Clinico-pathological evaluation of non-neoplastic and neoplastic skin lesions: A study of 100 cases

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Abstract

Introduction: Skin is the largest organ among all the organs of the body. The clinical manifestations of diseases of skin are vary in nature both in clinical presentations and behavior. It is necessary to cross talk between pathologist and dermatologist for better management of patients. Histopathological examination plays a significant role and the gold standard in providing accurate diagnosis for a variety of skin lesions.

Objective: 1. To evaluate histopathology as an ideal diagnostic method for vesiculobullous (non–neoplastic) and neoplastic (tumourous) skin lesions. 2. To establish the correlation between the microscopic pathological findings of various skin lesions with the presenting clinical features.

Materials and Methods: 100 patients of skin diseases were included for the study. Punch, excisional or incisional biopsy techniques were used to get the tissues. The tissue was obtained for detailed histopathological examination. The histological sections were stained with hematoxylin and eosin stains and histochemical stains were used as supplementary diagnostic tool.

Results: Out of 100 patients, 54% had vesiculobullous lesions, 22% granulomatous morphology and 24% were neoplastic. Epidermoid cysts included in benign neoplasm category and accounted for 37.5% of neoplasms. Squamous cell carcinoma was the most common malignant tumor (52.8%).

Conclusion: Histopathological study of skin biopsies helps to make an early and accurate clinically useful diagnosis in almost all of the normal looking or vesiculobullous or non neoplastic and neoplastic skin lesions, as the study of microscopic morphological features of different types of skin lesions had differentiating findings under the microscope.

Keywords: Vesiculobullous lesions, Histopathology, Pemphigus, Herpes.

Introduction

The skin is the largest organ of the body, comprising of Epidermis, dermis and hypodermis. Epidermis contains superficial lining epithelium. Dermis contains loose areolar tissue, blood vessels, sweat glands, sebaceous glands and root of hair follicles. Hypodermis contains mainly adipose tissue. Skin has important functions to perform like protection, temperature regulation and also metabolic. Among the out patients the patients with skin ailments form significant numbers and they constitute more numbers of hospital cases. They arise from the normal histological constituents of the skin. Different skin diseases comprise of non-specific, non infectious and infectious diseases to various types of benign and malignant tumorous (neoplastic) lesions. Vesiculobullous skin lesions are always the cause of concern to patients, clinicians and pathologists. Pemphigus vulgaris is an uncommon disease which is autoimmune in nature, but the most common among pemphigus group of skin diseases. Skin biopsy forms the fundamental basis for differentiation of similarly looking dermatological disorders and lesions, thereby giving valuable information to the pathologists to make a definitive diagnosis and more so to the dermatologist for better management of patients. Cytopathology is a good option in the outpatient dermatological practice,[1,2] but has many shortcomings. Cytological examination of vesiculobullous lesions of skin is generally done with Tzanck smears. The slides are stained by Giemsa, MGG, Leishmann or PAP stain. The morphology of the cells is studied with respect to size and shape of the nucleus, inclusions in the nuclei, multinucleation or hyperchromatism. The tumourous lesions of the skin are examined cytologically by FNAC technique with the help of MGG, H&E or PAP stain.

Clinical diagnosis alone may not be conclusive many a times and histopathology becomes a prime requisite for the definite diagnosis. Therefore this study was designed to evaluate histopathology as an accurate diagnostic method for different types of non- neoplastic and neoplastic lesions of the skin and to correlate the clinical and histopathological findings of various skin lesions.

Materials and Methods

A total of hundred cases with different types of clinical presentations of various skin lesions were selected for the study. The study was conducted at Department of Pathology RIMS, Raichur. Basic fundamental routine protocol was followed. A complete detailed history of the patients was taken down. Tzanck smears were prepared and stained. Various technical types of biopsies were done like incisional and excisional biopsies, so as to get the adequate tissues for morbid anatomy and histology lab processing, followed by microscopic examination. Thin 4 micron sections were taken and stained with hematoxylin and eosin (H and E) and with special stains as desired, like ZN stain. Histopathological diagnosis arrived was correlated with the clinical diagnosis.

Results

A total of 100 cases were studied, out of which 60% were male and 40% were female (Table 1). On microscopic study, 54% of cases were non neoplastic; 22% granulomatous lesions and 24% neoplastic lesions (Table 2). Histopathological examination of the tissue was done so as to arrive at a definitive diagnosis.

Table 1: Gender incidence of skin lesions

No. of cases	Male	Female
100	60	40
%	60	40

Table2: Types of skin lesions

Type	Percentage
Vesiculobullous	54%
Granulomatous	22%
Neoplastic	24%
Total	100%

In the present study, out of 54 cases of vesiculobullous lesions, 11 patients (20.3%) had herpes simplex infection; 14cases (25.9%) herpes zoster, 8 patients (14.8%) reported with molluscum contagiosum; 17 cases (31.4%) of pemphigus and 4 patients (7.4%) had bullous impetigo. Mean age of presentation was 23.5 years for herpes simplex and 42years for herpes zoster.

Patients with herpes simplex and herpes zoster infections presented to the OPD with chief complaints of painful irritant vesicular or bullous or combined lesions with a surrounding area which is erythematous and red with the history of short duration which averaged from two to seven days. Patients with herpes infections showed microscopic features of ballooning degeneration, multi- nucleated giant cells with irregular borders and bland or pale eosinophilic inclusion bodies containing nuclei, all of them molded into each other. Intraepidermal bullae filled with serous or clear fluid containing epithelial cells having intranuclear or intracytoplasmic inclusions, ballooning degeneration, cells with pale eosinophilic inclusion bodies in the cytoplasm were also detected. Seven patients with molluscum contagiosum were studied. On clinical examination the lesions were discrete, firm in consistency and papular with umblicated centers. Histopathological examination revealed acanthosis, hyperkeratosis and parakeratosis with cells having intracytoplasmic pale eosinophilic inclusion bodies were seen.

Patients with pemphigus vulgaris presented with bullous lesions present chiefly on the trunk and majority had mucosal involvement. Nikolsky sign was positive. Tzanck smears obtained from 17 cases of pemphigus showed free squamous cells (acantholytic) cells in small clusters or as single cells having hyperchromatic nucleus along with few giant cells. Histopathological examination revealed the important feature of suprabasal and intraepidermal bullae in Pemphigus vulgaris (14 cases) and Pemphigus foliaceous showed subcorneal and or intraepidermal bullae (3 cases). Bullous pemphigoid was seen in 4 children. The microscopic study revealed subcorneal pustules having many neutrophils with abscesses (microabscess) (Table 3).

Table 3: Types of non-neoplastic lesions

S. No.	Types of lesion	No. of cases	Percentage (%)
1	Herpes simplex	11	20.3
2	Herpes Zoster	14	25.9
3	Mollucum contagiosum	8	14.8
4	Pemphigus vulgaris	14	25.9
5	Pemphigus foliaceous	3	6.5
6	Bullous pemphigoid	4	7.4

Table 4: Types of Granulomatous Lesions

Type of lesion	No. of cases	Percentage (%)
Lupus vulgaris (tuberculosis)	12	58.2
Leprosy	10	41.8

Granulomatous skin lesions (Table 4) comprised of tuberculosis and leprosy. Out of the 24 cases, tuberculosis of skin (lupus vulgaris) was identified in 12 cases and leprosy in 10 cases. Clinically the patients presented with long standing non healing ulcers, nodular lesions or ulcerated plaques of long duration. Five of them gave past history of pulmonary tuberculosis. None of the patients gave any history with regard to exposure to an active leprosy case. Histopathological examination showed granulomas comprising of epitheloid cells, histiocytes, lymphocytes, fibroblasts with or without central caseation necrosis. Four of the sections were stained with ZN and were positive for acid fast bacilli (AFB) by ZN stain. Leprosy (Hansen's disease) cases were classified mainly as tuberculoid and lepromatous.[4] Seven cases showed features of tuberculoid leprosy and 3 of them lepromatous leprosy.

Table 5: Types of neoplastic lesions

Type of tumor	No of cases	Percentage (%)
Benign neoplasm	9	37.5
Malignant neoplasm	15	62.5

Neoplastic lesions (Table 5) were found in 24 cases. Epidermoid cysts were included in benign neoplasm

category as above. Clinically, patients presented with history of round to oval elevated or subcutaneous nodules, soft to firm in consistency measuring two to ten cms in size. Nine of the 24 neoplastic lesions were diagnosed as epidermoid cysts. Histopathological examination showed cyst wall lined by stratified squamous epithelium with the lumen showing keratin debris. Some of them showed mild to moderate acute and chronic inflammatory cells infiltrate. Malignant or cancerous lesions were seen more commonly in elderly population. Of the 15 malignant tumors there were 2 patients with malignant melanoma, 4 patients with basal cell carcinoma (BCC), 8 patients manifested with squamous cell carcinoma (SCC) and one patient with sebaceous glandular carcinoma (SGC) (Table 6). Clinically all of them showed features of chronic non healing ulceronodular type of growth with irregular indurated borders or as hard nodular growth with exudate and hard indurated margins. Microscopic examination showed malignant squamous cells with pleomorphic, vesicular or hyperchromatic nuclei and clumped chromatin and with prominent nucleoli. There was loss of polarity and many typical as well as atypical mitoses were noted. They showed various degrees of differentiations. Majority were Grade 2 moderately differentiated lesions.

Table 6: Types of malignant tumors

Type of malignant tumor	No. of cases	Percentage (%)
Squamous cell carcinoma (SCC)	8	52.8%
Basal cell carcinoma	4	26.4%
Malignant Melanoma	2	13.2%
Sebaceous carcinoma	1	6.6%

Four patients presented with single ulcerated lesions with hard raised indurated borders. They were seen either on the cheek, forehead and eyelid. Histological sections showed nests of blue tumor cells. The cytoplasm was scant to moderate, moderately hyperchromatic nuclei. As routinely observed they showed peripheral clearing. At almost all places the tumor cells in the nests show peripheral perpendicular arrangement. A diagnosis of Basal cell carcinoma was confirmed. Two male patients reported to the OPD with the history of recently changed pigmented lesion on the lower limb. Lesions showed brown to black appearance due to melanin pigment with irregular raised borders. Clinically they were diagnosed as melanomas. Both the cases had positive inguinal lymph nodes on FNAC for metastatic deposits. FNAC smears showed pleomorphic cells with eccentric round to oval irregular vesicular nuclei with prominent nucleoli. Histologically atypical pleomorphic round and spindle shaped tumor cells were seen infiltrating into dermis. The tumor cells were highly pleomorphic with moderate pigmented cytoplasm. The nuclei were pleomorphic vesicular with prominent nucleoli. Another patient reported to the Dermatology OPD with a moderately large ulcerated multinodular variegated growth with discharge on the chest wall. The lesion was superficially infected with bloody purulent discharge. The histological sections revealed the features of sebaceous carcinoma. Pleomorphic tumor cells were arranged in sheets, nests and cribriform pattern. Cells had abundant slightly eosinophilic cytoplasm and some with clear vacuolated cytoplasm infiltrating into lower dermis with increased pleomorphism or variation in size and shape. The nuclei were large vesicular, having characteristically prominent nucleoli and typical as well as atypical mitotic figures.

Discussion

It is immensely important to systematically perform the task of careful assessment of biopsy specimen.[3,4] Here it was extensive and systematic evaluation of various diseases of skin with more emphasis on vesiculobullous lesions. The mean age incidence of herpes simplex in the present study was 23.5 years but other authors observed mean years of incidence to be one to five years[5,6] and ten to twelve years[7] by Sehgal and Dube.[8] Clinically they both had similar results. Differentiation of herpes simplex and herpes zoster was made mainly on clinical characteristics. This was supported by microscopic examination of H&E sections which approved the clinical findings in all cases.

Pemphigus vulgaris presents with oral lesions in 50-70% of patients, and almost all patients have mucosal lesions at some point in the course of their disease. Mucosal lesions may be the sole sign for an average of 5 months before skin lesions develop, or they may be the sole manifestation of the disease. The diagnosis of pemphigus vulgaris should be considered in any patient with persistent oral erosive lesions,[6] with positive Nikolsky sign.

Tzanck smears preparation must be done from fresh bullous lesions.[3,4] The Tzanck smear is an important diagnostic tool in the evaluation of blistering diseases. It is most commonly used to distinguish viral diseases, such as herpes simplex, varicella, and herpes zoster, from non-viral disorders. It is important to note that Tzanck smears from vesicles of vaccinia and smallpox do not demonstrate multinucleated giant cells.[9] The smear is obtained by removing the 'roof' of the blister with a curved scalpel blade or scissors, and scraping the base to obtain the moist, cloudy debris. The material is then spread onto a glass slide, air dried, and stained with Giemsa or Wright stain. The diagnostic finding of viral blisters is the multinucleated giant cell. The giant cell is a syncytium of epidermal cells, with multiple overlapping nuclei; it is much larger than other inflammatory cells. A giant cell may be mistaken for multiple epidermal cells piled on top of each other.[1,10]

The findings in pemphigus skin diseases were similar to those observed by Sehgal and Dube and Naib.[11] Twelve patients were diagnosed as having Pemphigus vulgaris and two patients had Pemphigus foliaceous. Similar to other study, molluscum contagiosum were very small lesions clinically, and histological sections revealed characteristic intracytoplasmic inclusions[12] (Molluscum bodies). They were treated by simple enucleation. In the present study twelve cases of tuberculosis of skin (lupus vulgaris) were

reported. Bhambhani et al[13] observed –large number of patients to be children below the age of ten years. In our study the mean age was observed to be seventeen years.

The common site of occurrence of the tuberculous skin lesions as reported by Bhambani et al.[13] and Savin[14] was on the face - 40% and 80% respectively. This proved to be in accordance with the present study –wherein we also observed majority of them on the face. Raghuveer et al.[15] in their study –also had similar observations. Farshcian and Kheirandish[16] observed the mean age to be 48.5 years. The mean age of ten cases of leprosy in the present study was 32.5 years. Microscopic findings were diagnostic of Leprosy. Majority were tuberculoid type of leprosy. Our study findings matched to those studied by Layfield and Glasgow.[17]

Malignant tumors of skin were found to be more common on face, as in our study and presented clinically as chronic non healing ulcer. These findings were correlated with those observed by Dracopoulou et al[18] and Allen.[19] Fifteen malignant tumors studied were squamous cell carcinomas. Basal cell carcinoma (rodent ulcer) lesions were also observed and all of them were present on the face. This observation was similar to the findings by Allen and Malberger et al.[19,20] Two cases of malignant melanoma were seen. The age of presentation correlated with the observation made by Hadju[21-23] who suggested an age group of 41-60 years. The mean age recorded in our study was 48.50 years. This was contradictory to the observation by Perry et al.[24] which was in younger adults. The difference may be because of environmental and genetic predispositions. Histopathological examination showed obvious features of malignant melanoma like large tumor cells with pleomorphic nuclei and prominent nucleoli. Intranuclear pseudoinclusions were seen by us in FNAC smears of inguinal lymph nodes as observed by Perry et al.[24,25]

The sebaceous carcinoma was observed on the chest wall by us. The site of occurrence of sebaceous carcinoma as observed by other authors is eyelid.[26]

Sebaceous Carcinoma of Skin is a very rare, malignant tumor of the arising from the sebaceous gland. They are thought to occur due to sun damage. Common locations are the head and neck region, followed by the trunk, arms and legs. However, the tumors are most frequently seen on the eyelids and hence the term Meibomian Gland Carcinoma is used at this location.[25] The treatment of choice for this malignant skin tumor is surgical intervention; however, there is a chance of recurrence. The prognosis is poor for metastatic Sebaceous Gland Carcinomas.[26]

Cutaneous Immunofluorescence Testing

Immunofluorescence (IF) tests can be performed on sera or tissues obtained in the physician's office.[1,5] The direct IF test is performed on skin or mucosal biopsy specimens. All biopsy specimens are examined for the presence of bound immunoglobulins (IgG, IgM, IgA), complement C3, and fibrinogen.[5] The indirect IF test is performed on serum to detect the presence of circulating antibodies.[26] IF testing is particularly useful for confirmation of the following: blistering diseases, connective tissue diseases, and vasculitis. IF tests may be diagnostic when dermatopathologic studies are only suggestive, nonspecific, or negative.[27,28]

Conclusion

Histopathological examination of diseases of skin is very much informative for proper and accurate diagnosis of non neoplastic and neoplastic lesions of skin. This can be supplemented with other advanced modalities like histochemistry, immunohistochemistry and immunoflourescence. IF testing can be used as a confirmatory diagnostic tool in addition to histopathology for the diagnosis of blistering diseases, connective tissue diseases, and vasculitis. IF tests may be taken into considered when dermatopathologic studies are nonspecific, suggestive or negative. It helps to make an early and accurate clinically useful diagnosis in almost all of them with clinco-pathological correlation which can not be overemphasized.

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