

Recurrent Attack of Metformin Induced Bullous Pemphigoid

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Abstract

Bullous Pemphigoid is the large fluid filled blistering rare skin disease. This occurs when our immune system attacks the thin layer of inner tissue of outer layer of skin. Exact reason for the abnormal immune response is unknown, but this can be triggered by certain drugs like Phenacetin, Captopril, Ibuprofen, Penicillamine, etc. A 42 years old male patient of known diabetic mellitus joined in inpatient department of the hospital with chief complaints of itching, fluid filled blisters since 1 week over chest and lower limbs and scalp and gradually progressed to upper limb and face. On examination of past history, two months back he admitted in hospital with same complaints. He was treated with Corticosteroids, anti-histamine, vitamin supplement and antibiotics. Metformin is widely used as first line agent for treatment of type-2 diabetes mellitus. Drug induced Bullous Pemphigoid has been associated with many drugs, but Metformin is not one among them. Here we report a case on Metformin induced recurrent attack of Bullous Pemphigoid.

Keywords: Bullous pemphigoid • Metformin • Corticosteroids

Introduction

Bullous pemphigoid is an autoimmune, cutaneous sub-epidermal blistering disorder with antibodies against BP230 and BP180 antigens. The etiology for the precipitation of this disease is not clearly known [1]. Bullous pemphigoid is induced by many drugs, one of them is Gliptin category of diabetic drugs, but Metformin is not included [2]. Metformin is an anti-hyperglycemic agent of Biguanide class, which is a first drug of choice for type 2 diabetes and used for the managing of type-2 diabetes [3,4]. Bullous pemphigoid affects primarily elderly individuals from the fifth to seventh decade of life, with average onset of 65 years [5].

The autoantibodies against the components of skin can induce the blistering type of autoimmune disease. Autoimmune blistering diseases are two types: Blister in the epidermis (Pemphigus) and subepidermal blistering (Pemphigoid). Pemphigus, autoantibodies target (Dsg1) and (Dsg3) desmogleins, which play an important role in cell-cell adhesion between desmosomes and keratinocytes, thus cause blister formation with acantholysis [6].

Autoantibodies in Bullous pemphigoid target molecules which involves in connecting basal epithelial cells and basement membrane in hemidesmosomes, such as type XVII collagen (COL17, BP180), type VII collagen (COL7), dystonin-e (BP230), P200 and laminin 332 [7,8]. Furosemide, Nonsteroidal anti-inflammatory drugs (Ibuprofen), Captopril, Phenacetin, Penicillamine, Etanercept and systemic antibiotics have been associated with Bullous pemphigoid [9,10]. Topical Clobetasol Propionate 40 mg (0.05%) and Oral Prednisolone (0.5 mg/kg/day) is preferred for disease control of drugs induced Bullous Pemphigoid in patients [11]. This treatment was in support with European Dermatology Forum in collaboration with the European Academy of Dermatology and Venereology [12,13]. The well-established immunosuppressive medication is a purine analogue (Azathioprine), DNA-synthesis inhibitor (mycophenolatemofetil) and folate antagonist (methotrexate), Rituximab and Omalizumab, are advised as alternative treatment for Bullous Pemphigoid [11]. But these drugs would

have more adverse effects so patient must be monitored by physician [14,15].

Case Report

A 42-year-old male patient was admitted with chief complaints of itching, fluid filled blisters since 1 week over chest, lower limbs and scalp and gradually progressed to upper limb and face and he was admitted in local territory hospital of Warangal region.

Physical examination

On examination the patient was conscious coherent, afebrile with edema, fluid filled blisters over chest, upper limb, lower limb, on palms and face are found on body (Figures 1-3).



Figure 1. Formation of fluid filled blisters on hand.

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Figure 2. Formation of fluid filled blisters on palm.



Figure 3. Formation of fluid filled blisters on wrist back.

Clinical examination

All investigations were performed and revealed that Hemoglobin - 8.5 gms, RBS -189 mg/dL. Cutaneous examination was found to be fluid filled bullae over body but oral and genital mucosa spared. Nikolskys signs and Bullae sign was found to be positive.

Past history

Patient presented with a history of type II diabetes with uncontrolled glycemic status. His Fasting blood sugar level is 125 mg/dL, Post lunch blood sugar level is 190 mg/dL, with the medication of Metformin and Glimperide since last 7 years.

Previously, two months back patient admitted in hospital with similar complaints and treated with anti-histamines (Cetirizine 5 mg /OD) & Corticosteroid (Dexamethasone) 1 ml/OD. The etiology for the triggering of this disease was not examined and it was neglected during 1st time attack but after recurrent attack the examination for etiology of the disease was observed and determined.

During hospital admission, Management of blisters they treated with Inj. Dexamethasone-1 ml OD, Inj. Pantoprazole- 40 mg OD, Inj. Cefotaxim -1g BID, Tab. Cetirizine-5 mg BID, Tab Iron and folic acid-OD, Tab. Vit C- OD, Ont. Soframycin-OD topically, Ont. Betamethasone OD topically for 7 days and continued to take Glimperide-2 mg, BID and Insulin 5IU/OD.

Day to day examination of RBS was found to be declined as 2nd day- 195 mg/dl, 3rd day -173 mg/dl, 4th day - 168 mg/dl, 5th day- 160 mg/dl and it maintain constant for next 2 days, HbA1c was found to be 6.5 .

Patient relieved from symptoms and blisters are healing well, he was discharged with advice to continue Dexamethasone, Ont. Soframycin, Tab. Ceftirizine till follow up visit. After a week the blister are healing without any

scarring and next follow up for 3 months was clear with no new complaints was observed.

Discussion

Bullous pemphigoid is a cutaneous auto immune blistering disorder against the hemidesmosomal protein. BPAG1 and BPAG2 resulting in deposition of IgG in the basal cell-basement membrane region in a linear fashion way. Bullous pemphigoid mostly occurs in elderly patients, due to abnormal immune response. The etiology of this disease is still not clear. Bullous pemphigoid induced with several drugs like Furosemide, Spironolactone, Penicillin, Sulphasalazine and Gliptins. But Metformin was not reported Bullous pemphigoid, only one case report has been suggested still now. Metformin induced Bullous Pemphigoid can be very harmful. Many reports suggested that BP is caused by Gliptin, however this should be noted that patients were also taking metformin along with Gliptins. Gliptins inhibit the enzyme dipeptidyl peptidase, it has shown ubiquitously expressed in almost every organ systems, including skin [4]. The underlying pathogenesis of metformin can be related to increased levels of Transforming Growth Factor Beta (TGF- β) increase in esnophilia level. In the 1st reported case the Bullous Pemphigoid was reported after 12 days usage of Metformin and this currently case the Bullous Pemphigoid was reported after the continuous usage of 7 years. Based on the above evidences, usage of metformin for longer periods of time may also cause BP and an ultimate outcome can be fatal, if it is not diagnosed and not treated in time. The appropriate monitoring and alertness is required when new signs and symptoms are raised and absorbed to avoid such complication.

Conclusion

Diabetes mellitus is one of most prevalent chronic disease, the main drug of choice to treat type-2 diabetes is metformin which is the safest drug but it can also cause rare complication like bullous pemphigoid, which is irrespective to time span of usage of drug with greater implication. Timely detection and correct treatment choice can decrease fatal outcome.

Conflicts of Interest

Author declares that there is no conflict of interest.

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