

MULTILEVEL BLISTERING IN A CASE OF BREAST CARCINOMASoorya B.¹, Dr. Jayakar Thomas*² and Sivaramakrishnan S.¹¹Junior Residents, Department of Dermatology, Sree Balaji Medical College and Bharath University, Chennai 600044, India.²HOD and Professor, Department of Dermatology, Sree Balaji Medical College and Bharath University, Chennai 600044, India.***Corresponding Author: Dr. Jayakar Thomas**

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ABSTRACT

Bullous pemphigoid is a subepidermal autoimmune blistering disorder characterized by the production of auto antibodies against structural proteins of the dermo epidermal junction. Bullous pemphigoid is associated with multiple conditions including malignancy. We report a case of bullous pemphigoid with multilevel blisters associated with breast malignancy in 65 year old women.

KEYWORDS: Multilevel blisters, bullous pemphigoid, paraneoplastic dermatoses.**INTRODUCTION**

Paraneoplastic dermatoses are skin conditions due to neuromuscular or metabolic manifestations of certain internal malignancies. The paraneoplastic syndrome can affect any organs in the body. Some dermatoses are always associated with malignancy but in others, the association is not proved. Examples of paraneoplastic dermatoses are necrolytic migratory erythema, bullous pemphigoid, acanthosis nigricans, sweet syndrome, paraneoplastic pemphigus, dermatomyositis etc. But the association of bullous pemphigoid with malignancy is controversial.

CASE REPORT

65-year-old women came with complaints of fluid filled lesions over the upper back, arms, and chest for the past 1 month. The patient was apparently normal 1 year back following which she developed multiple fluid filled lesions over the upper back, arms and chest. The bulla subsequently eroded to leave raw areas which healed with both hyper and hypo pigmentation. For past 1 month, she developed similar fluid filled lesions over the back progressed to involve bilateral arms, chest, axilla, and groin. History of itching, pain and burning sensation were present over the lesion. No history of hemorrhagic bulla or pustules. No history of loss of weight and appetite. She is a known case of type 2 diabetes mellitus and systemic hypertension and on treatment. She was diagnosed to have right sided breast carcinoma 8 years back. For which right mastectomy was done, followed by radiochemotherapy given.

On examination - multiple tense bulla and vesicles were seen which broke open to form erosions with crusting and pigmentation over the upper back, bilateral arms, chest, axilla, and groin [Fig 1&2]. Nikolsky sign was negative. Bulla spreading sign was positive. Oral mucosa, palms, soles, scalp, genitalia and nails were normal. No enlarged lymph nodes palpable.

Routine investigations, peripheral smear, USG abdomen, chest x-ray, and stool for occult blood were normal. Biopsy from the lesion revealed hyperkeratosis, multilevel blistering – intraepidermal, suprabasal and subepidermal splits with lymphocytic and eosinophilic infiltration in the dermis [Fig 3]. Because of multilevel blisters repeat biopsy was done which revealed intraepidermal bulla with lymphocytic and eosinophilic infiltration in the dermis [Fig 4].



Figure 1: Clinical picture showing multiple erosions over the chest and arms and scar of right mastectomy.



Figure 2: Clinical picture showing multiple erosions and post inflammatory hypo and hyper pigmentation over the upper back.

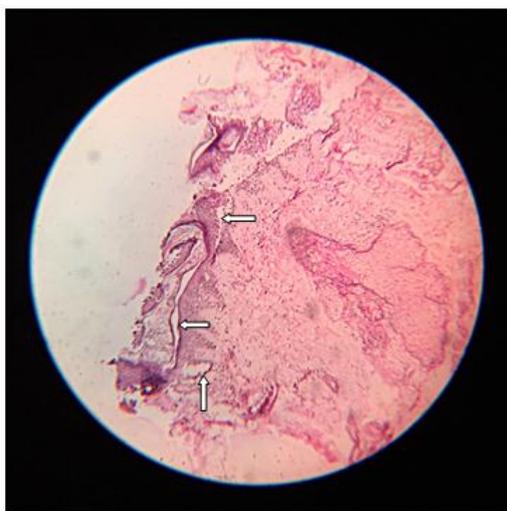


Figure 3: Histopathological picture shows multilevel split – intraepidermal, suprabasal and subepidermal with inflammatory infiltrates in the dermis.



Figure 4: Histopathological picture shows intraepidermal split with inflammatory infiltrates in the dermis.

DISCUSSION

Bullous pemphigoid (BP) was first differentiated from Pemphigus Vulgaris by Levers in 1953. It usually occurs in older age group mainly after 60 years. It is common in western countries. Environmental factors along with genetic susceptibility (HLA DQB1*0301 and DQ7) triggers this disease. Other precipitating factors are UV exposure, vaccination for influenza, infections (Cytomegalovirus, EBV, HHV-6, HHV-8, HBV, HCV, Helicobacter pylori and Toxoplasma gondii)^[1] surgery, electrical burns, drugs like furosemide, spironolactone, PUVA, enalapril, d-penicillamine, ampicillin, penicillin, cephalexin, sulfapyridine, fluoxetine, topical 5-FU, benzyl benzoate, anthralin etc and following radiotherapy.

Bullous pemphigoid is an acquired autoimmune disease in which autoantibodies are produced against the proteins of size 230 kD and 180 kD. Autoantibodies bind to the BPAG1 & 2 antigens and activate complement pathway. Components of complement starts with an inflammatory cascade which attracts leukocytes like neutrophils, eosinophils, mast cells and releases inflammatory mediators. Lysosomal enzymes and proteases are released from the inflammatory cells which lead to cleavage of the target antigens and cause hemidesmosomal disruption leading to blister formation.^[2] T cells mainly Th1, Th2, and Th17 are thought to produce autoantibodies indirectly and also releases inflammatory mediators.

BP usually starts as itchy urticarial wheals or as a nonspecific rash which precedes the development of bulla by several months. BP presents as tense bulla over the normal or erythematous skin. Bulla usually contains clear fluid but it can be hemorrhagic also. The bulla ruptures to leave erosion which heals with post inflammatory hypopigmentation and milia or the bulla gets reabsorbed with the roof settles like the skin graft. Commonest sites involved are lower abdomen, thighs, and flexors of forearm but it can occur anywhere in the body. The mucous membrane is involved in 30% of cases.

Variants of bullous pemphigoid are localized type (pretibial type, dyshidrosiform type and vulvar type), pemphigoid vegetans, lichen planus pemphigoides, pigmented type, erythrodermic type, pemphigoid nodularis, vesicular type, papular type, lymphomatoid papulosis like, TEN like, ecthyma like, occurring over the amputation stump, occurring in the radiotherapy site and associated with internal malignancy.

It is associated with other diseases like psoriasis, lichen planus, neurological disorders (Parkinson's disease, stroke, epilepsy, multiple sclerosis and myasthenia gravis),^[3] connective tissue disorders (rheumatoid arthritis, systemic lupus erythematosus and dermatomyositis), ulcerative colitis, diabetes mellitus and malignancy like squamous cell carcinoma,^[4] B-cell

lymphoma, solid organ malignancies (lung, breast, renal, bladder, colorectal, gall bladder, endometrial and esophageal).

Bullous pemphigoid is considered as paraneoplastic dermatoses. The incidence of paraneoplastic bullous pemphigoid is higher in Asian countries like Japan.^[5] HLA-DR13 is more common in patients with malignancy.^[6] Malignancy can present before or after or along with bullous pemphigoid. The relationship between malignancy and bullous pemphigoid is not known. But has been suggested that epitope spreading (injured carcinomatous mucosa exposing the normally sequestered BP180 antigens)^[7] or by anti BP180 antibodies prevents the binding of extracellular domain of BP180 antigen and laminin 332 resulting in epithelial cell disruption, increased motility of epithelial cells and malignancy.^[8] In some cases, there has been an improvement of BP following the treatment for malignancy.

Differential diagnosis of BP are pemphigus group of disorders, drug reaction, SLE, urticaria, arthropod bite, scabies, contact dermatitis and other subepidermal blistering disorders.

Histopathology from the bulla reveals subepidermal bulla with eosinophilic infiltrates. Rarely eosinophilic microabscess can be seen. Older bulla can reveal intraepidermal split due to re-epithelialization.

Linear deposition of C3 and IgG in the basement membrane zone are seen in direct immunofluorescence. Indirect immunofluorescence shows circulating IgG autoantibodies. The salt split technique shows antibodies bound on the epidermal side or roof. Other investigations are ELISA, immunoblotting, immunoelectron microscopy and immunoprecipitation.

This disease usually runs a chronic course with remission and exacerbation. The factors with poor prognosis are the age of onset after 80 years, associated with malignancy, serum albumin <3.6 g/dl, ESR > 30mm/hr, the requirement of >37mg of prednisolone at discharge and Karnofsky score ≤ 40.^[9]

Treatment - Topical steroid for localized type, systemic steroids, cyclophosphamide, azathioprine, methotrexate, dapsone, nicotinamide with tetracycline, MMF, leflunomide, chlorambucil, IVIG, plasmapheresis, and biologics like rituximab and appropriate treatment for the respective malignancies.

CONCLUSION

The relation between bullous pemphigoid and malignancy is still disputable. Bullous pemphigoid is considered as paraneoplastic dermatoses; hence internal malignancy has to be ruled out in every case. This case is reported because of the presence of multilevel blisters in bullous pemphigoid patient with malignancy of breast.

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