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Original Article

Interobserver Agreement in Histopathologic Diagnosis of Skin Lesions

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Abstract

Background: The concept of obtaining a second opinion is very popular in anatomical pathology, and multiple studies have shown its cost-effective benefits. This study aimed to determine the diagnostic discrepancy rate in skin biopsies in general pathology practice between first and second pathologists.

Materials and Methods: A retrospective study was conducted on 760 consecutive patients who underwent skin biopsies and subsequent pathologic review over a one-year period. Based on the initial pathologist's diagnosis, histopathological findings were primarily categorized as neoplastic or non-neoplastic. Neoplastic lesions were further divided into benign or malignant. A second pathologist reviewed all slides after codifying and without knowing the original diagnosis. Finally, the diagnoses provided by both pathologists were compared.

Results: According to a primary pathologist, 243 cases (31.97%) were non-neoplastic and 517 (68.02%) were neoplastic. Of the 517 neoplastic lesions, 218 cases (42.16%) were benign and 299 (58.83%) were malignant. The major discrepancies were observed in 1.23%, 5.5%, and 1.01% of non-neoplastic, benign neoplastic, and malignant neoplastic groups, respectively. Kappa coefficient was 0.908 for non-neoplastic, 0.857 for benign, and 0.878 for malignant lesions.

Conclusion: There was a high level of interobserver concordance in the histopathologic diagnosis of skin lesions in our study. We concluded that routine re-evaluation of all skin biopsies by a second pathologist may not be generally recommended except for cases needing aggressive therapeutic interventions to improve patient outcomes and quality of life.

Keywords: Second opinion, Pathology reporting, Skin disease, Discrepancy

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Background

Skin diseases are among the most common clinical problems, presenting with various lesions that vary from benign to life-threatening conditions (1). These lesions can be challenging to interpret, and accurate diagnosis of skin diseases relies on a close clinicopathologic correlation (2). As the disease progresses, skin lesions can evolve through various phases (3). Pathologic investigation is frequently used to support or confirm clinical diagnoses (4). Previous studies have reported considerable and repeatable diagnostic errors in the interpretation of skin biopsies (5). Diagnostic discrepancies contribute to approximately 10% of patient deaths by preventing or delaying appropriate treatment and are one of the leading causes of medical malpractice claims (6). It is critical to ensure accurate and timely diagnoses of patients to provide high-quality treatment, as diagnostic errors pose a significant threat to delivering high-quality care (7).

Seeking a second opinion serves as a decision-making tool for patients, physicians, and hospitals (8). For patients, it is a chance to obtain an alternative assessment of the diagnosis, treatment plan, or prognosis (9). The second opinion is a popular concept in anatomical pathology, with multiple studies demonstrating its cost-effectiveness (6). Although there are some controversies, most clinicians agree that obtaining a second opinion has helped reduce unnecessary procedures and interventions (6, 10). Histopathological diagnoses should be as accurate as possible, as the management and treatment of the patient rely heavily on the pathology report (11). Slide review by a second pathologist is one of the most reliable methods for reducing histopathologic errors. However, there is currently no gold standard to determine whether the first or second diagnosis is correct (6). If both pathologists reach the same conclusion clinician can continue therapeutic planning with greater

confidence (12). In cases of disagreement, referring to a multidisciplinary tumor board is considered the best approach (13). Although most discrepancies between primary and secondary reviews are minor without any severe impact on patient care, those that could impact prognosis and treatment have been reported in up to 7% of the cases (10, 14).

Despite the difficulties in the histopathologic diagnosis of skin samples, especially in centers where extensive use of immunohistochemistry (IHC) is not feasible, consultation with a general pathologist is not a routine method. Therefore, we decided to assess interobserver agreement and diagnostic discrepancy in the histopathologic evaluation of skin lesions to underscore the importance of consultation in general pathology practice to help achieve correct, reliable, and reproducible diagnoses.

Materials and Methods

This study was approved by the Ethics Committee of Urmia University of Medical Sciences and registered under the code: IR. UMSU.REC.1395.73.

This study was conducted retrospectively on 760 consecutive patients with skin biopsies referred to the Urmia University of Medical Sciences over a one-year period. Histopathology slides of the patients were retrieved from the pathology department archives. Based on the diagnosis provided by the initial pathologist, the histopathological findings were primarily categorized into neoplastic and non-neoplastic. Neoplastic lesions were further classified into benign or malignant, and each category was subsequently subtyped.

In the next step, all slides were re-evaluated by a second pathologist after being anonymized and codified. As previously mentioned, IHC is not available in all pathology centers; therefore, our consultation focused on histopathological diagnosis, without relying on complementary diagnostic methods. Finally, the diagnoses made by both pathologists were compared.

The results were expressed as mean ± standard deviation (SD). Statistical analysis was performed using SPSS software version 17. The statistical differences between proportions were determined using the Chi-square test, while numerical data were evaluated using analysis of variance (ANOVA), followed by Tukey's post hoc test. A *P*-value of less than 0.05 was considered statistically significant.

Results

According to the histopathologic diagnosis of the primary pathologist, 243 cases (31.97%) were non-neoplastic and 517 (68.02%) were neoplastic. Of the 517 neoplastic lesions, 218 cases (42.16%) were benign and 299 (58.83%) were malignant. Table 1 presents the diagnoses of both pathologists categorized as neoplastic versus non-neoplastic lesions.

Table 1. Interobserver Agreement on the Categorization of Skin Specimens

	First Pathologist	Second Pathologist	Agreement	*P* value
Neoplastic	517	506	97.87%	<0.001
Benign	218	206	94.95%	
Malignant	299	280	93.64%	
Non-neoplastic	243	224	92.1%	<0.001

In the non-neoplastic group, significant discrepancies (malignancy vs. non-neoplastic lesion) were observed in 1.23% of the cases. These included cases such as verrucous carcinoma vs. pyoderma vegetans and nonspecific change and Mycosis Fungoides vs. lupus discoid.

In benign neoplastic lesions, a major discrepancy was seen in 5.5% of cases, where a malignant lesion was diagnosed in the second review. These included:

- Three cases of squamous cell carcinoma (SCC) vs. keratoacanthoma, pseudoepitheliomatous hyperplasia, and actinic keratosis.
- Two cases of verrucous carcinoma vs. keratoacanthoma and seborrheic keratosis
- One case of malignant salivary gland tumor vs. inverted follicular keratosis
- One case of Bowen disease vs. eccrine poroma
- One case of carcinomatous transformation in seborrheic keratosis vs. keratoacanthoma.

The concordance between the two pathologists in diagnosing the three major groups of skin lesions (malignant neoplastic, benign neoplastic, and non-neoplastic) is illustrated in Table (2).

In the malignant group, a significant discrepancy (non-neoplastic lesions vs. malignancy) was seen in 1.01% of cases, including two cases of nonspecific changes vs. basal cell carcinoma (BCC) and malignant melanoma and one case of dermatitis versus Mycosis Fungoides.

Additionally, the second pathologist diagnosed 16 cases (3.35%) as benign neoplasms, which were initially diagnosed as malignant by the first pathologist. However, since this difference had no significant effect on the patients' prognosis or treatment, it was considered a minor discrepancy. For example, one case diagnosed as BCC by the primary pathologist was classified as trichoblastoma (a benign neoplasm) by the second pathologist. Since the treatment of both lesions required complete excision without further clinical intervention, this discrepancy was considered minor.

Of the 224 cases categorized as non-neoplastic by both pathologists, discrepancies in subtyping were observed in 41 cases (18.3%). Similarly, subtyping discrepancies were observed in 11.11% of 198 benign neoplastic lesions. These included:

- Two cases of dysplastic nevus were considered intradermal and compound nevi
- One case of intradermal nevus was diagnosed as

Table 2. Interobserver Agreement and Correlation on the Diagnosis of Skin Specimens

Second Pathologist First Pathologist	Non-neoplastic	Benign Neoplasm	Malignant Neoplasm	*P* value	Kappa
Non-neoplastic (243 cases)	92.18% (224 cases)	6.58% (16 cases)	1.23% (3 cases)	<0.001	0.908
Benign Neoplasm (218 cases)	3.66% (8 cases)	90.82% (198 cases)	5.50% (12 cases)	<0.001	0.857
Malignant Neoplasm (299 cases)	1.01% (3 cases)	5.35% (16 cases)	93.64% (280 cases)	<0.001	0.878

dysplastic nevus
- One case of keratoacanthoma was diagnosed as actinic keratosis
- One case of actinic keratosis was considered keratoacanthoma.

In the malignant group with diagnostic consensus (280 cases), subtyping discrepancies were found in 5% of cases. Examples included:
- Malignant salivary gland tumor vs. BCC
- SCC versus Bowen disease
- Two cases of BCC versus Basosquamous cell carcinoma and SCC.

The agreement rate in subtyping the skin lesions is presented in Table 3. The Kappa coefficient values for non-neoplastic, benign, and malignant lesions were 0.908, 0.857, and 0.878, respectively.

Table 3. Interobserver Agreement on Subtyping of Skin Lesions

Lesion Type	Agreement	Disagreement
Non-neoplastic Lesions (224 cases)	183 (81.69%)	41(18.3%)
Benign Neoplasms (198 cases)	176 (88.88%)	22 (11.11%)
Malignant Neoplasms (280 cases)	266 (95%)	14 (5%)

Discussion

Second opinions in medicine are commonly utilized to reach a consensus about the diagnosis and management of patients to improve their care (15). Given the high rates of diagnostic disagreements in certain skin biopsy samples, especially those involving challenging melanocytic proliferations, mandatory second opinions have been advocated (16). In this study, we evaluated the diagnostic concordance between general pathologists assessing the same skin lesions.

In the present study, most discrepancies were minor; nonetheless, a few major differences with significant clinical implications were identified. Interestingly, this discordance is comparable to that observed in studies evaluating breast biopsy diagnoses among pathologists (17). In the non-neoplastic group, discordant diagnoses were found in 19 cases (discrepancy rate: 17.82%), of which only three were major. These significant discrepancies included two cases of verrucous carcinoma and one case of Mycosis Fungoides, initially diagnosed as pyoderma vegetans, nonspecific changes, and lupus discoid, respectively. These findings are notable and strongly support the value of obtaining a second pathologist's opinion in critical cases. Consistent with the findings of Minig et al (18), it is clear that the prognosis and treatment plans for patients with these revised diagnoses are completely different from the original ones.

A major discrepancy was observed in the malignant neoplastic group in only three cases (discrepancy rate: 1.01%), including nonspecific changes vs. BCC and malignant melanoma and dermatitis vs. Mycosis Fungoides. In these cases, the differences in clinical course, prognosis, and treatment between the first and second diagnoses are significant. The definition of 'major discrepancy' varies across studies. Although most studies defined major discrepancy as a disagreement that alters the treatment plan (19, 20), some disagreements typically classified as minor (19) may still provide relevant information. These can lead to modifications in patient counseling regarding disease prognosis and help reduce patient and family anxiety.

Our findings regarding the impact of second opinions are consistent with those of Khazai et al, in which they reported minor discrepancies between the first diagnoses and second opinions of pathologists in reporting breast cancer results (17). However, the differences in our results were mainly related to the treatment plan and not the diagnosis. Conversely, major diagnostic differences were reported in 49.5% of 109 reviewed cases in a survey by Laliberté et al (18) and 38.5% of cases in the study by Regan et al (21).

Moreover, our study revealed significant interobserver discrepancies in subtyping skin lesions: 18.3% in non-neoplastic, 11.11% in benign neoplastic, and 5% in malignant neoplastic cases. Histologic subtyping has long been recognized as a common source of discrepancy in skin cancer diagnoses (22). Similar to our study, other studies have also reported disparities in serous, endometrioid, or sarcoma histology subtyping in women with uterine cancers (21, 22).

To the best of our knowledge, the present study is the first one to specifically investigate interobserver disagreement in the histopathologic diagnosis of skin biopsies that do not lead to treatment modifications. However, the study has some limitations. One limitation is that the pathologists' interpretations were conducted independently and only involved a single slide for each case. In clinical practice, multiple slides may be reviewed for each patient, and the second pathologist might be

informed of the initial diagnosis. Another limitation is the relatively small sample size (760 cases), which may affect the generalizability of the findings. More reliable and robust results can be obtained by studying more cases. Furthermore, the retrospective nature of data collection might lead to pathologists' misinterpretation, incomplete information, and patient loss to follow-up. Additionally, a subset of patients may not be referred to the second institution for further evaluation or a second opinion.

Conclusion

In summary, there was a high level of interobserver concordance in the diagnosis of skin lesions in our study. Therefore, routine re-evaluation of all skin biopsies by a second pathologist may not be generally necessary. However, given the presence of some significant differences with prominent clinical and prognostic implications, we recommend re-evaluating skin lesions in cases with strong clinical suspicion of malignancy or any uncertainty regarding the tissue diagnosis.

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Competing Interests

The authors declare no conflict of interests.

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