# CIPROFLOXACIN INDUCED BULLOUS PEMPHIGOID: A CASE REPORT

**Ravishankar AC[1*], Hiremath SV[1]**

[1]Dept of Pharmacology and Pharmacotherapeutics, JN Medical College, Belgaum, India.

**Summary**

Bullous pemphigoid (BP) is a idiopathic autoimmune disease of elderly characterized by formation of subepidermal blister, many drugs can induce BP.

We present a 45 year old woman of Indian descent who presented with history of rashes with vesicles which started upon taking ciprofloxacin. It was diagnosed as ciprofloxacin induced bullous pemphigoid by clinical examination and biopsy.

Onset of BP in patients less than 60 years is extremely rare and Ciprofloxacin is one of the very rare drugs that cause BP.

**Key Words:** Bullous pemphigoid, Ciprofloxacin, Subepidermal bulla.

***Corresponding author:**
Ravishankar A. C.,
Post graduate,
Dept of Pharmacology and Pharmacotherapeutics,
J N Medical College, Belgaum-590010, Karnataka, India.
Phone: 9590678578, Fax: 08312470759, e-mail: drchellaravi@gmail.com

## Introduction

Bullous pemphigoid (BP) is an autoimmune subepidermal blistering disease that predominantly affect elderly more than 60 years of age. It is characterized by formation of large tense blisters and immunologic finding of $C_3$ and IgG at the basement membrane zone.[1]

It is associated with tissue bound and circulating autoantibodies against hemidesmosomal bullous pemphigoid antigens BP230 (BPAg1) and BP180 (BPAg2). The precise role of bullous pemphigoid antigens in the pathogenesis of bullous pemphigoid is not completely clear. BPAg1 (BP230) is an intracellular component of the hemidesmosome; BPAg2 (BP180, type XVII collagen) is a transmembranous protein with a collagenous extracellular domain, they promote dermoepidermal cohesion.[2]

**Clinical features**: Can be classified in to two phases

**Non bullous phase** - Patient may have mild to severe intractable pruritis which may be associated with eczema, papular and/or urticarial lesions.

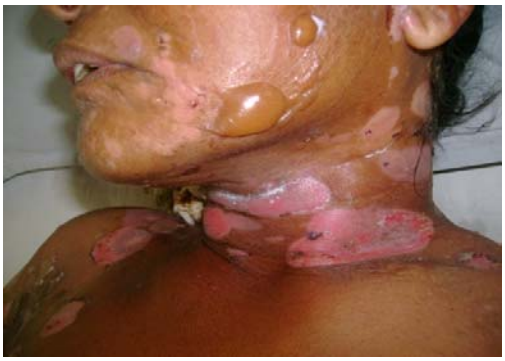
**Bullous phase** – Characterized by formation of vesicles and tense bulla containing clear fluid which occurs on normal/erythematous skin. Lesions have symmetrical distribution mainly over flexural aspects of limbs and lower trunk. Residual postinflammatory changes include hypo & hyperpigmentation. Oral cavity is involved in 30% of individuals.[3]

## Case Report

45 year old women of Indian descent presented with 15 days history of rashes with vesicles all over the body. Patient gave history of burning micturation from last one month, for which she was started on Tab ciprofloxacin 500 mg twice daily. Patient took medication for 7 days, on $8^{th}$ day of medication patient developed intense itching all over the body following which she developed vesicles first over both lower limbs which gradually spread to other parts. There was no history of any other drug intake.

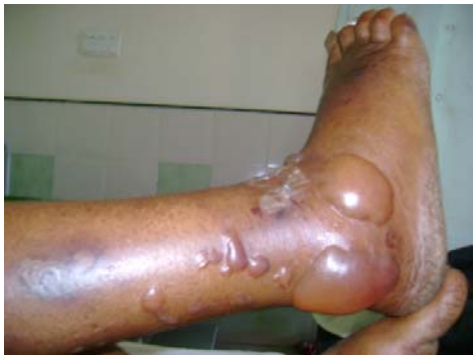
On examination – Patient was afebrile, conscious, alert, oriented. Blood pressure was 110/70 mmHg. Cutaneous examination revealed multiple tense bullae and vesicles present over face, chest, back, upper limb, flexural aspects of limbs and lower trunk. Multiple raw areas due to rupture of bullae were present on back and upper limbs. On systemic examination, no abnormality was detected.

**Figure 1**



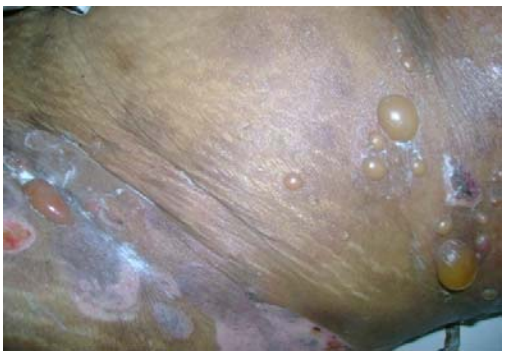
**TENSE BULLAE OVER FACE**

**Figure 2**



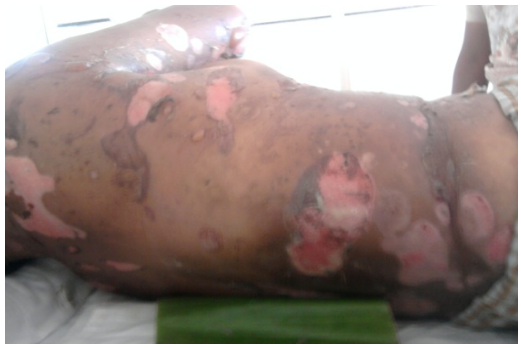
**BULLAE OVER RIGHT LOWER**

**Figure 3**



**FLEXURAL ASPECT OF LEFT LOWER LIMB AND LOWER TRUNK**

**Figure 4**



**MULTIPLE RAW AREAS DUE TO RUPTURE OF BULLAE**

**Investigations**

Haemoglobin – 12 gm%, Total count – 10,100 (N – 70, L- 15, E – 15), Absolute Eosinophil Count – 1612, Peripheral smear shows eosinophilia, Blood urea – 24, serum creatinine – 0.8, Total protein – 6.4, Serum albumin – 2.8, Serum A: G – 0.8

HIV 1 & 2 - Negative

Urine microscopy – WBC: 12 – 15 / high power field.

**Tzanck smear** – Smear show good number of neutrophils, few lymphocytes, eosinophils, plenty of RBC's

**Immunofluorescence report –**
IgG moderately strong linear BMZ band,
C3 strong linear BMZ band,
IgM, IgA, Fibrinogen negative.
Impression: features suggestive of bullous pemphigoid

**Biopsy report –**
Section studied showed structure of skin comprised of epidermis and dermis. At the edge of biopsy there is a subepidermal bulla. Dermis showed perivascular lymphocytic and eosinophilic infiltrate. Impression – features suggestive of bullous pemphigoid.

**Differential Diagnosis**

Pemphigus,
Subepidermal blistering disorders include

Cicatricial pemphigoid,
Herpes gestationis,
Epidermolysis bullosa acquisita,
Linear IgA dermatosis,
Dermatitis herpetiformis.[4]

## Discussion

Bullous pemphigoid(BP) is an idiopathic disorder. Many drugs have been known to induce BP. Drug-induced BP presents similarly to idiopathic BP except that it is temporally related to a drug, systemic or local, and it normally clears after discontinuation of the inciting agent. There have been at least 30 systemic drugs described in association with drug-induced BP.[5] (Table 1)

**Table 1 Medications reported to induce bullous pemphigoid**

| |
|---|
| Actinomycin D, Amoxicillin, Ampicillin, Anti-influenza vaccine, Arsenic, Azapropazone Captopril, Chloroquine, Clonidine, Dactinomycin, Enalapril, Furosemide, Flupenthixol, Gold thyosulfate, Ibuprofen, Interleukin-2, Mefenamic acid, Methyldopa, Nadolol, Omeprazole, Penicillamine, Penicillin, Phenacetin, Placental extracts, Potassium iodide, Practolol, Psoralens with UVA, Risperidone, Salicylazosulfapyridine, Sulfonamide, Tetanus toxoid, Thiopronin, Tiobutarit, Tolbutamide. |

Thiol compounds and sulfonamide derivatives have been commonly implicated whereas most other drugs have only occasionally been reported. [5] Ciprofloxacin induced BP is a very rare case.

**Diagnosis**

Usually done mainly on clinical features

Light microscopy (Histological features) – show subepidermal blister accompanied by dermal inflammatory infiltrate composed of eosinophils and mononuclear cells.[3]

Immunofluorescence microscopy – Provides clues that are essential and sufficient for diagnosis. It demonstrates presence of fine, linear, continuous deposits of IgG &/or C3 along the epidermal basement membrane.[3]

**Treatment**

Topical and sytemic corticosteroids are the mainstay of treatment. For localized BP, very potent topical steroids can be tried. Recommended initial dose of prednisolone
– in localized or mild disease is 20mg/day or 0.3mg/kg/day
– in moderate disease 40mg/day or 0.6mg/kg/day can be given
– in severe disease 50 – 70mg/day or 0.75 – 1mg/kg/day can be given. Dosage can be reduced over the course of a few weeks to 15 – 20 mg/day. Majority can be managed on less than 10mg/day prednisolone which can be slowly withdrawn by reducing 1mg/month.[6]

Use of Immunosuppressants is a matter of debate - Azathioprine, Methotrexate, Chlorambucil can be given at a dose of 0.1mg/kg/day, Cyclophosphamide 1-3mg/kg/day, Cyclosporine 1-5mg/kg/day or Mycophenolate mofetil 1.5 – 3 grams/day can be given

The combination of nicotinamide (500 – 2000 mg/day) and minocycline or doxycycline has been tried as a therapeutic alternative when obvious contraindication to corticosteroids exists.[3] (Table 2)

**Table 2- Therapeutic Approach for a case of Bullous pemphigoid**

| **Mild &/or localized disease** | **Extensive/ Persistent disease** |
|---|---|
| - Super potent topical steroids<br>- Nicotinamide + Tetracycline/Minocycline<br>- Dapsone<br>- Topical immunomodulators ( Tacrolimus) | -Oral corticosteroid<br>- Immunosupressant agents like Azathioprine<br>- Intravenous immunoglobulin<br>- Plasma exchange<br>- Rituximab |

## Conclusion

Bullous pemphigoid is a disease of elderly more than 60 years, but condition can occur in those under 40 years. Literature survey indicates that no case of BP have been reported in 40 – 60 year age group. We have a 45 year old female patient with ciprofloxacin induced BP, which is an extreme rarity.

## Acknowledgement

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Written informed consent is taken from the patient in her own language for examination and publication.

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**Consent:** Written informed consent taken from the patient in her own language