

Reliability Of Skin Biopsy Pathology

Patricia E. Boiko, MD, and Michael W. Piepkorn, MD, PhD

Background: The diagnosis of skin disease by histologic examination is regarded as the reference standard upon which therapy and follow-up are determined. Our study investigated the reliability of skin biopsy diagnosis requested by family physicians and physicians' assistants.

Methods: Biopsy diagnoses by a community-based pathology group were reinterpreted by our study dermatopathologist on a sample of 119 skin biopsies randomly selected from the 1844 biopsies performed by family physicians and physicians' assistants at a large Washington State health maintenance organization during a 4 $\frac{1}{2}$ -year period.

Results: There were 107 exact matches and 3 mismatches of premalignant lesions and 6 mismatches of benign diagnoses. In addition, two melanomas diagnosed by the community-based pathologists were interpreted as benign by our study dermatopathologist. A third melanoma diagnosed by the community-based group was interpreted as a poorly differentiated squamous cell cancer by the university dermatopathologist. The weighted kappa, 0.83, indicated excellent interrater agreement.

Conclusion: Although our study showed excellent interrater concordance of skin biopsy interpretation, there was disagreement about three melanomas between a community-based general pathology group and our study dermatopathologist. The melanoma disagreement is consistent with previous studies that found poor interrater agreement for early melanomas. The community-based pathologists were uncertain about two of these melanomas, and as part of their quality control and review procedures requested confirmation by an expert pathologist, who agreed with the melanoma diagnosis. Family physicians are justified in requesting a second opinion (if not automatically requested by a community laboratory) when the histopathologic diagnosis is not in concordance with the clinical history or impression or when the pathologist is unsure of the diagnosis. (J Am Board Fam Pract 1994; 7:371-4.)

Family physicians perform skin biopsies to confirm clinical suspicions of skin diseases, especially skin cancer. The diagnosis of skin disease by a pathologist's interpretation of histologic findings is regarded as the reference standard upon which clinical acumen, therapy, and follow-up are determined.^{1,2} The value of a skin histopathologic diagnosis, however, depends on the assumption that microscopic changes in the skin correlate with the natural history of disease. For example, the histologic criteria for melanomas were developed using proven melanoma metastasis cases.³

The reliability of a pathologist's diagnosis is influenced by the ability of the pathologist, the adequacy of the skin specimen (including type of biopsy, area, staining, and sectioning), and the cur-

rent classification system. It is important to know the reliability of a pathologist's diagnosis when that diagnosis is being used as the basis for treatment and follow-up, especially for malignant melanomas.

Family physicians often do not have a university dermatopathology specialist available but rely on community-based general pathology groups. The purpose of this study was to determine the reliability of skin biopsy diagnoses by a community-based general pathology group for biopsies performed by family physicians and physicians' assistants.

Methods

The study was based at Group Health Northwest (GHNW), a family practice staff model health maintenance organization in Spokane, Washington. At the completion of this study there were more than 50,000 patient members of GHNW. Family physicians and physicians' assistants performed 1844 biopsies from January 1988 through June 1992.

These specimens were interpreted by a 10-member community-based pathology group. In this group there were 1 board-certified dermatopathologist and 2 other pathologists who had ad-

Submitted, revised, 3 May 1994.

From the Department of Family Medicine (PEB), and the Departments of Medicine and Pathology (MWP), University of Washington School of Medicine, Seattle. Address reprint requests to Michael W. Piepkorn, MD, Division of Dermatology, Department of Medicine, RM-14, University of Washington School of Medicine, Seattle, WA 98195.

This project was supported in part by a National Institutes of Health National Research Award (Boiko).

ditional training and interest in skin diseases. A request form accompanying the biopsy specimen usually had the patient's name, age, sex, site of biopsy, and a clinical diagnosis or question. As part of the quality control and review procedure, all biopsies with an uncertain or malignant diagnosis were reviewed by a second member of the group. If the malignant diagnosis was still in question, the slides were sent for confirmation to an outside expert university dermatopathologist.

This study was based on a random sample (182 of the 1844 biopsies) plus 11 malignant melanomas. Seventy-one of the slides either could not be found or were in a storage area where access was too difficult to obtain given the limited resources of this study; 69 of these specimens were from the years 1988 and 1989. Of the remaining 122 slides obtained from the pathology group, three slides did not match with the correct person or specimen code from the list.

The reliability of the pathologists' diagnoses was determined on a sample of 119 biopsy specimens. Our study dermatopathologist was board certified in dermatology and pathology. He was blinded to diagnosis and did not know that most melanomas were included, believing that he was given a random sample of all lesions. He based his diagnosis only on the specimen and received no clinical information. Diagnoses were coded for both groups using the SnoMed coding system.

Agreement between raters occurred when either the diagnosis codes matched exactly or review of the original biopsy report and our study dermatopathologist's data sheet revealed synonymous diagnoses.⁴ Disagreement or mismatches were classified if the rater's codes and review of the reports did not produce a synonymous diagnosis.

Interrater reliability was calculated using a weighted kappa, which quantifies the level of agreement beyond chance and allows for disagreements to be weighted as to seriousness.⁵

Results

There were 107 exact matches of the 119 reviewed (Table 1). The weighted kappa (0.83) indicated excellent interrater agreement.⁶

Of the mismatches (Table 2), two melanoma skin cancers were diagnosed by the community-based pathology group but were diagnosed by our study dermatopathologist as an inflamed compound nevus and a junctional nevus. The community-based pathologists noted difficulty in making the melanoma diagnoses and had them confirmed by an outside melanoma pathology specialist. Another melanoma diagnosed by the community-based pathologists was interpreted as a poorly differentiated squamous cell cancer by our study dermatopathologist. After the results were shared with the community-based pathologists and our study dermatopathologist, this slide was reviewed again by our study dermatopathologist, who confirmed it to be a melanoma and reasoned that he had misinterpreted it because the cells were squamoid in appearance and nearly devoid of pigment.

In two cases the community-based pathologists diagnosed actinic keratosis, whereas our study dermatopathologist diagnosed seborrheic keratosis. In another case the community-based pathologists diagnosed verruca planus, but our study dermatopathologist interpreted it as an actinic keratosis. There were six mismatches of benign diagnoses.

Interpretation of the 119 biopsies occurred among the community-based group of 9 general pathologists, 1 dermatopathologist, and 1 outside

Table 1. Interobserver Agreement between Community-based Pathologists and Study Dermatopathologist on 119 Biopsy Specimens.

Community-based Pathologists	Study Dermatopathologist				
	Melanoma	Basal or Squamous Cell Cancer	Premalignant	All Benign	Benign Mismatches
Melanoma	8	1	0	2	0
Basal or squamous cell cancer	0	6	0	0	0
Premalignant	0	0	2	2	0
All benign	0	0	1	91	6
Benign mismatches	0	0	0	0	0

Exact matches 107, mismatches 12. Observed weighted proportion agreement=0.949. Expected weighted proportion agreement=0.70. Weighted kappa=0.83.

Table 2. Diagnosis of Mismatches and Their Clinical Importance.

Community-based Pathologists	Study Dermatopathologist	Clinical Importance
Benign		
Lipoma	Skin tag	None, both removed
Adnexal neoplasm	Fibrous papule	None, both removed
Intradermal nevus	Epidermal inclusion cyst	None, both removed
Scar	Lichenoid dermatitis	Removal vs. steroid treatment
Lichen simplex chronicus	Dermatofibroma or angiofibroma	Steroid treatment vs. removal
Granuloma annularae	Dermatofibroma	Intralesional steroids vs. removal
Premalignant		
Verruca planus	Actinic keratosis	Cryotherapy for both, but the actinic keratosis requires closer follow-up for squamous cell cancer
Actinic keratosis	Seborrheic keratosis	Cryotherapy for both, but the actinic keratosis requires closer follow-up for squamous cell cancer
Actinic keratosis	Seborrheic keratosis	Cryotherapy for both, but the actinic keratosis requires closer follow-up for squamous cell cancer
Malignant		
Melanoma	Poorly differentiated squamous cell cancer	Melanoma requires wider excision and determination of metastasis than squamous cell cancer
Melanoma	Junctional nevus	Melanoma requires wider excision and determination of metastasis vs. no further treatment or follow-up
Melanoma	Inflamed compound nevus	Melanoma requires wider excision and determination of metastasis vs. no further treatment or follow-up

expert melanoma pathology specialist, whereas our 1 study dermatopathologist read all 119. Also, the community-based pathology group often had the added information of site of biopsy, age and sex of the patient, and clinical diagnosis or question. It is not known what the interrater reliability was among the community-based pathologists. Of the 12 mismatches, 5 general pathologists and the 1 dermatopathologist read those biopsies from the community-based pathology group. Two of the melanomas mismatched were read by the dermatopathologist in the community-based group and the other by a general pathologist.

Not all biopsies from a random sample were obtained, with the majority of those unavailable from the years 1988–1989. The diagnoses assigned in 67 of the 71 unavailable slides were also among the diagnoses assigned to the study slides except three benign diagnoses: pilar tumor, folliculitis, and psoriasis. Also, if the study was limited to 1990–1992, the kappa value increases ($k=0.98$).

Discussion

We found excellent interrater agreement between a community-based pathology group and a study university dermatopathologist even though the difficulties in diagnosing early melanomas and precancerous lesions were underscored. The in-

terobserver agreement in this study was better than that reported in the literature overall but is consistent with the difficulty of histopathologic diagnosis of early melanomas and precancerous lesions.³ Early melanomas and precursor lesions of melanomas elicit poor interrater agreement even in areas where there is a high incidence of melanoma and even among dermatopathology specialists.^{7,8}

In our study, two melanoma skin cancers were diagnosed by the community-based pathology group, but our study dermatopathologist diagnosed them as inflamed compound nevus and junctional nevus. The community-based pathology group noted difficulty in making the diagnoses of the two malignant melanomas and had the diagnoses confirmed by a university-based melanoma pathology consultant. This consultant also noted that these cases were questionable but agreed ultimately with the malignant melanoma diagnosis. Clinically, the community-based pathologists' diagnosis of melanoma would be considered the correct (most reliable) diagnosis after having been confirmed by the consultant pathologist. Whether these lesions would become metastatic (validity), however, is not known.

In the case of the diagnosis disagreement in which the community-based group noted a mela-

noma and our study dermatopathologist indicated poorly differentiated squamous cell cancer, the community-based pathologists knew the clinical history and past diagnosis of melanoma in the patient. Our study dermatopathologist reviewed the case again and confirmed it to be a melanoma, which he had misinterpreted because of certain aberrant features (see Results section).

Table 2 shows the clinical importance of the mismatches. The benign mismatches were of minimal clinical importance. The premalignant and malignant mismatches potentially have considerable importance; inadequate follow-up of an actinic keratosis could lead to a squamous cell cancer or death from an inadequately treated melanoma.

This study also provides a context in which family physicians can better understand the reliability of skin histopathology. Even though skin lesions are more reliably diagnosed by histopathologists than are lesions from the breast, endometrium, and liver and lymph nodes, there is not perfect agreement.⁹ In fact, agreement has been as low as 58 percent ($k = 0.34$) in a study of interobserver agreement of dysplasia in melanocytic nevi.¹⁰ Higher agreement rates have been found by other researchers, but their selection of histology specimens was not random, and the pathologists agreed on histologic criteria for dysplasia in advance.^{11,12}

Conclusion

Although this study showed excellent interrater concordance of skin biopsy diagnosis, there was disagreement about three melanomas between a community-based pathology group and a study university-based dermatopathologist. This finding is consistent with results of previous studies, which demonstrated poor interrater agreement for early melanomas. The community-based pathology group found diagnostic certainty of two of these melanomas to be questionable, and as part of their quality control and review procedures they requested confirmation by an expert consultant pathologist, who agreed with the melanoma diagnosis.

If there is no automatic second opinion requested by a community laboratory for clinically suspicious or pathologically diagnosed skin cancers, family physicians are justified in the request of a second opinion. Second opinions should be considered when the histopathologic diagno-

sis is not in concordance with the patient's clinical history or the physician's clinical impression or when the pathologist is unsure of the diagnosis.

Sherry M. Connors, Kelly Tripp, Group Health Northwest; L.R. Bernard, MD, and Vera Pillers at Pathology Associates, Spokane, Washington, provided data collection and entry. Tom Koepsell, MD, Eric Larson, MD, and Karl Weyrauch, MD, provided study design and editorial review; Bobko Industries, Seattle, Washington, provided computer software assistance.

References

1. Cassileth BR, Clark WH Jr, Lusk EJ, Frederick BE, Thompson CJ, Walsh WP. How well do physicians recognize melanoma and other problem lesions? *J Am Acad Dermatol* 1986; 14:555-60.
2. Curley RK, Cook MG, Fallowfield ME, Marsden RA. Accuracy in clinically evaluating pigmented lesions. *BMJ* 1989; 299:16-8.
3. Price NM, Rywlin AM, Ackerman AB. Histologic criteria for the diagnosis of superficial spreading malignant melanoma: formulated on the basis of proven metastatic lesions. *Cancer* 1976; 38:2434-41.
4. Carter RL, Leider M. A dictionary of dermatologic terms. 4th ed. Baltimore: Williams & Wilkins, 1992.
5. Armstrong BK, White E, Saracci R. Principles of exposure measurement in epidemiology. New York: Oxford University Press, 1992:107-9.
6. Fleiss JL. Statistical methods for rates and proportions. 2nd ed. New York: John Wiley and Sons, 1981:223-5.
7. Schmoeckel C. How consistent are dermatopathologists in reading early malignant melanoma and lesions "pre-cursor" to them. An international survey. *Am J Dermatopathol* 1984; 6(Suppl):13-24.
8. Heenan PJ, Matz LR, Blackwell JB, Kelsall GR, Singh A, ten Seldam RE, et al. Interobserver variation between pathologists in the classification of cutaneous malignant melanoma in western Australia. *Histopathology* 1984; 8:717-29.
9. Penner DW. Quality control and quality evaluation in histopathology and cytology. *Pathol Ann* 1973; 8:1-19.
10. Piepkorn MW, Barnhill RL, Cannon-Albright LA, Elder DE, Goldgar DE, Lewis CM, et al. A multi-observer, population-based analysis of histologic dysplasia in melanocytic nevi. *J Am Acad Dermatol*. In press.
11. Rhodes AR, Mihm MC Jr, Weinstock MA. Dysplastic melanocytic nevi: a reproducible histologic definition emphasizing cellular morphology. *Mod Pathol* 1989; 2:306-19.
12. Clemente C, Cohran AJ, Elder DE, Levine A, MacKie RM, Mihm MC, et al. Histologic diagnosis of dysplastic nevi: concordance among pathologists convened by the World Health Organization Melanoma Programme. *Hum Pathol* 1991; 22:313-9.