Plan Pregnancy by Age and Stage

Melanoma *from page 1*

There is an accumulation of recent data showing a lack of effect of pregnancy on melanoma survival, when studies control for Breslow depth of invasion (Cancer 1985;55:1340-4; Lancet 1991;337:1164-5).

► **How long must a woman who has been treated for melanoma wait before becoming pregnant?** "My answer is always that it depends on the stage of your disease plus your age," she said. The risk of death associated with cutaneous melanoma is greatest with high-risk lesions greater than 3 mm in depth, although most melanomas that are treated are 1 mm or less.

A study reporting that 83% of patients with metastatic disease present within 2 years of initial diagnosis recommended a 2-year interval between melanoma surgery and pregnancy (Lancet 1991;337:653-5). Opinions differ about the waiting period, with some physicians, including Dr. Bolognia, opting for a 3-year delay in a young patient with a high-risk lesion.

"The scenario that I see fairly frequently is the woman who is 40 years of age, has waited to have children, and has an in situ lesion," she said. "I tell them they can go ahead and try to get pregnant now and that we don't have to wait the 2 years. The way I think, the older the patient and the thinner the lesion, the more I am going to decrease the time they have to wait."

► **Does the prognosis differ if the cutaneous melanoma is diagnosed when the patient is pregnant?** For early-stage disease (American Joint Committee on Cancer stages I and II), there is no difference in prognosis, Dr. Bolognia said. Although some retrospective series have suggested a worse prognosis, at least nine controlled studies have shown no effect on survival with pregnancy-associated cutaneous melanoma, when controlled for Breslow depth.

► **What can be done to minimize the depth of melanomas identified in pregnant women?** Physicians should lower the threshold for performing a biopsy of suspicious pigmented lesions in pregnant women. "If you have a lesion that is worrisome to you, do a biopsy; don't say you'll wait until after the baby is born," she said.

Of multiple studies, three have shown increased tumor thickness for melanomas diagnosed during pregnancy, but this observation could be due to a variety of reasons, including a delayed diagnosis resulting from the belief that moles change during pregnancy; relative immunosuppression; and the effects of hormones or growth factors, she said.

Her approach to the pregnant patient with melanoma is to perform a complete history plus skin and lymph node examination, to excise the lesion with the recommended margins, and to discuss sentinel lymph node (SLN) biopsy if there are no palpable nodes or if the Breslow depth is 1-4 mm. If signs or symptoms of metastatic disease are present, or if it is a high-risk lesion, then ultrasound or MRI is recommended. Use of MRI is accepted in the second and third trimesters, said Dr. Bolognia, who reported no conflicts of interest.

A combination of radioactive technetium-99m sulfur colloid (Tc-99m SC) plus isosulfan blue dye is used to increase the sensitivity of SLN mapping and biopsy. However, a recent article recommended the use of only Tc-99m SC in pregnant women because of the risk of allergic reactions (up to 2%) and life-threatening anaphylaxis (0.7%-1.1%) associated with the blue dye (Cancer 2003;97:2130-3).

Women should be advised of this potential risk, but reassured that the radiation exposure with Tc-99m SC is in a very safe range. A small series of nine women who underwent SLN biopsy during pregnancy for melanoma (six patients) or breast cancer (three patients) observed no adverse reactions and nine healthy, term babies (Ann. Surg. Oncol. 2007;14:218-21).

► **If a pregnant woman has metastatic melanoma, what is the chance that the child will also develop melanoma?** If the placenta is involved, the chance of fetal metastasis is about 20%-35%, with the majority of these babies not doing well, Dr. Bolognia said. Melanoma is the tumor that most frequently metastasizes either to the placenta or the fetus, and accounts for at least half of tumors with fetal involvement. ■

Tape Test Helps Distinguish Melanoma From Atypical Nevi

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — Melanoma proved genetically distinguishable from atypical nevi when cells were collected from the stratum corneum using a custom-designed adhesive tape in a poster presentation at the annual meeting of the American Association for Cancer Research.

Molecular analysis of tape-collected RNA identified an expression pattern of 20 genes that was 100% sensitive, 90.6% specific, and 92.4% accurate in detecting both in situ and invasive melanoma in 66 skin samples, reported Dr. William Wachsman of the oncology/hematology division of the University of California, San Diego.

If confirmed in further studies, the technique could be used to obtain a skin sample "noninvasively and painlessly" and to receive an objective diagnosis based on a validated genetic biomarker. "This technique could become the preferred first line for evaluating pigmented lesions suspicious for melanoma," Dr. Wachsman said in an interview.

The 20-gene cluster used to develop the Epidermal Genetic Information Retrieval (EGIR) system (DermTech International) was selected from an original array of 350 differentially expressed genes put to the test in a preliminary comparison of 18 lesions that proved to be melanoma and 18 ultimately diagnosed as atypical nevi.

In both the preliminary study and the 66-sample testing set, suspicious pigmented lesions and normal skin regions were tape stripped four times using EGIR-specific adhesive film designed by DermTech scientists. Total RNA was then isolated from the tape strips and amplified using microarray technology.

The resulting pattern analysis could distinguish melanomas from normal skin samples as well as from atypical nevi. Furthermore, at least three distinctive groups of atypical nevi were discernable, suggesting the potential of characterizing low- and high-grade nevi.

The finding could have significant diagnostic implications, reducing the number of unnecessary skin biopsies and taking some of the guesswork out of melanoma identification, said Dr. Harold Rabinovitz, a coauthor on the study and a dermatologist in private practice in Plantation, Fla.

Currently, dermatologists can distinguish melanoma from an atypical nevi with about 60% accuracy. The levels of sensitivity and specificity obtained in the study, 100% and 90.6%, respectively, are "very, very high, and exciting," Dr. Rabinowitz said in an interview.

"The plan is for the RNA samples obtained via EGIR-based tape stripping to be sent to a CLIA [Clinical Laboratory Improvement Amendments] lab for testing. In 3-5 days, the physician will receive a report back that, based on genetic profiling, shows the probability of the lesion in question being a melanoma," he said.

The company plans to develop a point-of-care application of the technology, so that results would be available while the patient waits in the physician's office.

Dr. Wachsman is an uncompensated adviser to DermTech. Dr. Rabinovitz disclosed that he is a consultant, independent contractor, and advisory board member for DermTech. He also serves as a consultant, medical coordinator, and/or clinical investigator for other technologies aimed at melanoma diagnosis. The first author on the study was Dr. Sherman Chang, director of molecular biology for DermTech in San Diego. ■

Jury Remains Out on NSAIDs' Effect on the Risk of Melanoma

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Does regular use of aspirin or other NSAIDs protect against melanoma?

The question remains wide open following the presentation of two large, well-controlled studies that drew diametrically opposite conclusions at an international investigative dermatology meeting.

Investigators found no association between melanoma risk and overall use of NSAIDs.

DR. ASGARI

"The study designs are very different, and each has its strengths and weaknesses. You can't say one is better than the other," session cochair Dr. Suephy Chen, director of the dermatology clinical outcomes and research unit at Emory University, Atlanta, said in an interview.

Dr. Clara Curiel-Lewandrowski presented a case-control study involving 400 cutaneous melanoma patients and 600 controls matched for gender, age, and neighborhood.

The primary study hypothesis, based upon preliminary data, was that statin therapy would reduce the risk of developing melanoma by upward of 30%. That didn't happen. In fact, there was no indication that long-term use of statins reduced melanoma risk, according to Dr. Curiel-Lewandrowski of Harvard Medical School, Boston.

But the study was also designed to look at NSAID use. The prevalence of a history of more than 5 years' duration of NSAID use, regardless of frequency, was 18% in melanoma patients, compared with 24.2% in controls.

After adjustment for baseline melanoma risk factors, this translated into a 27% relative risk reduction in conjunction with more than 5 years of NSAID use.

The risk reduction seen with long-term NSAIDs was driven mainly by aspirin use. More than 5 years of aspirin use was reported by 13.3% of the melanoma group and 21.2% of controls. This worked out to an adjusted 44% relative risk reduction.

In a separate presentation, Dr. Maryam M. Asgari presented a prospective cohort study involving 63,809 participants in the National Institutes of Health–sponsored Vitamins and Lifestyle (VITAL) study.

On a detailed questionnaire administered at study entry, participants self-reported their NSAID consumption during the prior 10 years. They also listed their melanoma risk factors, including family history of melanoma, a personal history of three or more severe sunburns during ages 10-20 years, having had moles removed, and red or blond hair color.

During an average follow-up of 5 years, 349 new cases of melanoma occurred. After adjusting for melanoma risk factors as well as indications for NSAID use, investigators found no association between melanoma risk and overall use of NSAIDs, duration of use, or dosage. NSAID use did not influence tumor invasion, Breslow Depth, or risk of metastasis, said Dr. Asgari, a dermatologist and Moh's surgeon in the division of research at Kaiser Permanente, Oakland, Calif.

The study was funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Cancer Institute. ■