Melanoma Masqueraders Call For Low Index of Suspicion

BY BETSY BATES
Los Angeles Bureau

SANTA BARBARA, CALIF. — The melanomas that students are taught to recognize in medical school are often tough to miss—ugly, misshapen, and black, maybe with tinges of blue and red.

In real life, it's not always that easy, Clay J. Cockerell, M.D., said at the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

"This disease will teach you a lot," said Dr. Cockerell, president of the American Academy of Dermatology and professor of dermatology and pathology at the University of Texas Southwestern Medical School in Dallas.

Prototypic, evil-looking melanomas do exist, but generally they herald metastatic disease. And while the ABCDs—and now "E" for evolution—can help identify melanomas sooner, the sensitivity for diagnosis by clinical appearance alone still hovers between 48% and 67% in most studies.

"I'd be willing to bet almost every person in this room has missed a melanoma clinically at least once in their career," Dr. Cockerell surmised.

The diagnostic challenge is only getting more difficult, he said.

"In my own experience looking at hundreds and hundreds of slides under the microscope, there's no question we're seeing far more melanomas than we used to. We're also seeing melanoma at smaller stages in evolution and melanoma that has unusual features," he said.

These days, if it's black and asymmetrical, "to me, it's melanoma until proven otherwise," no matter its size, Dr. Cockerell said.

Some entities that can mimic melanoma include a halo nevus, solar lentigo, traumatized blue nevus, seborrheic keratosis, pigmented basal cell carcinoma, pigmented Bowen's disease, pigmented squamous cell carcinoma, and thrombosed angioma.

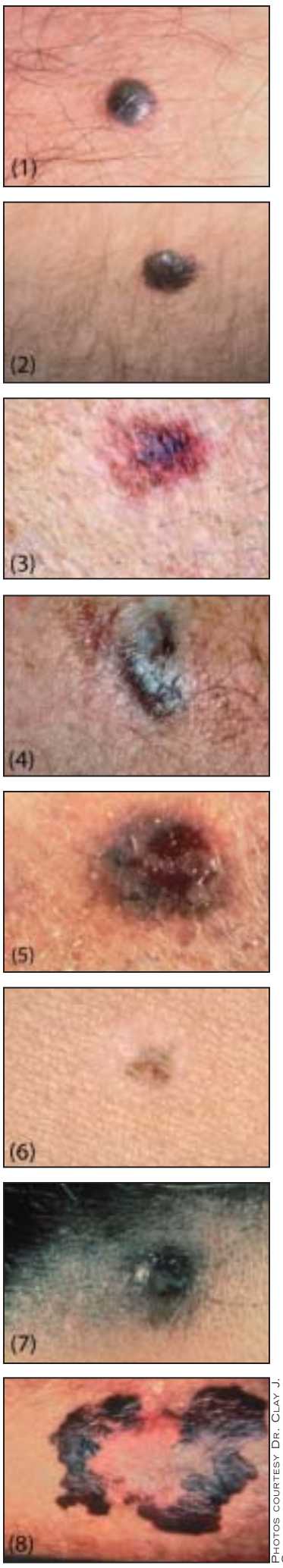
In a study of 1,784 histologically proven primary melanomas, Dr. Cockerell and associates found 583 that were not clinically suspicious. In these "wolf-in-sheep's-clothing" cases, the presumed diagnoses included nevi, basal cell carcinoma, Bowen's disease, pigmented seborrheic keratosis, and lentigo, among others (Am. J. Dermatopathol. 1991;13:551-6).

Unfortunately, the histologic diagnosis can be murky as well.

Spitz nevus is a well-known mimicker of melanoma, although Dr. Cockerell uses the "Mary Poppins rule" to decide on management. A Spitz-like lesion in a child must be "practically perfect in every way" in terms of meeting criteria for melanoma to draw Dr. Cockerell's concern, while in an adult, the opposite is true.

More perplexing is desmoplastic malignant melanoma, which may have a very "banal" appearance both clinically and under the microscope, he said.

In such a case, characteristic spindle cells may be scarce, while the overall picture is of minimal cytologic atypia. A key to identifying it is nesting within the epidermal component, Dr. Cockerell said. ■



PHOTOS COURTESY DR. CLAY J. COCKERELL

Answer Key:

1. irritated blue nevus; **2.** nodular melanoma; **3.** melanoma with halo; **4.** dermatofibroma; **5.** pigmented basal cell carcinoma; **7.** pigmented basal cell carcinoma; **8.** pigmented Bowen's disease

Jury Out on Value of Sentinel Node Biopsy for Melanoma

BY TIMOTHY F. KIRN
Sacramento Bureau

VANCOUVER, B.C. — According to an informal poll, most melanoma experts would want a sentinel node biopsy if they had melanoma, despite the fact that sentinel node biopsy results have now been followed out for 5 years, and were not shown to increase long-term survival.

The poll was taken by Merrick Ross, M.D., at the Sixth World Congress on Melanoma, following a presentation of the 5-year results of the 1,973-subject, Multicenter Selective Lymphadenectomy Trial.

The Multicenter Selective Lymphadenectomy Trial found no statistically significant difference in 5-year survival rates between those who had sentinel node biopsy and those who did not (87% vs. 86%), the primary end point of the trial, said Donald L. Morton, M.D., the originator of the procedure. Dr. Morton is the chief of science and medicine at the John Wayne Cancer Institute, Santa Monica, Calif.

However, subanalysis of the data from the trial suggested enough benefit that if sentinel node biopsy were considered a new drug, it would warrant Food and Drug Administration approval, Dr. Morton asserted.

One of the commentators, John Thompson, M.D., said he agreed. Assessment of the sentinel node for evidence of migrating melanoma cells "is likely to be appropriate and important for the foreseeable future," said Prof. Thompson, executive director of the Sydney Melanoma Unit at the Royal Prince Alfred Hospital, Camperdown, Australia, and another principal investigator in the trial.

The other commentator, however, disagreed strongly. The trial was designed to look for a difference in survival, and it failed to show one, said J. Meirion Thomas, M.D., of the sarcoma unit of the Royal Marsden Hospital, London. "We must stop burying our head in the sand," Dr. Thomas said. "At the present time, this procedure offers patients no benefit."

Dr. Ross, chief of the melanoma section at the M.D. Anderson Cancer Center, Houston, and an advocate of the procedure, asked the approximately 200 melanoma experts present in the room: "If you had melanoma, would you want a sentinel node procedure?" About 90% of the audience raised their hands, indicating they would.

The Multicenter Selective Lymphadenectomy Trial looked at patients who had melanomas with greater than a 1.0-mm Breslow thickness. It randomized about 60% of the patients to wide local excision with a sentinel node biopsy, which was followed by regional lymphadenectomy if a positive sentinel node was found. About 40% of the patients were randomized to a watch-and-wait group, in which they received a wide local excision only, and were followed. If the followed patients developed a palpable node, they then underwent regional lymphadenectomy. The median time of follow-up of the patients was 59 months.

Although there was no difference in overall survival, there was a difference in disease-free survival (78% vs. 73%), Dr. Morton said.

The analysis also showed that there was a similar rate of positive nodes in both groups (16%); that node positive patients overall had lower survival at 5 years (71% vs. 88%); and that when patients needed regional lymphadenectomy, those in the sentinel node biopsy group had fewer positive nodes at lymphadenectomy than did those in the watch-and-wait group (an average 1.6 vs. 3.4), among other findings.

Moreover, 5-year survival among those with positive nodes was significantly higher in those patients with a positive sentinel node and immediate lymph node dissection than it was among the patients who had a delayed complete dissection (71% vs. 55%).

Taking the data all together, no evidence suggested that the sentinel node biopsy was inaccurate, or that it was unsafe in any way. The data further suggested that there were some patients whose disease was caught while it was still limited to the sentinel node, and that these patients were cured, Dr. Morton said.

"There is a very short window of opportunity here where in fact there is a small, but definite subset of patients who have their disease limited to the sentinel node, and their removal aborts the blood-borne and distant metastasis," he said.

Sentinel node biopsy is important also because it removes uncertainty for many patients, and it allows for more accurate cancer staging of patients, which is critical information for conducting clinical trials, he added.

The reason the trial may have shown no effect on overall survival may be because it enrolled too few patients to make a clear difference, Prof. Thompson suggested.

Dr. Morton agreed. The $90-million trial has had far fewer deaths (13%) than were expected when the trial was designed over a decade ago, when the only information they had to go on to decide how many patients might be needed was the historical rate at the John Wayne Cancer Institute, he said.

The real issue is the accuracy of sentinel node biopsy, given that it has shown no benefit, Dr. Thomas said. The false-negative rate has been shown to be about 13%. The false-positive rate is not known, but by extrapolating from various data sources, it can be estimated to be anywhere from 12% to 22%, and those patients are getting unnecessary lymphadenectomies.

"There is no survival advantage, and they shouldn't be looking at those other measures," he said.

Dr. Ross, on the other hand, said he was not dismayed by the lack of a survival advantage in the trial.

"Overall it is a better way to treat patients because you are identifying and removing disease early," he added. ■