

## CASE REPORTS

# TOXIC EPIDERMAL NECROLYSIS AND AGRANULOCYTOSIS: RARE ADVERSE EFFECTS OF CIPROFLOXACIN

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### ABSTRACT

*Ciprofloxacin is one of the most commonly used antibacterial agents with relatively few side effects. Serious adverse reactions reported with ciprofloxacin are rare with an incidence of 0.6%. Recently we came across two rare adverse effects of ciprofloxacin, viz. toxic epidermal necrolysis and agranulocytosis. To our knowledge, a total of seven cases have been reported in the literature documenting an association between oral ciprofloxacin administration and toxic epidermal necrolysis. One case of granulocytopenia, four of pancytopenia and fifteen of leucopenia worldwide have been reported. With the use of ciprofloxacin becoming more and more widespread, these two rare but fatal complications of ciprofloxacin should be borne in mind.*

**Key words:** Adverse drug effects, agranulocytosis, ciprofloxacin, toxic epidermal necrolysis

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### INTRODUCTION

Ciprofloxacin is a 4 Quinolone antibiotic active against a broad range of bacteria. It is a relatively safe drug.<sup>[1]</sup> Side effects occur in 10% of patients and are generally mild. Adverse reactions rarely require discontinuation of therapy.<sup>[1]</sup> Common side effects include nausea, vomiting, diarrhea, headache, dizziness, agitation, sleep disturbances and hypersensitivity reactions.<sup>[2]</sup> Rarely, it has been associated with

agranulocytosis, toxic epidermal necrolysis, photosensitivity reaction, renal damage and acute renal failure.<sup>[3]</sup> We report a case of ciprofloxacin induced toxic epidermal necrolysis and agranulocytosis in a 25-year old housewife.

### CASE REPORT

A 25-year old housewife presented with fever, conjunctival soreness and multiple erythematous discrete confluent blanchable macules and papules all over the body, four days after the intake of ciprofloxacin for urinary tract infection. The drug was discontinued and on the second day of her admission, the patient developed bullous lesions over the face, neck and upper limbs, which progressed to involve the abdomen, chest, back and lower limbs. Bullae subsequently

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ruptured to leave large raw painful areas [Figure 1]. Nikolsky's sign was positive. Erosions of palate and buccal mucosa with crusting of lips and nasal cavity were present. The patient was kept under isolation with all aseptic precautions. Autoclaved banana leaves were used to minimize skin trauma. The patient developed leucopenia (total count- 1,100 cells/cu.mm) and neutropenia (absolute neutrophil count- 65 cells/cu.mm) for which granulocyte colony stimulating factor was given for five days and the counts returned to normal. The patient developed septicemia (skin and blood cultures showed heavy growth of staphylococcus aureus) on the third day of admission, which was treated with IV meropenem 1 g three times daily for fourteen days. She recovered completely within 2 months [Figure 2].

## DISCUSSION

Toxic epidermal necrolysis is a potentially life threatening skin disease characterized by an extensive detachment of the epidermis with sub epidermal blister formation and severe constitutional symptoms. It is usually associated with multi system involvement and a high mortality between 20% and 66% in the acute

phase.<sup>[4]</sup> Drug reactions are the most frequent cause.<sup>[4]</sup> Other etiologies include infection, malignancies and vaccination.<sup>[5]</sup> The average incidence of toxic epidermal necrolysis is 0.5 to 1.4 per million per year.<sup>[5]</sup>

Females appear to have a greater predilection for developing toxic epidermal necrolysis than males.<sup>[6]</sup> Though the main culprit drugs include sulfonamides, antiepileptic drugs, ampicillin, allopurinol and NSAIDs, toxic epidermal necrolysis is rarely reported with ciprofloxacin.<sup>[6]</sup>

Agranulocytosis is another rare life threatening complication of ciprofloxacin.<sup>[3]</sup> The overall incidence of non chemotherapy drug induced agranulocytosis ranges from 2.6 to 10 cases per million patients exposed to drugs per year.<sup>[7]</sup> Neutropenia usually leads to severe sepsis, requiring IV broad spectrum antibiotic therapy, as in our patient. The severity of neutropenia and its duration may also impact negatively on the outcome. Hemopoietic growth factors have been shown to shorten the duration of neutropenia in drug induced agranulocytosis. With appropriate management, the mortality rate is around 5%.<sup>[7]</sup>



**Figure 1:** Toxic epidermal necrolysis (pre-treatment)



**Figure 2:** Toxic epidermal necrolysis (post-treatment)

In our patient, we came across two rare life threatening complications of ciprofloxacin, viz., toxic epidermal necrolysis (TEN) and agranulocytosis. There have been reports in the past regarding the fatal outcome of ciprofloxacin induced TEN.<sup>[8,9]</sup> We did not use corticosteroids or other immunosuppressive drugs and still the outcome was favorable.

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