule.

The ABCD rule, launched in 1985, is a form of gross clinical analysis that "has served us well" in the early recognition of melanoma, said Dr. Marghoob, a dermatologist at Memorial Sloan-Kettering Cancer Center, New York. But it has shortcomings: There is morphologic overlap with dysplastic nevi, resulting in many unnecessary excisions, and ABCD criterion does not fit for many thin melanomas.

To test the utility of the ugly duckling sign when applied by a diverse group of people, Dr. Marghoob and his coinvestigators assembled a portfolio of digital photographs of the backs of 12 patients at high risk for melanoma. Each of the patients had at least eight dysplastic nevi on the back. In five patients, one of the skin lesions was a melanoma, which was removed and histologically confirmed after the pictures were taken. The photo spread included whole-back overview images as well as clinical close-ups of a total of 145 lesions.

The lesion raters consisted of 13 general dermatologists, 8 dermatologists with special expertise in pigmented lesions, 5 nurses, and 8 secretaries and other nonclinical hospital staff. They were asked if any of the 145 nevi differed from the others on the patients' backs.

There was excellent agreement on the ugly duckling sign among observers. All five melanomas but only 3 of 140 benign nevi were identified as ugly duckling lesions by at least two-thirds of the raters. The sensitivity of the ugly duckling sign—that is, the percentage of melanomas identified as "different"—was 100% for the experts, 89% for the general dermatologists, 88% for the nurses, and 85% for the nonclinicians. For the overall group, the sensitivity of the ugly duckling sign was 90% (Arch. Dermatol. 2008;144:58-64).

That 85% sensitivity when the ugly duckling sign was applied by nonclinicians is much higher than the percentage seen in studies of the ABCD method, Dr. Marghoob observed. "Could this be a new public health message? "[Something] along the lines of, 'Look for the ABCD features, but if you see a lesion that looks [different from] the surrounding lesions on your skin—even if it doesn't have the ABCDs—see a dermatologist.' "

He noted that the overall melanoma survival rate in the United States has soared from less than 60% in 1970 to greater than 90% in 2008, mainly as a result of improved detection of early disease, since there are still no effective systemic therapies for advanced melanoma.

If a lesion looks different from the surrounding lesions—even if it doesn't have the ABCDs—see a dermatologist.

DR. MARGHOOB

In 1965, only about 60% of melanomas were diagnosed when localized to the skin, compared with more than 80% today. And although only about 35% of melanomas were less than 1 mm thick at diagnosis in 1976-1980, by 2000 that figure had climbed to 60%.

Widespread adoption of the ugly duckling sign could help improve early diagnosis of melanoma. Total body photography, dermoscopy, confocal microscopy, and short-term mole monitoring via a stepped-up schedule of office visits in selected patients are additional tools likely to lead to further improvements, he said.

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Omalizumab Shows Efficacy for Urticaria

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Treatment with an antibody to IgE led to improved symptoms in patients with urticaria in two pilot studies and a case series reported at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

The antibody, omalizumab, probably is effective for urticaria because of the role that IgE-mediated activation of basophils and mast cells has in causing the disorder. Omalizumab is a recombinant, humanized antibody that binds to human IgE, and therefore has the potential to block this urticaria trigger. This was tested in a study of 20 patients with chronic idiopathic urticaria who were randomized to treatment with either omalizumab or placebo at Johns Hopkins Medical Center in Baltimore, Dr. Laura M. Gober reported in a poster at the meeting.

In a second, independent study, 12 patients with chronic, autoimmune urticaria were treated with omalizumab in an open-label study at the National Allergy, Asthma & Urticaria Centers of Charleston (S.C.), reported Dr. Allen P. Kaplan.

And results from a case series presented at the meeting showed that 22 patients in a single practice treated with omalizumab for asthma had resolution of their food allergies, reported Dr. Caroline Watson, an allergist in private practice at the Allergy & Asthma Care Center in Los Angeles.

Omalizumab (Xolair) is marketed by Genentech Inc. and Novartis Pharmaceuticals Corp. as a treatment for asthma. The urticaria study at Johns Hopkins was sponsored by Genentech, and Dr. Kaplan's study in Charleston was sponsored by Novartis; the case series reported by Dr. Watson did not have commercial sponsorship. Dr. Gober, Dr. Kaplan, and Dr. Watson reported having no financial relationships with the two companies, but the senior researcher in the Johns Hopkins study, Dr. Sarbjit S. Saini, has served as a consultant to Genentech and Novartis.

The controlled study at Johns Hopkins enrolled 20 patients with chronic, idiopathic urticaria who had active disease despite receiving standard antihistamine treatment. The patients ranged in age from 22 to 64 years. They were randomized to receive either the approved dosage for treating asthma or placebo, reported Dr. Gober and her associates. Treatment was by subcutaneous injection every 4 weeks for 16 weeks, and then patients were followed for an additional 8 weeks.

The average urticaria severity scores were identical at baseline in both treatment arms. Both the physician-rated and patient-rated scores among the patients treated with omalizumab were significantly reduced, compared with the placebo group as quickly as 2 weeks after the initial dose, and stayed significantly lower throughout the balance of the study.

After 16 weeks of treatment, following the final dose, the patients in the omalizumab group showed "marked improvements" in their scores for quality of life, emotions, and functioning, compared with the placebo group, and they also had a significant increase in number of symptom-free days. After 16 weeks of treatment, an average of 50% of days were symptom free in the omalizumab-treated patients, compared with an average of about 5% of days in the placebo group.

These benefits were maintained during the next 8 weeks without treatment, but severity scores in the omalizumab group began to increase from their level during active treatment. There were no reports of serious adverse effects with omalizumab.

Further study is needed to find the optimal omalizumab regimen in those with chronic idiopathic urticaria, said Dr. Gober, a pediatric allergist at Johns Hopkins.

The open-label study at the National Allergy, Asthma & Urticaria Centers of Charleston included 12 patients with chronic autoimmune urticaria who remained symptomatic despite high-dose treatment with a nonsedating antihistamine and hydroxyzine. After 4 weeks on placebo, they received a standard dose of omalizumab every 2 or 4 weeks for 16 weeks. This produced complete resolution of symptoms in seven patients and partial improvement in four patients, and had no effect in one patient, said Dr. Kaplan, a professor of medicine at the Medical University of South Carolina, Charleston.

In Dr. Watson's case-series study, the impact of omalizumab on food allergies was assessed in 82 patients with asthma who received regular treatment with omalizumab as patients at the Allergy & Asthma Care Center. In this group, 46 also had a history of a food allergy, and 22 of these patients reported exposure to the triggering food. All 22 patients reported a substantial reduction in symptoms following their food exposure when treated with omalizumab, Dr. Watson noted in a poster.

The patients were allergic to fish, shellfish, tree nuts, egg, soy, dairy, avocado, and wheat. Allergic reactions that were reduced in the patients included asthma, angioedema, anaphylaxis, atopic dermatitis, rhinosinusitis, and urticaria. ■

Becaplermin Tied to Cancer Death Risk

The risk of death from cancer may be increased in patients prescribed becaplermin (Regranex) more than three times, according to statement by the Food and Drug Administration issued last month.

Becaplermin is made by Johnson & Johnson's Ethicon division and is used to treat diabetic leg and foot ulcers. It was approved in 1997.

In a posting on its Web site, the agency said it recently was informed of a study—an analysis of a health insurance database—that found an increase in the number of cancer deaths in patients taking becaplermin. The database contained information on adult patients with diabetes who had no history of cancer. The authors compared patients taking becaplermin with those who did not. There were more cancer deaths in those prescribed the drug three or more times. It is not clear whether there was an increase in new cancer cases, said the FDA.

Johnson & Johnson had already been monitoring a potential cancer link, as becaplermin, a recombinant form of human platelet–derived growth factor, inherently had the potential to accelerate disease. Growth factors cause cells to divide more rapidly, said the FDA.

A long-term safety study completed by Johnson & Johnson in 2001 found more cancer in patients prescribed the drug.

The agency said patients should not stop taking the drug. Instead, "the risk of using Regranex should be weighed against the benefit for each individual patient." The agency has not yet decided whether the new data will lead to any labeling changes.

—Alicia Ault