

Histopathological Spectrum of Vesiculobullous Lesions of the Skin: Study at a Tertiary Care Hospital

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ABSTRACT

Background: Vesiculobullous lesions are one of the predominant groups of skin lesions. They are the primary morphological patterns of skin reaction to various external and internal pathologic stimuli. Various types of pathologic processes can lead to development of vesiculobullous eruptions over body.

Methodology: This observational study was conducted in Department of pathology and department of dermatology. 72 patients who presented with vesiculo bullous lesions of skin not related to infectious aetiology were enrolled for the study. Clinical details and histopathological findings were analyzed.

Results: Pemphigus group of disease comprised the major proportion comprising 38 cases (52.9%), out of which 31 cases were pemphigus vulgaris (43.1%), 4 cases were pemphigus foliaceus (5.6%) and 3 cases were pemphigus vegetans (4.2%). Bullous pemphigoid was the second most common type and was found in 10 biopsies (13.9%).

Conclusion: Punch biopsy of the skin is a simple, inexpensive, safe OPD procedure, causing minimal discomfort to the

patient. Histopathological features are conclusive in majority of vesiculobullous lesions of skin; thus it forms the primary diagnostic modality in the management of such patients where the facility for immunofluorescence technique is not available.

Key word: Vesiculobullous, Skin Biopsy, Pemphigus, Blisters.


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INTRODUCTION

Vesiculobullous lesions are one of the predominant groups of skin lesions. They are the primary morphological patterns of skin reaction to various external and internal pathological stimuli. Various types of pathologic processes can lead to development of vesiculobullous eruptions over body. They may occur in many dermatoses, which include various inflammatory, infective, autoimmune, drug induced as well as genetic.¹

Vesicles and bullae are fluid filled cavities formed within or beneath the epidermis. Vesicles are less than 0.5 c.m. in diameter and bullae are blisters greater than 0.5 c.m. in diameter.^{2,3} They occur in all the layers of epidermis from stratum corneum to basal and sub-epidermal layers.

Blistering of skin is an obvious sign of disease & can be encountered in a wide variety of clinical settings in which vesicles or bulla are formed during the course of the disease e.g. dermatitis, burns, bullous impetigo, lichen planus etc. Some of these have an immunological mechanism. It is therefore necessary to diagnose & treat the condition early. Mortality and morbidity in various vesiculobullous lesions differ greatly; therefore accurate diagnosis is important. The diagnosis of these diseases is facilitated by use of battery of tests that includes histopathology,

immunofluorescence & electron microscopy. Using these techniques, it is possible to differentiate similar appearing bullous disorders.

Most commonly employed technique for diagnosis of vesiculobullous lesions is punch biopsy as it is safe, simple, inexpensive and minimally invasive OPD procedure without any major complications, causing minimal discomfort to the patient and no scarring. The greatest diagnostic accuracy is obtained by correlating the clinical and histopathological findings.^{4,5}

Thus present study was carried out to study histopathological changes in vesiculobullous disorder of the skin by light microscopy and to correlate clinical and histopathological aspects of vesiculobullous lesions of skin.

MATERIALS AND METHODS

In this study we have included 72 cases of vesiculo bullous lesions which were analyzed with clinical details and histopathological findings.

Only the lesions which showed vesicles and bullae clinically have been included in this study. The relevant clinical history and pathological findings were recorded.

All the patients were examined by dermatologist thoroughly before biopsy was performed. Biopsies were carried out under aseptic conditions under local anaesthesia with or without sedation.

The obtained biopsies were then gently fixed overnight in 10% neutral buffered formalin solution, processed and slides were prepared.

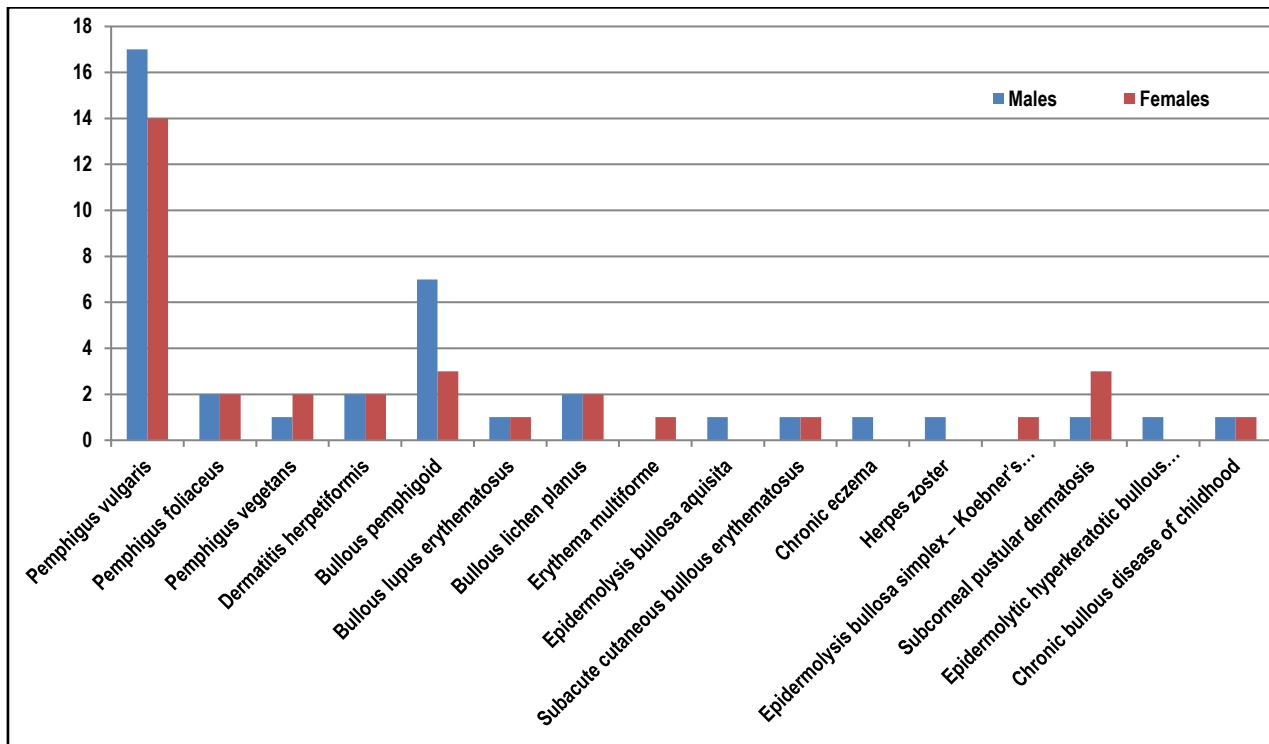


Fig 1: Frequency And Gender Distribution of Various lesions In Study

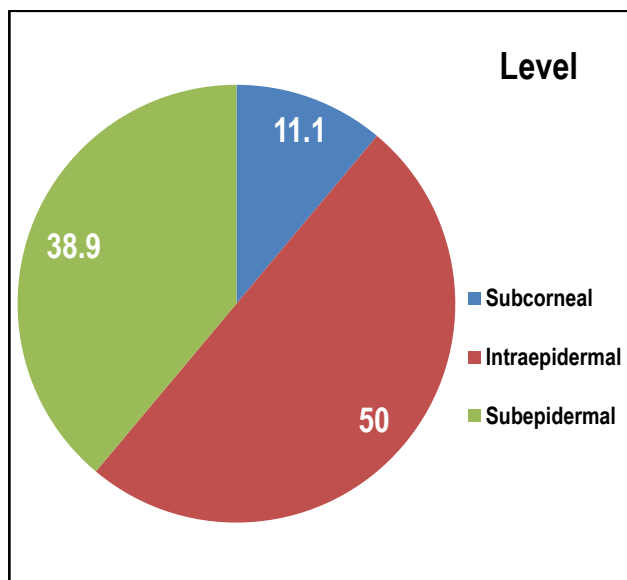


Fig 2: Biopsy finding with respect to level of separation

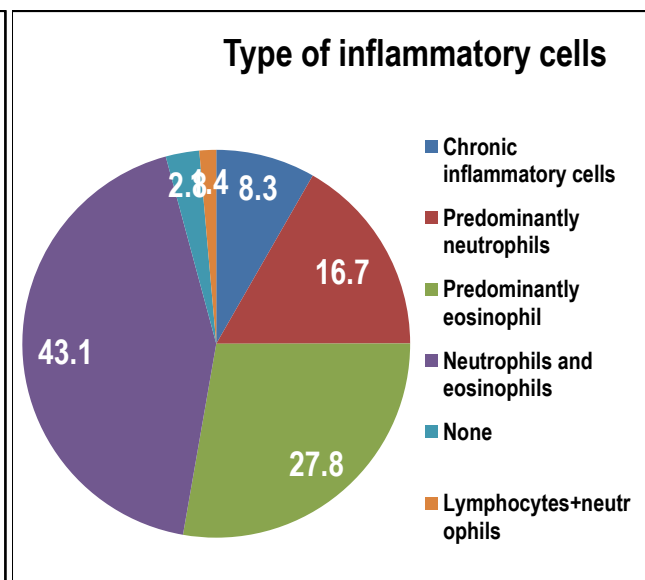


Fig 3: Biopsy finding with respect to predominant type of inflammatory cells

OBSERVATIONS AND RESULTS

In the present study of 72 skin biopsies obtained from the patients, who were clinically known to be non-infectious, Pemphigus group of disease comprised the largest group comprising of 38 cases (52.9%), out of which 31 cases were pemphigus vulgaris (43.1%), 4 cases were pemphigus foliaceus (5.6%), 3 cases were pemphigus vegetans (4.2%). Bullous pemphigoid was the second most common type and was detected in 10 biopsies (13.9%). [Fig 1]

In the present study, there was a slight male predominance with 39 (54.17%) males and 33 (45.83%) females with overall male to female ratio 1.18:1. Pemphigus vulgaris and bullous pemphigoid were found most commonly in males whereas cases of subcorneal pustular dermatosis, pemphigus vegetans and Erythema multiforme were commoner in females. [Fig 1]

Of all the patients biopsied for vesiculo bullous lesions more than half were in their adulthood. Pemphigus vulgaris were detected

most commonly in third decade of life. Bullous pemphigoid predominated in the late adulthood and old age. Upper limb was the most common overall site involved in all lesions whereas oral mucosa involvement was mostly seen in pemphigus vulgaris (15 out of 31 cases). In Pemphigus vulgaris, bullous pemphigoid and pemphigus foliaceus, skin involvement was mostly generalized. On histopathological examination 50% of the lesions were found to be intraepidermal, whereas sub epidermal blisters were encountered in 39% cases (Fig 2). Acantholysis was seen in 37.5% of cases.

Considering the types of inflammatory cells in all bullous diseases chronic inflammatory cells were found in Bullous Lichen Planus, Erythema multiforme and Herpes zoster. Dermatitis herpetiformis, Bullous lupus erythematosus and Subacute cutaneous bullous erythematosus showed predominantly neutrophils. The inflammatory cell type was predominantly eosinophil in Pemphigus foliaceus, Pemphigus vegetans, Bullous pemphigoid, chronic eczema and chronic bullous disease of childhood. No inflammatory cells were seen in Epidermolysis bullosa simplex – Koebner's variety and in Epidermolytic hyperkeratotic bullous erythroid form erythroderma. Epidermolysis bullosa aquisita showed both lymphocytes and neutrophils. (Fig 2,3)

DISCUSSION

The vesiculobullous lesions are the alarming skin condition where blister formation occur at various levels and clinically present as blisters. Histopathological examination is an important tool in the diagnosis of these.

Clinical correlation with histopathological examination is sufficient for the diagnosis though immune-fluorescence helps in confirmation.⁶

In the present study 72 cases were examined. Of these; 39 (54.17%) were male and 33 (45.83%) were female with majority of cases presenting in adulthood which is comparable with study of Thejaswi Krishnamurthy et al.⁷

Pemphigus Vulgaris is observed to be the commonest and largest group of vesiculobullous lesion in present study comprising of 31 cases which accounts for 43.1% of the cases followed by Bullous Pemphigoid comprising of 10 cases which accounts for 13.9% of the cases which is comparable with the studies of Khan W A et al., Khannan C K et al., Arundhati S et al. with the frequency of 60% and 16.6%, 38% and 26%, 38.2% and 16.2% respectively.⁸⁻¹⁰

Distribution of lesions in the present study was seen mainly in upper limb, back and chest, followed by lower limbs. Lesions in upper limbs were seen in 58 cases. Back lesions were seen in 57 cases and chest lesions in 55 cases. Lower limbs showed lesions in 54 cases. The least common site of lesions was in genitals which were present only in 8 cases.

In our study, 38 cases of Pemphigus were diagnosed, 31(81.6%) of which were of pemphigus vulgaris, 4 (10.5%) were of pemphigus foliaceus and 3 (7.9%) were of pemphigus vegetans which is similar to the study conducted by Arya et al¹¹ showing 70 cases of pemphigus out of which pemphigus vulgaris was the predominant type with 43 cases (61.4%) followed by 25 cases (35.7%) of pemphigus foliaceus and 2 cases (2.9%) of pemphigus vegetans.

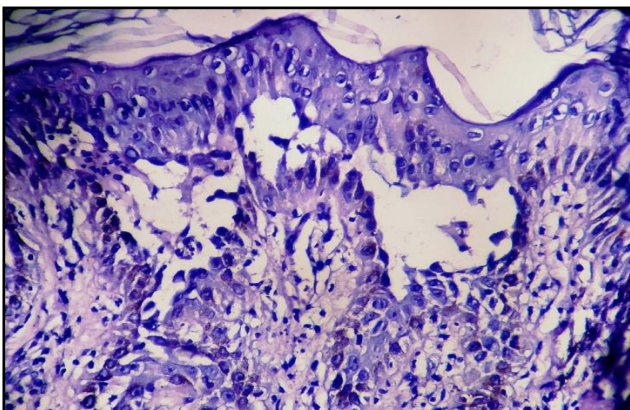


Fig 4: Suprabasal intraepidermal separation in pemphigus vulgaris (100 X magnification, H&E Stain)

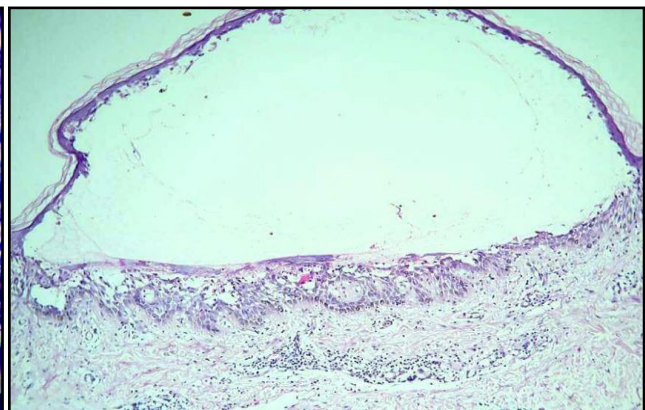


Fig 5: Pemphigus foliaceus with intact bulla, few acantholytic cells and eosinophilic spongiosis (40 X magnification, H&E Stain)

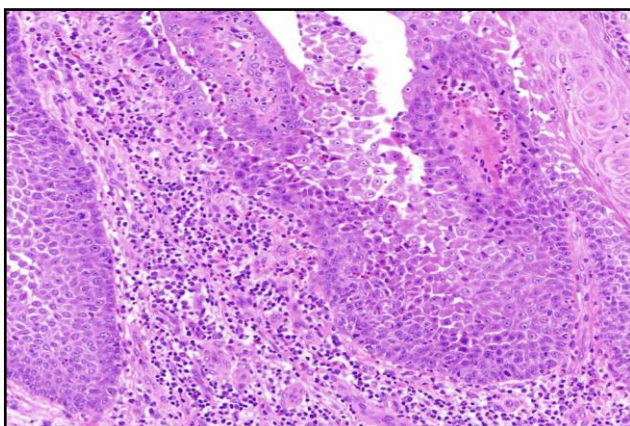


Fig 5: Intraepidermal spongiosis and acantholysis in Pemphigus vegetans (100 X magnification, H&E Stain)

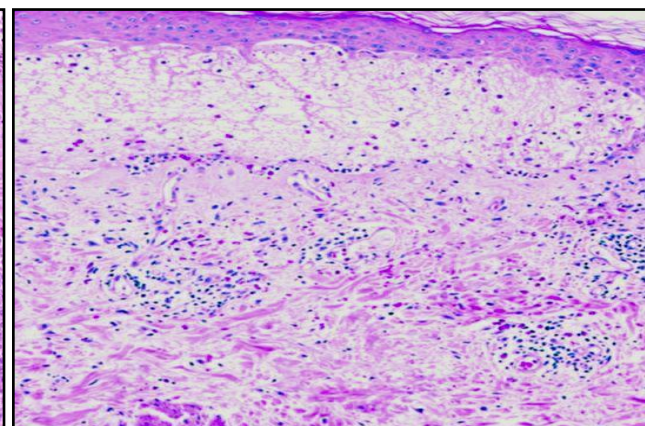


Fig 6: Subepidermal blister in bullous pemphigoid containing few eosinophils with fibrin(100 X magnification, H&E Stain)

Pemphigus Vulgaris

Of the 31 cases of pemphigus vulgaris in the present study, 17 were in males and 14 in females which is comparable with the study conducted by Arya et al.¹¹ showing male preponderance in the ratio of 1.4:1 (25 males and 18 females).

The age distribution of pemphigus vulgaris was wide and varied between 21 to 70 years, with maximum number of cases in third decade, which is similar with study by Rosenberg et al.¹², Sehgal V N¹³ and Arya et al.¹¹ Our study showed that 17 cases (54.8%) had mucosal involvement out of the 31 cases, similar to study by Arya et al, showing mucosal involvement in 31 out of 43 (72.1 %) cases of pemphigus vulgaris.¹¹

Of the 31 cases of pemphigus vulgaris, 25 cases (80.7%) showed intra-epidermal suprabasal vesicles [Fig 4] and 6 cases (19.3%) showed mid-epidermal vesicles. Mid epidermal vesicles were seen in old bullae, due to regeneration of the cells from the floor of the bulla. Acantholysis was seen in 87.1% cases as groups of cells or single cells within the bulla cavity. Dyskeratosis, basal layer budding and pseudo-epitheliomatous proliferation was not seen in any of the cases. An inflammatory infiltrate was present in the bulla cavity in 18 cases (58.1%). Neutrophils and eosinophils were seen in 6 cases (19.3%) and lymphocytes and neutrophils in 6 cases (19.3%). 6 cases showed chronic inflammatory infiltrate. Similar results were reported by Arya et al.¹¹

Pemphigus Foliaceus (pf)

Pemphigus foliaceus was diagnosed in 4 cases only, with upper limbs, chest and lower limbs being involved in all cases. No oral lesions were seen. Genital lesion was seen in 1 of them. In the study by Arya et al there were lesions in trunk in 4 cases (56%) and involvement of extremities in 12 cases (48%). In their study, 4% cases showed mucosal involvement. The gender distribution in the present study was 1:1 with 75% of the cases being in between 21 to 50 years, which is comparable with the study by Arya et al, who reported 80% cases of pemphigus foliaceus in the age group of 21-60 years.¹¹

Of the 4 cases of pemphigus foliaceus studied, all showed acantholysis [Fig 5]. Sub corneal bulla was seen in 3 cases (75%), one showed separation in upper epidermis. Dyskeratosis, basal layer budding and pseudo epitheliomatous proliferation was not seen in any of the cases. An inflammatory infiltrate was present in the bulla cavity in 2 cases (50%). Neutrophils and eosinophil was predominant inflammatory cell in 2 cases (50%). The observation were similar with the study conducted by Arya et al.¹¹ who reported acantholysis in 96% cases of pemphigus foliaceus, sub corneal bulla in 60% cases, sub granular cleavage from middle epidermis in 24% cases and inflammatory infiltrate in the bulla cavity in 53.5% cases. Neutrophils were predominant in 9 cases (20.9%) and eosinophils in 11 cases (25.6%).¹¹

Pemphigus Vegetans (pve)

There were 3 cases of pemphigus vegetans, 2 of them were young adults and third was in 8th decade. Of these, 2 were females and 1 was male. Arya et al.¹¹ saw 2 cases of pemphigus vegetans both of which were between the age group 21-60 years. The patients had lesions in upper limbs, back, chest, abdomen and buttocks. No oral or genital lesions were seen.

The level of separation in the present study was intra epidermal and the mechanism of separation was acantholysis and spongiosis (Fig 6). The inflammatory cells were predominantly eosinophils. Both cases of pemphigus vegetans in the study by

Arya et al showed hyperkeratosis, papillomatosis and irregular acanthosis with intra-epidermal eosinophilic abscesses. Suprabasal lacunae with a few acantholytic cells were seen.

Bullous Pemphigoid (bp)

This was the second most common group in the present study with the number of cases being 10. 4 of them were in 51 to 60 years age group which was similar to that of Korman.¹⁴ Rest were evenly distributed between 21 to 70 years. The cases showed a male predilection, with 7 patients being males and 3 females. Lesions were seen mainly in upper and lower limbs, back, chest and abdomen. Genital and oral lesions were seen in 1 patient. This finding is in contrast to that of Laskaris et al, who said that oral mucous membrane involvement is never a presenting feature.¹⁵

Histologically these lesions were characterised by sub epidermal bulla with infiltration rich on erythematous base and poor on non-erythematous base as reported by Korman and Fisler et al.^{14,16} Bulla contained few eosinophils with fibrin net as was seen by Varigos.¹⁷ The type of inflammatory cells seen was predominantly eosinophils in 60% and neutrophils with eosinophils in 20% and neutrophils and lymphocyte in other 20%. The mechanism of separation could not be assessed as the basement membrane cannot be visualized by light microscopy accurately (Fig 7).

Subcorneal Pustular Dermatosis (scpd)

There was 4 cases of scpd in the present study and these cases had a wide range of age distribution throughout adulthood to old age. The cases showed a female predominance with female: male ratio being 3:1. None of the cases showed genital / oral lesions. This lesion is characterised by subcorneal pustule with polymorphs which was similar to that reported by Sneddon et al.¹⁸

Dermatitis Herpetiformis (dh)

Our study had a total of 4 cases of dh (5.6%) which were evenly distributed between 21 to 60 years. It was most common in and around 4th decade as quoted by Smith Zone.¹⁹ The same authors have quoted that male: female ratio = 1.5:1. However, our study showed an equal sex predisposition (1:1). One patient showed scalp and face lesions. The others had lesions in extremities and trunk. Histologically they showed sub epidermal bullae which were similar to that described by Eng & Moncado.²⁰ 2 cases showed micro abscesses at dermal papilla. The inflammatory cells were predominantly neutrophils.

Bullous Lichen Planus (blp)

There were 4 cases of bullous lichen planus in the present study. The cases were evenly distributed between 21 to 60 years and showed no sex predisposition. All cases had lesions in trunk and limbs. There were no oral or genital lesions. Histologically, sub epidermal bullae were seen with degeneration of basal cells, bands of chronic inflammatory cells in epidermal dermal junction as shown by Gawkrödger et al.²¹ Bullous lichen planus must be distinguished from Lichen Planus Pemphigoides as given by Gawkrödger et al.²¹

Erythema Multiforme (em)

There was only 1 case of Erythema Multiforme in a 25 years old female with lesions on face and upper limbs but no mucosal involvement, who also had history of viral infection before onset of this. According to Cho et al.²² it affects males more commonly, with a male: female ratio ranging from 3:2 to 2:1. Histologically, subepidermal bulla was seen with superficial chronic inflammatory infiltrate in the upper dermis with papillary edema basal cell layer

showed vacuolar degeneration which was similar to that reported by Thejaswi Krishnamurthy et al.⁷

Epidermolysis Bullosa

There were 2 cases of epidermolysis bullosa – one of them was aquisita and the other was of Koebner's variety. The first case was seen in a 45 years old male and the Koebner's variety was seen in a 9 years old female child. Epidermolysis bullosa is seen mainly in infants. The aquisita variety showed lesions in trunk, limbs as well as oral lesions whereas Koebner's variety showed lesions in limbs, back and scalp. Histologically, subepidermal bulla was seen which were similar to that described by Pearson.²³

Bullous Lupus Erythematosus (ble)

We had 2 cases of Bullous lupus erythematosus which were aged between 31 to 60 years. 1 was male and the other was female. The patients did not have any oral or genital lesions. Histologically, there were subepidermal bullae with predominantly neutrophilic infiltrate.

Subacute Cutaneous Bullous Erythematosus (scbe)

There were 2 cases of Subacute cutaneous bullous erythematosus in our study, which were aged between 41 to 60 years. One was a male and the other female. Both the patients had oral lesions in addition to lesions elsewhere in the body. Histologically, there were subepidermal bullae with predominantly neutrophilic infiltrate in both the cases.

Chronic Eczema (ce)

We had 1 case of chronic eczema in a male aged 58 years. The patient had lesions in lower limbs. Histologically, intraepidermal bullae were seen with predominantly eosinophilic infiltrate. The mechanism of separation was spongiosis.

Herpes Zoster (hz)

There was 1 case of herpes zoster seen in a 22 years old male patient with lesions on the chest. Histologically we saw intraepidermal bullae with chronic inflammatory cells and reticular degeneration as consistent with the published literature.

Chronic Bullous Disease of Childhood (cbdc)

We had 2 cases of which were diagnosed as chronic bullous disease of childhood based on clinical manifestation who were aged in the first two decades, one male and other female. One of the patients had oral lesions in addition to lesions elsewhere in the body. Both the cases showed subepidermal bullae with predominantly eosinophilic infiltrate.

Epidermolytic Hyperkeratotic Bullous Ecthysiform Erythroderma (ehbee)

We had 1 case of Epidermolytic hyperkeratotic bullous ecthysiform erythroderma who was a 15 years old male. This patient had lesions in limbs as well as genitals. Subepidermal bullae were seen without any inflammatory cells.

CONCLUSION

Punch biopsy of the skin is a simple, inexpensive, safe OPD procedure, causing minimal discomfort to the patient. Histopathological features are conclusive in most of the primary cases of vesiculobullous lesions of skin. Analysis of morphological features in addition to the clinical features is useful to reach at a conclusive diagnosis in most of such lesions. Clinical examination along with histopathological examination of skin forms primary diagnostic modality in the management of patients with vesiculobullous lesions of skin where the facility for immunofluorescence technique is not available.

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