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ORIGINAL RESEARCH

HISTOPATHOLOGICAL STUDY OF VESICULOBULLOUS SKIN LESIONS– A PROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Skin is the largest organ of the body and various diseases can commonly involve the skin out of which vesiculobullous lesions form one of predominant group. Histopathological study of bullous skin lesions andto knows the incidence of bullous lesions and to study bullous lesions in relation to age and sex.

Materials and Methods: A prospective study of vesiculobullous disorders were studied over aspan of 24 months from July 2019 to June 2021. A total of 48 skin biopsies from patients with vesiculobullous skin lesions were sent to the Department of Pathology, Guntur Medical College, Guntur. Punch biopsies were taken for histopathological diagnosis. H& E staining was done.

Results: In the present study pemphigus foliaceus is the most common vesiculobullous disorder (35.41%) followed by pemphigus vulgaris in 18.75% of cases. Majority of patients presented between 31-40yrs of age with female prepondarance. Subcorneal blister was noted in pemphigus foliaceus and suprabasal blister was seen in pemphius vulgaris.Dermoepidermal junction separation was seen in bullous pemphigoid, dermatitis herpitiformis, and bullous SLE.

Conclusion: Vesiculobullous disorders represent a heterogeneous group of dermatoses with female preponderance and peak incidence inthird decade. Pemphigus foliaceus

constituted the most common subtype of vesiculobullous disorder in this study followed by Pemphigus vulgaris.

Keywords: Skin, VesiculoBullous lesions.

INTRODUCTION

Skin is the largest organ of the body and various diseases along with its manifestations can commonly involve the skin out of which vesiculobullous lesions form one of predominant group. Vesicles and bullae are fluid filled cavities formed within or beneath the epidermis. Vesicles are less than 0.5cm in diameter and bullae are blisters greater than 0.5 cm in diameter. Vesicles and bullae occur in many skin diseases involving all the layers of epidermis from stratum corneum to basal layers and subepidermally. Each entity in this group has distinct clinical features and lesions share number of histologic features but only some extent have common pathogenic mechanism E.g.; Bullous pemphigoid and Pemphigus Vulgaris are autoimmune in nature, whereas epidermolysisbullosa is inherited disease caused by non-immunologic mechanism. Wide variety of pathologic processes can lead to development of vesiculobullous eruptions over body. They may occur in many dermatosis, which include various inflammatory, infective, autoimmune, drug induced as well as genetic.

Present study was carried out to study histopathological changes by light microscopy in vesiculobullous disorder of the skin and to study the incidence and distribution of the disease amoung different age groups.

MATERIALS & METHODS

Patients with bullous lesions of skin, who visited the department of dermatology Guntur Medical College, Guntur between July 2019 to June 2021 (2yrs), were included in this prospectivestudy. The age of the patients varied from birth to 80 yrs. After taking the history and evaluating the patient clinically, punch biopsy was taken from fresh and early vesicle with perilesional skin and was subjected to histopathological examination

For performing the Skin Biopsy, the site selected for biopsy was cleaned with spirit and infiltrated with local anaesthetic, 2% xylocaine. Punch biopsy was taken from fresh and early vesicle with perilesional skin. Skin biopsy was taken from the patient and was fixed in 10% buffered formalin andhistopathologicalexamination was done. H & E stain was used to stain histopathological sections.

RESULTS

It was a prospective study done in Department of Pathology GMC, Guntur and the duration of study was from July 2019 to June 2021(2yrs).Total skin biopsies obtained during this period - 160. Bullous lesions of skin obtained during this period - 48 (30%). Out of total 48 cases (Figure 1) studied 17/48 (35.41%) constituted Pemphigus foliaceus, followed by Pemphigus vulgaris 9/48 (18.75%), Bullous pemphigoid constitute 8/48 (16.66%), Dermatitisherpetiformis 2/48(4.16%) and dariers disease 4/48 (8.33%) respectively. Hailey-Hailey 3/48 (6.25%), TEN 1/48 (2.08%), Bullous SLE 2/48(4.16%), Bullous Lichen planus 1/48 (2.08%), Epidermolysisbullosa 1/48 (2.08%)**.** The highest incidence was seen in 3rd decade (27.08%). Lowest incidence was seen in 1stdecade(2.08%) youngest patient was 5

years old boy [Table 1] Female: Male ratio in various vesiculo bullous lesions was 29:19 (1.52:1) with female preponderance in pemphigus vulgaris and pemphigus foliaceus, Hailey Hailey disease, Bullous SLE.

Majority of Pemphigus foliaceus were in the age group of 31- 60 years - 12/17 (70.58%), 8/9 cases(88.88%) of Pemphigus vulgaris were in the age group of 21-60 yrs. Out of the 8 cases of Bullous pemphigoid, maximum number of cases 6/8 (75%) were in the age group of 61-80 yrs and 2/8 cases (25%) were in the age group of 41-50 yrs [Table 1] Bullous SLE and Epidermolysis Bullosa were seen in the age group of 1- 20yrs. Erythema multiforme were seen between 21-50yrs. Bullous Lichenplanus, Dermatitis herpetiformis, TEN, Dariers disease and Hailey-Hailey were seen between 31- 60yrs.

DISCUSSION

The immunobullous diseases are a group of autoimmune diseases in which components of the epidermis and basement membrane zone are the focus of attack, resulting in the formation of cutaneous and mucosal blisters. Several disorders fall under the categoryof immunobullous diseases and are broadly classified as intra-epidermal and sub-epidermal blistering disorders. Intra-epidermal blistering disorders, apart from those mediated by immunological mechanisms, include inherited disorders like Darier's and Hailey-Hailey disease. Secondary damage by severe intercellular edema can also cause acantholysis, as seen in spongiotic dermatitis and transient acantholyticdermatosis.

In a similar fashion, sub-epidermal blistering disorders include mechanobullous disorders like epidermolysisbullosacongenita, in addition to the immunobullous lesions. Though, various primary cutaneous diseases present clinically with vesiculobullous lesions, their etiology, pathogenesis, severity and course differs. Therefore, accurate diagnosis of these diseases are essential for appropriate management to avoid or minimize associated morbidity and mortality.In the present study, the maximum numbers of subjects (52.08%) were in 3rd and 4th decades. There was a slight female predominance in present study with female to male ratio was 1.52:1.

Pemphigus Foliaceus: It is the most common lesion in our study.Out of the fourty eight cases(48),seventeen cases(17) that is 35.41% of the total cases are of pemphigus foliaceous, It usually develops in middle aged individuals. PF between 21 to 30 years of age Arya et al observed pemphigus foliaceus, lesions to involve trunk, extremities, and face, which was similar to our present study.[1] There was female preponderance of the disease with M:F ratio of 1:3.2.AnirudhaVasantacharyaKushtagi et al study has shown M:F ratio of 1:1.5 with slight female preponderance which is similar to our present study.[2]

Histopathology showed epidermal spongiosis (76.47%) and subcorneal collections of neutrophils with sub-corneal bulla (88.23%) [Figure 2], cleft or acantholytic cells (70.58%). Dermal inflammation with few neutrophils, lymphocytes and eosinophils is seen in 58.82% of cases of pemphigus foliaceus. Of the 25 cases studied by Arya SR et al, (1992 to 1996) 96% showed acantholysis, subcorneal bullae was seen in 60% and subgranular cleavage in middle epidermis in 24% of casesArya et al and L. Jubojevics et al reportedacantholysis and suprabasal blister to be the feature of pemphigus vulgaris and subcorneal blister in the pemphigus foliaceus.[1,3] These observations were similar to our present study.

Pemphigus vulgaris: The second most common lesion of the fourty eight cases involved in the study was pemphigusvulgaris with 9 cases (47.5%).In Khandari et al, Fernadez et al studies pemphigus vulgaris are more common than pemphigus foliaceus.[4,5] However Aboobaker et al series, in Oxford, UK showed cases of Pemphigus foliaceus and pemphigus vulgaris in equal proportion.[6] In our study pemphigus foliaceus (35.41%) is more common than pemphigus vulgaris (18.75%) While our study showed low prevalence of pemphigus vulgaris which is around 18.75% of the cases. This variation may be due to geographic distribution of bullous diseases. In the present study M:F ratio in cases of pemphigus vulgaris was 1:2 with female preponderance. Michael Muerer et al in his study pemphigus vulgaris, had a sex ratio of M: F has 1:4 with the female preponderance.[7] Bedi et al observed that pemphigus vulgaris is more prevalent in the younger age group in india with female preponderance.[8] Similar results were observed in our study. The histological findings in the present study showed well-formed supra basal bullae, [Figure 3] with a row of tomb stone appearance. The bullae contained acantholytic cells single or in clusters. Only in one case there was eosinophilsinterspersed with acantholyticcells in the bullae. Inflammatory exudates containing mainly eosinophils, few neutrophils and lymphocytes around adnexae, were seen in 8/9 cases (88.8%) of the cases.Histopathology [Table 2] showed 8/9 cases (88.8%) with a suprabasal blister and 7/9 cases (77.7%) showed acantholysis extending into follicular epithelium.Seema et al observed similar findings in edition to eosinophilicspongosis in few cases.[9] Emmerson and Wilson in their histological study of Pemphigus vulgaris described eosinophilicspongiosis as the earliest pathological change, even earlier than the acantholytic change in the epidermis.This was similar to our study.[10]

Bullous pemphigoid: The third most common lesion observed in our study group was bullous pemphigoid [Figure 1] (08/48 cases, 16.6%) with the predominant age group between 61-70years (4 cases). This is in cordinance with the studies conducted by Anirudha Vasantacharya et al where bullous pemphigoid was with male predilection and was seen commonly between 60 to 70 years of age.[2]

The risk of developing Bullous pemphigoid increases with age and is higher in men. The present study very well correlates with above observation. Although earlier studies (Keil J. Korman et al) and literature from western countries, have shown bullous pemphigoid to be the most common autoimmune blistering disorder, in our study it was third most common lesion next to pemphigus foliaceus and pemphigus vulgaris.[11] The affected patients were predominantly males (62.5%). Histopathology [Figure 5] showing a subepidermal bulla (8/8cases) in all the cases. Superficial dermal edema is seen in 3/8cases Dermal inflammation with predominant eosinophilic infiltration is seen in (6/8cases). Two cases showed mixed inflammatory infiltrate comprising of eosinophis, lymphocytes and neutrophils.

Dariers disease (Keratosis follicularis): In the present study a case of darier's disease was seen accounting for 8.33% of all the cases. (4/48 cases). M:F ratio is 1:1 in our study. The histopathology showed acanthosis, hyperkeratosis, papillomatosis, dyskeratotic changes, corps&ronds, grains and suprabasal lacunae. Dermis and hair follicles showed chronic inflammatory infiltrate. Out of the 4 cases, 3 are at the age group between 31-40yrs, 1 is at the age group between 41-50yrs. In the studies by Bedi BMS et al and Garg BR et al the age groups ranged between 10-51yrs in all the cases.This is in concerance with the present

study.[8] Whereas in the studies conducted by AnirudhaVasantacharya Kushtagil et al the age group was between 10-40yrs.[2]

Hailey-Hailey disease: In the present study 3 cases were diagnosed as Hailey-Hailey disease amoung 48 cases accounting for 6.25% of all the cases. Arundhati et al reported 1case (1.5%) and Jindal et al reported 1 case (1.6%) of haileyhailey disease in their study of 68 cases and 60 cases of vesiculobullous disorders respectively.[12,13] Incidence of HHD is slightly higher in the present study than in other studies.

Vesicles and papules are located on the erythematous base in all the cases. In the present study histopathology showed suprabasal blister, acantholytic cells arranged individually and in clusters with villi protruded into the cavity of bulla. Above the bullous cavity, cells of the detached epidermis showed only slight separation, giving the detached epidermis the appearance of a dilapidated brick wall. Dilapidated brick wall is formed due to partial detachment of keratinocytes in the epidermis. Arundhatiet al also reported villi and acantholytic cells in 100% of the cases.[1]

Bullous SLE: Two cases are diagnosed in our study constituting 4.16% of all the cases. One patient was 18 year old female who had presented with pruritic raised lesions over the extensor aspect of both upper extremities. Some of these lesions developed into blisters. The patient also gave history of photosensitivity. Histopathology showed a sub epidermal vesicle and a lymphocyte predominant perivascular inflammatory cell infiltrate with the evidence of mild vasculitis within the superficial layers of dermis. Anne. H. Kettler et al in their study reported a case of 34-yearsold female having bullous systemic lupus erythematosus with a subepidermal bulla and neutrophilic papillary micro-abscesses.[14]

Dermatitis herpetiformis: In the present study two cases of dermatitis herpetiformis were seen accounting for 4.16% of all the cases. The patient in the study were between 31-50yrs. Olbricht et al observed dermatitis herpetiformis between 2nd and 4th decade and have demonstrated papillary micro-abscesses containing predominantly neutrophils in almost all the cases on histology and they were common in males.[15]

On Histopathology subepidermal blister, neutrophilic and few eosinophilic leukocytes in the papillary dermis forming microabcesses at the tips of the dermal papillae were noted.Both the cases were males.Histopathology showed presence of the unilocularsubepidermalblister[Fig 6}. In addition dermal papillary micro abscesses with predominant neutrophils and fibrin was seen. These are similar to the studies of Jindal et al.[12]

Toxic epidermal necrolysis: TEN is widely but not universally regarded as the severe end of the spectrum of erythema multiforme major or Stevens Johnson syndrome. The patient presented clinically with blisters over upper limb, lower limb, trunck. Lesions are occupying more than 30% of the body surface without involvement of mucosa. If blistering involved less than 30% of the body surface with the involvement of mucosa then it favours the diagnosis of Steven Johnson Syndrome clinically. These clinical features are suggestive of TEN. One case out of 48 cases in our study is diagnosed a TEN. It constitutes 2.08% of the total cases. The patient is male and of 40yrs age. Histopathology showed sub epidermal blister and epidermal necrosis. Dermal inflammation is sparse. Few extravascated RBC are seen in the cavity. These features are suggestive of diagnosis of TEN.

Bullous lichen planus: In our present study, one case of Bullous Lichen planus was seen accounting for 2.08% of all the cases encountered in this study. Vesicles were flaccid and

present on the neck, upper extremity and lower extremity. Oral lesions were present and blisters were seen on nonerythematous skin. Nikolsky sign and bulla spread sign are negative. Similar clinical presentation was also noted by Verma et al and normal skin was also involved in their study. The histopathology showed a subepidermal blister and the cavity contained mixed inflammatory infiltrate comprising dense lymphocytic infiltrate along with eosinophils and neutrophils. Dense lymphocytic dermal infiltrate was seen papillary dermis; however other changes of lichen planus were not seen. Predominance of lymphocyte was seen by Verma et al.[16] This led to the diagnosis of BLP.

Epidermolysisbullosa [mechanobullous] group: Paller. A.S et al and Furve M et al in their separate studies reported blistering disorders with history of minimal trauma in 25 and 32 cases respectively 80% of them showed sub-epidermal blisters with scantly inflammatory infiltrate and fragmented basal keratinocyte.[17,18] Present study comprised only One case of Epidermolysisbullosa with the incidence of 2.08% Biopsy was done in this case and microscopic examination revealed similar histological features with subepidermal blisters with minimal mixed inflammatory infiltrate and few degenerated keratinocytes.

CONCLUSION

Vesiculobullous disorders represent a heterogeneous group of dermatoses with protean manifestations classified according to location as suprabasal, intraepidermal, sub corneal and sub epidermal group with female preponderance and peak incidence in the third decade. Pemphigus foliaceus constituted the most common subtype of vesiculobullous disorder in this study followed by Pemphigus vulgaris and bullous pemphigoid.

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