Significance of Single Vs Multiple Skin Biopsies

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Skin biopsy is an important investigation but the results are not always conclusive. Our aim was to evaluate the diagnostic value of single and multiple skin biopsies in dermatological diseases. The study was prospective and comparative. We examined 798 skin biopsies in 572 patients. Biopsy was taken from one or more sites and fixed, processed, sectioned and stained. Diseases with diagnostic histopathology were evaluated and the percentage of patients in whom a biopsy was taken from a single or multiple sites was calculated. Biopsies were taken from 310 males and 262 females, aged between three to eighty years. Histopathology was diagnostic in 66.6%, 78.6% and 90.9% patients when one, two or three biopsies, respectively, were taken. The difference between one and two biopsies was highly significant, especially in autoimmune bullous diseases and lichen planus. In eczemas, cutaneous tuberculosis, sarcoidosis and lupus erythematosus there was no significant difference when biopsy was taken from one or two sites. Skin biopsies from two sites yield better histopathological results than a single biopsy, especially in autoimmune bullous diseases and lichen planus. Single biopsy is sufficient in eczemas, tuberculosis, sarcoidosis and lupus erythematosus. Larger sample size is required to know the significance of three biopsy sites.
Key Words:Skin biopsy, Multiple skin biopsies, Significance

Microscopic examination of skin is the most important laboratory investigation used by the dermatologists for diagnostic and management purposes. All lesions cannot be definitely diagnosed by this method. Many a time histopathological features are suggestive rather than diagnostic of the clinical disease. In other cases they may even be non-specific. Multiple skin biopsies may be helpful when a biopsy taken from a single site is inconclusive[1,2,3,4].

Our aim was to evaluate the diagnostic value of skin biopsies when they were taken either from a single or from multiple sites, and to know their significance in various groups of dermatological diseases.

Patients and methods

Between February 2000 and December 2001, seven hundred and ninety eight skin biopsies performed in 572 patients were examined in the Department of Dermatology, King Edward Medical College/Mayo Hospital, Lahore. Age, sex, clinical history and examination along with a provisional diagnosis or a differential diagnosis was provided in each case. Biopsy sites were chosen by the clinical dermatologist with an experience in dermatopathology (Ist author) in each case. In every patient either one site or more than one site (2 or 3) were marked. Three sites were only chosen if the disease manifested variable features in the same person. After an informed consent, a punch (4 m.m) or an elliptical skin biopsy was taken from the marked sites. The biopsy specimen was fixed in 10% formalin, processed, sectioned and stained with haematoxylin and eosin. Special stains like periodic acid-Schiff (PAS), Gram's, Ziehl Neelsen, Giemsa and Congo Red were used whenever required in special circumstances. The microscopic findings were recorded in the histopathological section of the Dermatology Department, King Edward Medical College/Mayo Hospital, Lahore. The findings were reconfirmed by the histopathologists at the pathology department of King Edward Medical College, Lahore.

A biopsy report was considered to be diagnostic when it revealed typical features of a disease or if the features correlated with the provisional clinical diagnosis or one of the given differential diagnoses. It was not regarded as diagnostic if non-specific findings were seen or if the histopathological details could be a feature of more than one skin disease and were not conclusive.

The results of skin biopsies were placed in different groups in two stages. In the first stage, the number of patients with diagnostic histopathological report was separated from those patients with non-specific or inconclusive report. Those with a diagnostic report were subdivided, depending upon the number (one, two or three) of skin biopsies performed in these patients. In the second stage, those diseases or groups of diseases were analyzed in which histopathology was diagnostic. In each disease we calculated the percentage of patients in whom a biopsy was taken from a single site and the percentage of cases in whom the biopsies were taken from two or three different sites.

All the collected data was tabulated and analyzed in a database. Where appropriate, statistical analysis was made using Fisher's exact test.

Results

Skin biopsies were taken from 310 males and 262 females, aged between three to eighty years. Table I shows number and percentage of patients in which histopathology was diagnostic when skin biopsy was taken from one, two or three sites. Statistical analysis revealed that when skin biopsies were taken from two sites instead of one, the difference in histopathology results was highly significant ($p < 0.003$), while the difference between the results of two and three biopsy sites, respectively, was not significant ($p > 0.1$).

Results of various diseases when skin biopsy was taken from one or two sites are shown in Table-II. The table does not include naevi, benign tumours and miscellaneous diseases, where the number of patients in each disorder varied between one and five and only a single biopsy was taken in almost all the cases. Autoimmune bullous disorders and lichen planus showed highly significant difference ($p<0.01$ and 0.001 respectively) when biopsies were taken from two sites instead of one. In eczemas, cutaneous tuberculosis, sarcoidosis and lupus erythematosus there was no significant statistical difference ($p>0.3$, 0.05, 0.4 & 0.8 respectively) between the histopathological results of one and two skin biopsies. In psoriasis, squamous and basal cell carcinomas and mycosis fungoides, statistical difference was again not significant ($p > 0.2$ in psoriasis and > 0.1 in others).

Diseases in which biopsy was taken from three sites include a wide variety of disorders like eczema, lichen planus, lichen nitidus, lupus erythematosus, infections (leprosy, syphilis and leishmaniasis), autoimmune bullous disorders (pemphigus and dermatitis herpetiformis), psoriasis, prurigo, leucocytoclastic vasculitis, panniculitis, necrobiosis lipoidica and keloid. One case with a differential diagnosis of syphilis, drug rash and psoriasis showed interface dermatitis on histopathology while another patient with a provisional diagnosis of actinic reticuloid gave a non-specific picture on microscopy

Table I. Diagnostic histopathology in single and multiple skin biopsies

Skin biopsy sites	Number of Patients	Patients with diagnostic histopathology n(%)
One	368	245(66.6)
Two	182	143(78.6)
Three	22	20(90.9)

Table II. Diagnostic histopathology in different diseases in patients with one and two skin biopsies

Diseases	Patients with single biopsy n	Diagnostic histopathology n(%)	Patients with two biopsies n	Diagnostic histopathology n(%)
Eczemas	28	26(92.86)	15	13(86.86)
Cutaneous tuberculosis	31	27(87.09)	12	7(58.33)
Sarcoidosis	13	13(100)	17	15(88.23)
Deep mycoses	6	3(50)	6	2(33.33)
Lichen planus	15	11(73.3)	12	12(100)
Lupus erythematosus	19	15(78.9)	6	5(83.3)
Autoimmune bullous diseases	67	45(67.16)	16	16(100)
Prurigo	5	5(100)	8	8(100)
Psoriasis	13	5(38.4)	9	6 (66.6)
Pityriasis rubra pilaris	3	1(33.33)	7	4(57.14)
Vasculitis	19	19(100)	-	-
Squamous cell carcinoma	10	5(50)	3	3(100)
Basal cell carcinoma	12	7(58.3)	2	2(100)
Mycosis fungoides	9	3(33.33)	3	3(100)

Discussion

Skin biopsy examination under a light microscope has always been an important diagnostic tool used by the physician in the management of dermatological diseases. Expectations of receiving a histopathological results which is diagnostic or at least helpful in making a decision are high. It is not always possible to meet these expectations. Many a time the histological picture of a disease shows non-specific features or does not correlate with the clinical findings[5]. There could be many possibilities for this lack of clinico-pathological correlation. The biopsy sample may not be a true representation of the active disease process, or the disease may be in its different phases of evolution or may be partially treated. The biopsy site chosen may be inappropriate. Another possibility of inability to reach a conclusive diagnosis may be lack of representation of the histological sections cut from the biopsy tissue[6]. Adequate

clinical information is also pertinent for a correct histological diagnosis.

In our study, we took measures to minimize the possibilities that could lead to a lack of clinico-pathological correlation. Every patient was seen by the first author to mark the biopsy site. Clinical information was evaluated. Treatment was withheld, whenever possible, if it could mask or change the histological features. In case of lack of any change in the microscopic features of skin tissue, it was cut again and another section made.

Usefulness of multiple skin biopsies have been mentioned in various diseases in different studies[1,2,3,4]. At times, repeated biopsy samples are required to reach a conclusion[1,7]. Our study reveals that when skin biopsies were taken from two sites instead of one, they were diagnostic in a greater percentage of patients and the difference was statistically highly significant ($p<0.003$). The reason for this disparity may be that the tissue is not the true representative of the active disease process at the microscopic level. Only those biopsy tissues were recut that lacked any microscopic changes. One may need to make many sections to increase the chances of getting a positive result[6]. When reports of biopsy taken from three sites were compared with those taken from two sites, the difference was not statistically significant ($p> 0.1$). This appears to be due to the small sample size in the former case. We may need to study larger number of patients with three biopsy sites to ensure that this lack of difference is genuine or not.

Analysis of different groups of diseases revealed that in cases of eczemas, cutaneous tuberculosis, sarciodosis and lupus erythematosus, it did not matter whether biopsy was taken from a single site or two sites because the difference in results was not statistically significant. It can also be seen (table II) that all the cases of prurigo and vasculitis could be diagnosed on histopathology. In all the above mentioned diseases, appropriate selection from a single site should suffice. In cases of psoriasis and the malignant tumours like squamous and basal cell carcinomas and mycosis fungoides, again there was no statistically significant difference whether the biopsy was taken from one or more sites. But since the number of patients was small, a larger number of cases are required to know the real value of this observation.

In autoimmune bullous diseases and lichen planus when biopsy was taken from two sites, the chances of a diagnosis on histopathology increased significantly. This difference could be due to various reasons. Difficulty in diagnosis arises when the roof of a blister is damaged during the biopsy procedure or processing. If a fresh blister is not available at the time of biopsy, the location of the vesicle may also change during its evolution. Secondary infection also creates problem at times. Therefore single biopsy in case of a bullous disorder might be less fruitful than multiple ones. Lichen planus shares its different histopathological features, like basal cell degeneration, lymphocytic infiltrate and colloid bodies, with other diseases. Multiple biopsies may increase the chances of manifesting greater number of features which together are specific for lichen planus and rule out other diseases. We need more studies to see whether multiple skin biopsies in individual diseases or groups of diseases can produce better results or not.

Conclusion

Multiple skin biopsies generally yield better histopathological results than single biopsies. Skin biopsy from a single site is sufficient in reaching a diagnosis in cases of eczema, cutaneous tuberculosis, sarcoidosis and lupus erythematosus. In autoimmune bullous diseases and lichen planus, a biopsy taken from two sites significantly increases the chances of reaching a diagnosis on histopathology. To know the diagnostic significance of three biopsy sites, a larger number of patients need to be studied.

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