Influence of evaluation of clinical pictures on the histopathologic diagnosis of inflammatory skin disorders

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Background: Clinical information on histologic referral sheets is usually very limited, and particularly for inflammatory skin disorders, dermatopathologists often ask referring physicians for clinical correlation.

Objective: In this study we tested the value of clinicopathologic correlation in the histopathologic diagnosis of inflammatory skin disorders.

Methods: One-hundred biopsy specimens were digitalized and stored on 3 DVDs along with the clinical images. All cases were evaluated by 9 independent full-time dermatopathologists, initially without looking at the clinical pictures and subsequently after checking them. All diagnoses were finally compared with the "reference" diagnosis established in Graz, Austria, and the results were statistically analyzed.

Results: After evaluation of the clinical images, the number of dermatopathologists making a correct diagnosis was increased in 70 cases, unchanged in 25 cases, and decreased in 5 cases. The total number of correct diagnoses increased from 332 (diagnoses before evaluation of clinical pictures) to 481 (diagnoses after evaluation of clinical pictures), with a 16.6% increase in the total.

Limitations: The computerized setting is different from real-life dermatopathology and physical examination of patients.

Conclusion: Our study clearly shows that clinical pictures should be added to biopsy request slips of inflammatory skin disorders whenever possible, as they allow a better interpretation of histopathologic findings. (J Am Acad Dermatol 2010;63:647-52.)

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INTRODUCTION

During routine practice, dermatopathologists often ask referral physicians for clinical correlation (clinical pictures or presentation of patients) before making a histologic diagnosis of inflammatory skin disorders. Clinical information on histologic referral sheets is usually very limited. In addition, as more surgical biopsies are performed by physicians without formal dermatologic training, proposed clinical diagnoses are often imprecise, particularly concerning inflammatory diseases of the skin.

On the other hand, clinical images may be considered the "gross macroscopy" of dermatopathology, and morphology and distribution of lesions play a crucial role in the evaluation of a cutaneous histopathologic specimen.[1]

Digital photography has transformed the world of photography; digital pictures can be sent easily per e-mail or be stored and forwarded on other electronic media. A digital camera is available in the vast majority of dermatological practices or other medical offices. Particularly for pigmented skin tumors, the feasibility of teledermatology has been successfully evaluated in several studies, even with the use of cellular phone–based cameras.[2-6]

The current study was performed to verify whether the evaluation of clinical pictures increases the accuracy of dermatopathologic diagnosis of inflammatory skin disorders.

CAPSULE SUMMARY

- Clinical information on histologic referral sheets is usually very limited.
- Histopathologic diagnosis of inflammatory skin disorders is improved by review of clinical pictures.
- Clinical pictures should be added to biopsy request slips of inflammatory skin disorders whenever possible.

MATERIAL AND METHODS

Design of the study

One-hundred cases were selected from the files of the Research Unit Dermatopathology of the Department of Dermatology, Medical University of Graz, Austria. Cases represented 99 inflammatory skin disorders and one example of early-stage mycosis fungoides, a typical simulator of inflammatory dermatoses. Cases were selected as follows: all cases of inflammatory skin disorders for which clinicopathologic correlation was necessary to make a definitive diagnosis (mentioned in the histologic report) were retrieved for the period 2001 through March 2008. To have the widest spectrum of inflammatory disorders, only the most recent case of a given entity was included, with the exception of peculiar clinicopathologic variants (eg, both pustular and plaque-type psoriasis were included). A total of 1811 cases matched these criteria (total number of biopsies in the same period: 416,048; estimated number of biopsies of inflammatory skin disorders: 45,000). Cases with insufficient biopsy specimens, cases without or with bad clinical pictures, cases in which clinical pictures were not synchronous with the biopsy, and cases without unequivocal final diagnosis were excluded.

The "gold standard" for evaluating diagnoses was represented by the final diagnosis made at the Department of Dermatology in Graz, which was based on clinical and histopathologic features, complete laboratory analyses, results of ancillary studies such as immunohistochemistry or immunofluorescence analyses, clinical history, and follow-up data.

All biopsy specimens were digitalized at the highest resolution (40×) by using the Aperio ScanScope system, and were stored on 3 DVDs along with the clinical information as available on the original biopsy request slips. Clinical images (one or two per case) were included in a separate folder. We decided to limit the number of clinical images to one or two to have a setting easily reproducible in routine practice. In all images, patients were rendered unidentifiable.

All cases were evaluated by 9 independent full-time dermatopathologists with different backgrounds (dermatology or pathology). Evaluation of the 100 cases took place as follows: digital slides were first studied with knowledge of the clinical information provided, but without looking at the clinical pictures. Each observer gave a main diagnosis, a maximum of 5 differential diagnoses, and the "level of confidence" of the main diagnosis (expressed according to a scale from 0 to 100, with 100 representing a "completely confident" diagnosis, whereas 0 represented a total lack of confidence). The same process was then repeated after checking the clinical pictures. All diagnoses were finally compared with the "reference" diagnosis and the results were statistically analyzed. A diagnosis was considered correct only if it was specific. For example, "lichenoid dermatitis" was not considered correct in a case of lichen planus, and "vasculitis" was not considered synonymous for "livedo vasculitis". In fact, the aim of the study was to check whether the addition of clinical pictures could allow dermatopathologists to avoid using generic terms such as those just mentioned and, instead, to generate specific diagnoses.

The original clinical descriptions and/or diagnoses included on the biopsy request slips and in the clinical data provided to the observers in this study were provided by a very heterogeneous group of physicians, including general practitioners, general surgeons, dermatology residents, and dermatologists in private practice (usually with main focus on dermatologic surgery).

Statistical analysis

We used the McNemar test for the comparison of paired proportions. A paired *t* test was used for the comparison of confidence levels with and without clinical information. For this type of analysis we used only those cases in which a correct diagnosis was made. All given *P* values are two tailed and a *P* value

Table I. Summary of results stratified according to the different dermatopathologists

Observer	Correct DG (−)	Correct DG (+)	Change wrong DG (−) to correct	Change correct DG (+) to wrong	*P* value (Correct DG [−]/[+]), change DG	Change No. of DD in correct DG (−/+)	*P* value (change in No. of DD in correct DG)	Change LC in correct DG (−/+)	*P* value (change of LC in correct DG)
1	31	58	29	2	<.001	2.58-.68	<.001	7.9-89.3	<.001
2	21	50	31	2	<.001	0.67-0.14	.005	73.6-92.4	<.001
3	46	59	15	2	.004	0.80-0.26	<.001	43.8-85.0	<.001
4	44	60	21	5	.003	0.75-0.20	<.001	82.9-96.0	<.001
5	49	61	12	0	.002	0.20-0.06	.049	64.9-85.7	<.001
6	25	44	19	0	<.001	0.80-0.20	.0014	79.6-94.8	<.001
7	35	44	12	3	.04	0.94-0.14	<.001	73.7-94.5	<.001
8	42	51	14	5	.07	1.50-0.43	<.001	69.7-81.5	<.001
9	39	54	20	5	.001	Np	Na	Np	Na
Total	332	481	173	24	<.001	1.03-0.26	<.001	70.1-89.9	<.001

DD, Differential diagnoses; *DG*, diagnosis; *LC*, level of confidence; *Na*, data not available; *Np*, data not provided.
Correct DG (−): Number of correct diagnoses before evaluation of clinical pictures.
Correct DG (+): Number of correct diagnoses after evaluation of clinical pictures.
Change wrong DG (−) to correct: Number of cases for which, after evaluating the clinical pictures, a wrong diagnosis has been changed to the correct one.
Change correct DG (+) to wrong: Number of cases for which, after evaluating the clinical pictures, a correct diagnosis has been changed to the wrong one.
P value (correct DG [−]/[+], change DG): Statistical analysis of correct diagnoses before and after evaluation of clinical pictures and of number of diagnoses changed from wrong to correct or from correct to wrong.
Change of number of DD in correct DG (−/+): Change of number of differential diagnoses in cases for which the correct diagnosis had been established before evaluating the clinical pictures.
P value (change in number of DD in correct DG): Statistical analysis of change of number of differential diagnoses in cases for which the correct diagnosis had been established before evaluating the clinical pictures.
Change of LC in correct DG (−)/(+]): Change of level of confidence in cases for which the correct diagnosis had been established before checking the clinical pictures.
P value (change of LC in correct DG): Statistical analysis of change of level of confidence in cases for which the correct diagnosis had been established before checking the clinical pictures.

less than .05 was regarded to indicate statistical significance.

RESULTS

A summary of the results is provided in Tables I and II. One participant did not provide data on differential diagnoses and level of confidence. All other 8 observers provided complete data. There were no clear-cut differences between dermatopathologists with different backgrounds in dermatology or pathology.

The majority (≥ 5) of the dermatopathologists made the correct diagnosis in 32 and 54 cases before and after evaluation of the clinical pictures, respectively. After evaluation of the clinical pictures, the number of dermatopathologists making a correct diagnosis was increased in 70 cases, unchanged in 25 cases, and decreased in 5 cases. The total number of correct diagnoses increased from 332 (diagnoses before evaluation of clinical pictures) to 481 (diagnoses after evaluation of clinical pictures), with an increase of 149 correct diagnoses representing 16.6% of the total. After clinical pictures were checked, 173 wrong diagnoses were changed to the correct ones, whereas 24 correct diagnoses were changed to wrong ones. These differences are statistically significant ($P < .001$).

Both the number of differential diagnoses and the level of confidence improved for all dermatopathologists after evaluation of clinical pictures (decrease in the number of differential diagnoses from 1.22 per case to 0.44 per case and increase in the mean level of confidence from 61.8 to 80.8). Of more interest, in cases in which the correct diagnosis was made before evaluation of the clinical pictures, the number of differential diagnoses decreased in a statistically highly significant way after their evaluation ($P < .001$). In a similar way, the level of confidence of diagnoses that were correct before checking the clinical pictures increased after their evaluation ($P < .001$). Interestingly, in cases in which the histopathologic diagnosis was correct before the clinical pictures were evaluated, the number of differential diagnoses and level of confidence were better both before and after checking the clinical images.

Physicians referring the 100 biopsy specimens included in this study provided a correct clinical diagnosis (mostly mentioned with other differential

Table II. Total number of cases diagnosed correctly before and after evaluation of clinical pictures, stratified according to the number of observer making the correct diagnosis and compared to the correct clinical diagnoses mentioned on the referral sheets

No. of observers	Total No. of cases with correct diagnosis *before* clinical evaluation*	Total No. of cases with correct diagnosis *after* clinical evaluation*
9	3 (2)	7 (5)
8	4 (3)	9 (6)
7	7 (4)	22 (8)
6	10 (3)	8 (4)
5	8 (6)	8 (1)
4	9 (4)	12 (4)
3	13 (3)	11 (2)
2	17 (3)	10 (0)
1	15 (2)	5 (0)
0	14 (0)	8 (0)

*No. of cases with correct clinical diagnosis mentioned on referral sheet shown in parentheses.

diagnoses) in 30 cases; only a clinical description or a wrong clinical diagnosis was provided in 19 and in 50 cases, respectively, and one referral sheet was not filled out at all (data on correct diagnoses are summarized in Table II).

DISCUSSION

In patients with inflammatory dermatoses, skin biopsies are usually performed to confirm clinical diagnosis. However, the dermatological skills of physicians performing skin biopsies is highly variable, ranging from experienced dermatologists (who will likely choose biopsy mostly for cases that are unclear clinically) to residents and general practitioners, among others. Non-dermatologists are more likely to misdiagnose skin diseases than are dermatologists.[7] Particularly when physicians are less experienced, the level of clinical description and diagnosis provided on the biopsy request slips may be very poor. It is a common experience among dermatopathologists worldwide that referral sheets are mostly incompletely completed (when they are filled out at all) and that in most cases the quality of information provided is poor. In fact, in the group of 100 biopsies included in this study, the correct clinical diagnosis was mentioned with other differential diagnoses on the referral sheet of only 30 cases. The need for appropriate clinical correlation and clinical images has already been underlined.[8,9] Recently, the usefulness of clinicopathologic correlation for the histopathologic diagnosis of melanocytic skin tumor was demonstrated,[3,6] and it was suggested that all biopsy specimens of clinically difficult pigmented lesions should be assessed histopathologically with knowledge of the clinical picture.[10] In this context, we stress that dermatopathology is macroscopic and microscopic pathology of the skin, and that evaluation of clinical presentation (macroscopy) represents a crucial step in the diagnostic process.[1] In fact, a study by Massone et al[11] using virtual histological slides of 46 cases from daily routine suggested that lack of clinical information hinders a proper diagnosis in a distinct proportion of cases of inflammatory skin conditions; Berman, Elgart, and Burdick[12] demonstrated that inclusion of clinical history improves the histologic diagnosis made using virtual microscopy.

The cases included in this study represent a small proportion of all cutaneous biopsies, but highlight a common problem in the histopathologic diagnosis of inflammatory skin disorders. Although during the period of this study the need for clinicopathologic correlation was specifically mentioned in the histopathologic report only in approximately 4% of all biopsies of inflammatory conditions, in the majority of the histologic reports of inflammatory skin disorders a spectrum of differential diagnoses is usually provided, even if the need of clinicopathologic correlation is not always explicitly mentioned. Our results clearly indicate that evaluation of clinical pictures significantly improves the accuracy of histopathologic diagnoses in this particular field of dermatopathology. There were no clear-cut differences between dermatopathologists with different backgrounds in dermatology or pathology, indicating that full-time dermatopathologists benefit from the possibility of evaluating clinical pictures regardless of their original field of specialty training.

Even in cases in which a correct histopathologic diagnosis was made without knowledge of the clinical features, the level of confidence of dermatopathologists clearly increased, and the number of differential diagnoses decreased, implying a decrease in the number of additional investigations that would be required for establishing a final diagnosis (eg, ancillary techniques such as special stains, immunohistology). In a similar way, a decrease in the number of differential diagnoses means less need of further investigations (eg, re-biopsy, immunofluorescence studies). This, of course, implies a decrease in the costs of management for a given patient, one of the main limiting factors in modern medicine. This aspect is even more important if we consider that the costs of providing clinical pictures is limited, as small, inexpensive cameras can be used for taking pictures of thousands of patients, and most storage media can

be reutilized an unlimited number of times (taking and organizing pictures, however, costs additional time for physicians or other staff).

Of course, we are aware that a study such as this one has some limitations. First of all, evaluation of digital histopathologic sections is not the same as evaluation of routine specimens at the microscope. Similarly, evaluation of clinical pictures is not equal to clinical examination of a patient. In addition, clinical pictures represent a "frozen moment" in the life of lesions of dermatological disorders and do not give information about their evolution. However, the high resolution of digital histopathologic sections is considered sufficient for digital consultations and for organization of self-assessment courses or similar didactic activities, and digital pictures are used routinely to illustrate clinical features of skin diseases at hundreds of scientific meetings. Feasibility of virtual histologic slides for diagnosis of different pathologic conditions, including inflammatory skin disorders, has been demonstrated in several studies.[11-18] In a study by Koch et al,[19] residents in dermatology or pathology performed similarly when making histopathologic diagnoses of skin diseases using either the conventional or the virtual microscope, although subjectively they liked the first one better. In our study, the dermatopathologists performing this study did not complain about the quality of digital sections or pictures. Another limitation consists in the impossibility of cutting additional sections of tissue or in the ability to perform additional stains. Finally, we would like to emphasize that our study included only cases that were histopathologically difficult, and for which the need for clinicopathologic correlation for a proper diagnosis was mentioned in the histopathologic report. Some of these entities represented skin diseases for which histopathologic analysis does not provide crucial diagnostic information. These diseases undergo biopsy almost exclusively by physicians without sufficient experience in dermatological disorders (mostly young residents and general practitioners); nonetheless, these cases, too, represent a diagnostic challenge for dermatopathologists sitting at the microscope. All of these limitations, as well as the intrinsic difficulties associated with histopathologic diagnosis of cutaneous inflammatory disorders,[11,20] probably account for a score lower than expected by the 9 dermatopathologists. On the other hand, even considering the limiting factors just mentioned there was a statistically highly significant improvement in the number of correct diagnoses, number of differential diagnoses, and level of confidence, thus showing that even under these conditions, the addition of clinical pictures clearly helps in making a better histopathologic diagnosis of inflammatory skin disorders. Interestingly, all cases in which none of the 9 observers in our study made the correct diagnosis were referred with a wrong clinical diagnosis as well (Table II), thus underlining once again that, in order to make histologic diagnoses of inflammatory skin diseases, in assessing histopathologic criteria, dermatopathologists also rely on clinical information.

We believe that our study confirms common sense, clearly showing that clinical pictures should be added to biopsy request slips of inflammatory skin disorders whenever possible, as they are an integral part of dermatopathology (macroscopic dermatopathology). Dermatopathologists, on the other hand, must be conversant with clinical presentation of inflammatory skin disorders, a notion that is already an integral part of the curriculum for board certification in dermatopathology in different countries.

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