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Case Study

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CASE SERIES ON AUTOIMMUNE-BULLOUS DISEASE

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ABSTRACT

The autoimmune bullous disease is a rare disorder affecting skin and mucosa. In an autoimmune disease, the body's immune system which normally protects the body against foreign invaders mistakenly attacks the skin cells resulting in the formation of blisters. A blister is an accumulation of fluid between cells of the epidermis and upper epidermis. The cause of the blister could be either genetic or immunological. Based on its location of intraepidermal and subepidermal, pemphigus Vulgaris constitute intraepidermal immunobullous disease whereas bullous pemphigoid is a subepidermal immunobullous disease.

Bullous pemphigoid is a chronic autoimmune skin disorder resulting in generalized, pruritic, bullous lesions, and Pemphigus Vulgaris is an uncommon, potentially fatal, autoimmune disorder characterized by intraepidermal blisters and extensive erosions on apparently healthy skin and mucous membrane. Treatment strategies for both bullous pemphigoid and pemphigus Vulgaris include Topical and systemic corticosteroid initially and long term maintenance therapy with immunosuppressants.

To observe the treatment pattern, a case series with three cases on pemphigus Vulgaris and one case on bullous Phemphigoid is highlighted and analyzed below.

KEYWORDS – Autoimmune, Bullous Pemphigoid, Pemphigus, Corticosteroid, Case Report.

INTRODUCTION

Autoimmune Bullous diseases are rare disorders affecting the skin and mucous membranes. These diseases are mediated by pathogenic autoantibodies directed against keratinocyte adhesion molecules. A majority of these antigens are demmosomal and hemi-desmanal transmembrane glycoproteins which participate in epidermal cell and epidermal dermal adherence.[1] Bullae are elevated, fluid-filled blisters >= 10mm in diameter and the common types of the autoimmune bullous disease include pemphigus Vulgaris, pemphigus vegetans, pemphigus foliaceous, pemphigus erythematosus and paraneoplastic pemphigus of intraepidermal origin whereas Bullous Pemphigoid, Dermatitis Herpetiformis, Epidermolysis bullosa acquisition,Linear Immunoglobulin A disease, Pemphigus gestations on subepidermal origin.[2]

Pemphigus Vulgaris(PV) is an autoimmune blistering condition that usually affects the oral mucosa and is characterized by autoantibodies directed against the desmoglein component of the keratinocytes.[2] Pemphigus Vulgaris is most commonly encountered than BP in India. PV is usually characterized by acantholysis (loss of keratinocytes to keratinocytes adhesion). The process of acantholysis is induced by circulatory autoantibodies to intercellular adhesion molecules.[3] Lesions are most commonly found in an area subjected to frictional trauma such as the cheek mucosa, pharynx, larynx, esophagus, genital mucosa as well as the skin in where blisters are seen.

The most growing of blistering disorders is the bullous pemphigoid. It is present most often in the elderly aged above 70 years and is diagnosed based on clinical, histological, and immunological criteria. The incidence is between0.2 and 0.3 per 100000 person year. Clinically it presents diffuse eczematous, pruritic, hives-like lesions, with the subsequent emergence of tense bullae or blistering lesions usually filled with clear fluid.

Antibodies against structural components of keratinocyte proteins BP180 and BP230 immunoglobulin are shown as historical indications of the subepidermal blist and the immunofluorescence. The clinical variant of BP includes localized, Nodular, Vegetating, Erosive, Erythrodermic, Juvenial, and drug-induced.[4] This paper highlights the treatment pattern [both pharmacological and non-pharamcological]of two different categories of autoimmune bullous disease

CASE REPORTS

Case 1(Pemphigus vulgaris)

A 47-year-old male patient was admitted with vesicle and bullae complaints distributed through the trunk, flexor, orbit, nose, oral mucosa, and anus. Laboratory testing showed that White blood cells=12.6x10^9/L**[4-10 x 10^9/L]**, Platelets=322x10^9/L**[100-300 x 10^9/L],** Hemoglobin=13.4gm/dL**[12-16g/dL]**. Electrocardiogram registered sinus tachycardia and X-ray — Increased broncho-vesicular marks and patient with discharge erythematous lesions in the eyelid .pharmacological management include Inj. Ciprofloxacin 200 mg IV BD, Inj Metronidazole 500 mg IV BD, Ranitidine 50 mg IV BD, Inj. Dexamethasone 8 mg IV OD, Tab. Chlorpheniramine 4 mg PO BD, Tab. BCT, Tab. Vitamin C BD, Tab. Calcium 300mg, Inj. Cefotaxime 1 g IV BD was started from the 4th day and stopped after the antibiotic course had been completed. On the 7th day, the combination of antibiotics {Inj. Ciprofloxacin and Inj. Metronidazole} were halted. Ampicillin 1 g IV BD and Inj.Gentamicin 80 mg IV BD} was initiated in conjunction with Tab. Cyclophosphamide 50 mg PO 1-0-0. The Inj. Dexamethasone frequency was changed to 2 mg on the first day and 4 mg on the next day due to deteriorating health conditions.

Case 2(Pemphigus vulgaris)

A 46-year-old female patient was admitted for the 6th cycle of DCP Pulse therapy with itching and lesion complaints in B / L palms and legs after local inspection new pemphigus lesions were discovered in her scalp, hands, and palms. Her Fasting Blood Sugar = 212 mg / dL**[70-100mg/dL]** in hematological examination. Pharmacological treatment for the patient includes Inj. Dexamethasone 100 mg IV OD, Tab. Cyclophosphamide 100 mg PO OD, Tab. Loratidine 10 mg PO OD, Tab. Doxycycline 100 mg PO BD, Tab. Multivitamin OD, Tab. Metformin SR 500 mg PO OD, Protein supplement, and Hydrocortisone Cream.

Case 3 (Bullous phemphigoid)

A 78-year-old female patient was admitted for the past 4 months with the complaint of itchy vesicles primarily near the surface of the trunk and flexor. Laboratory inquiry reveals Hemoglobin=9.9gm / dL**[12-16mg/dL].** Pharmacological management was initiated with Inj. Ampicillin 1gm IV BD, Inj. Gentamicin 80 mg IV BD, Inj. Ranitidine 50mgIV BD, Tab. Chlorpheniramine Maleate 4 mg PO BD, Tab. B Complex BD, Tab. Ferrous Sulphate PO BD, Tab. Calcium 300mgPO BD, Inj. Dexamethasone 4 mg IV OD, Tab. Albendazole 400 mg PO STAT, Tab. Vitamin C PO BD, Syp. Potassium Chloride 10ml PO TDS, Tab. Cyclophosphamide 50 mg PO OD, Tab. Ciprofloxacin 500mgPO BD. Inj. Dexamethasone level has been increased due to the recurrence of vesicles. Povidone Iodine Ointment 5% W / W SOS, Liquid Paraffin L / A TID .

Case 4 (Pemphigus vulgaris)

A 38-year-old female patient was admitted for the 4th cycle of DCP with non-healing erosion symptoms on the lower lips for the past 6 months. The hematological analysis indicates Hemoglobin=11.5gm / dL**[12-16mg/dL]**, Serum Creatinine=0.6mg / dL**[0.7-1.4mg/dL]**, Serum Total Protien =5.8mg / dL**[<6.8mg/dL]**, Serum Total Albumin=3.7mg / dL**[3.8-5g/dL].** The view of the Eelctocardiogram shows Sinus Tachycardia and Chest X-Ray PA shows correct pure cardiac opacity.

The pharmacological approach consisted of Tab. Prednisolone 10mg PO OD, Tab. Cyclophosphamide 50mg PO OD is given for the first four days and is converted to Inj. Cyclophosphamide on 5TH day, Tab. Glimepiride 1mgPO BD, Tab. Enalapril 2.5 mg PO OD, Tab. BCT PO BD, Tab. Vitamin C PO BD, Tab. Ferrous Sulphate PO BD, Tab. Calcium 300 mg PO TDS, Inj. Dexamethasone 100 mg IV OD, Tab. Ranitidine 150 mg PO BD was given for the first three days and is converted to Inj. Ranitidine 2ml IV BD, Tab. Alprazolam 2.5 mg PO HS.

DISCUSSION

According to the IPPF(International Pemphigus and Pemphigoid Foundation) guidelines, the aim of treatment in Bullous Pemphigoid is to make the disease tolerable to an individual patient (reduction of blister formation, urticarial lesions, and pruritis).[5] Corticosteroids aim to suppress the inflammatory process, antibiotics examples tetracycline, sulphones are used usually. Other immunosuppressive treatments aim to suppress the production of pathogenic antibodies example high dose corticosteroids, azathioprine, methotrexate, cyclophosphamide, and cyclosporins.[6]

In case 3 with the differential diagnosis of Bullous Pemphigoid the pharmacological management includes a systemic corticosteroid therapy as per the guidelines along with immune modulated treatment which includes cyclophosphamide. The combined therapy of oral or Intravenous cyclophosphamide with pulsed intravenous dexamethasone was reported to have more benefit(less steroid-sparing effect) than individual corticosteroid therapy alone (mainly prednisolone).

Guidelines for the management of Pemphigus Vulgaris as per IPPF aims to induce disease remission followed by a period of maintenance treatment using minimum drug doses. The common pharmacological treatment includes oral corticosteroids, pulsed intravenous corticosteroids,

and adjuvant drug(Azathioprine, oral cyclophosphamide, mycophenolate mofetil, gold, methotrexate, cyclosporine, tetracyclines, etc.[6]

In case 1 and case 2 pulsed intravenous corticosteroid therapy with a high dose of corticosteroid (dexamethasone) provided to achieve more rapid and effective disease control compared with conventional oral dosing along with cyclophosphamide as a combination of pulse therapy to reduce long term maintenance of corticosteroid doses and corticosteroid side effect. Due to the risk of hemorrhagic cystitis with prolonged administrations of cyclophosphamide usually, the option for the drug is switched to azathioprine or methotrexate after a time period of 6months.

In case 4 the pharmacological approach indicates the maintenance therapy with low dose corticosteroids (10mg tablet Prednisolone) and adjuvant immune-modulatory agent cyclophosphamide. The aim of combining adjuvant drugs with corticosteroid is to reduce the chance of remission of disease and lower the steroid side effects.

For rapid improvement of conditions in both the cases of autoimmune bullous diseases The inclusion of non-pharmacological options alongside can benefit the patients, it includes.[7]

- ✓ Avoiding contact sports that could cause the skin to become damaged
- ✓ Using a soft toothbrush and avoiding crisp, hard, hot or spicy foods to protect the oral mucosa
- ✓ Usage of talcum powder liberally to prevent the skin from sticking to the bedsheet
- ✓ Frequent changing and laundering of towels, sheets and body linen in hot water to prevent secondary infection
- ✓ Attending pain management courses
- ✓ Practicing exercise and relaxation techniques

In both cases of Pemphigus Vulgaris and Bullous Pemphigoid, pulse therapy combined with an immunosuppressant has shown to be more promising than an individual high dose of corticosteroids alone. Maintenance therapy is more essential in both diseases to prevent the severity of symptoms.

CONCLUSION

Pemphigus Vulgaris is a chronic mucocutaneous autoimmune bullous disease with IgG antibodies directed against desmoglein 1 and 3 and degrading the intercellular adherence in stratified squamous epithelia mainly skin and oral mucosa. British association of dermatologists recommends two-stage management by induction of remission and maintenance of remission to reduce the severity of symptoms and is mostly accepted pattern of treatment.

Bullous pemphigoid is an acquired autoimmune subepidermal bullous disease where autoantibodies are directed against the basement membrane zone of the skin and the antigen[igG]-antibody[BP230 AND BP180] interactions result in subepidermal blister formation. Since the disease is self-limiting and usually remits within 5 years, the focus of treatment should be on reducing the blisters, lesions, and pruritis.

The main challenge in both diseases to the patients includes coping with the relapses and flare-ups, side effects of drugs, itching, and burning of skin erosions mainly, So clinicians should focus equally on non-pharmacological and pharmacological treatments. This case report aims at raising awareness of the disease and highlighting treatment patterns, as well as advocating referral to a dermatologist, given its potential severity.

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