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Case Report

Fatal case of ciprofloxacin-induced toxic epidermal necrolysis

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ABSTRACT

Ciprofloxacin is a very commonly used antibiotic. Mild to moderate gastrointestinal side effects commonly reported whereas serious reactions such as Steven–Johnson syndrome and toxic epidermal necrolysis (TEN) are very rare. We report the fatal case of 25 years female who had TEN after ingestion of tablet ciprofloxacin. This case report highlights the need to be critically aware of this rare, but life-threatening side effect of this commonly prescribed antibiotic.

Keywords: Ciprofloxacin, Toxic epidermal necrolysis, Causality

INTRODUCTION

Cutaneous drug reactions are the most common type of adverse drug reaction (ADR) occurring in 2-3% of hospitalized patients.[1] Toxic epidermal necrolysis (TEN) and Steven–Johnson syndrome (SJS) are rare but severe adverse cutaneous drug reactions; most commonly triggered by medications and are characterized by fever and mucocutaneous lesions leading to necrosis and sloughing of the epidermis. SJS and TEN are distinguished chiefly by severity and percentage of body surface involved. The term "SJS/TEN" is used to refer collectively to SJS, TEN, and SJS/TEN overlap syndrome.[2] Early diagnosis, immediate discontinuation of offending drug, supportive therapy, and prevention of ocular complication and infection gives best results in the management of TEN. Systemic glucocorticoid therapy consisting prednisolone 1-2 mg/kg given early in the evolution of the disease, but for a short period.[3] Other immune modulators like cyclosporine (3-4 mg/kg/day), cyclophosphamide (100-300 mg/day intravenously for 5 days) can be used. Sometimes, plasma exchange and immunoglobulins can be used to complete remission of the condition.[4]

Fluoroquinolones represent approximately 11% of antibiotics prescribed worldwide on an out-patient basis to treat infections such as urinary tract infections, lower respiratory tract infections, and bronchitis.[5] Ciprofloxacin, a first generation fluoroquinolone is among the commonly prescribed antimicrobial agents because of activity against

broad range of bacteria and a low ADR profile, with mainly gastrointestinal side effects. Cutaneous reactions such as pruritus, urticaria, flushing, hyperpigmentation, rash, and SJS/TEN are some of the rare side effects due to ciprofloxacin with an incidence of <1% in patient population.[6,7] Here, we report a fatal case of ciprofloxacin-induced TEN.

CASE REPORT

A 25-year-old female patient presented with a sore throat to a local private practitioner who prescribed her tablet ciprofloxacin 500 mg twice a day. After 3-4 days, she started developing multiple oral erosions in the entire oral cavity and 1-2 days later developed multiple reddish-brown lesions followed by fluid filled vesicles all over the body with dryness and peeling of lip mucosa, redness, and discharge from both eyes which was accompanied by fever also. For these complaints, she again consulted the same practitioner. He gave her oral medications including methylprednisolone and ranitidine. Some injectable was also given for which no records were available. There was only partial improvement in the condition. So, patient came to tertiary care hospital casualty after a week and got admitted in skin ward.

On local examination, multiple erythematous to hypopigmented macules and varying sized patches of 0.3 cm × 0.5 cm-2 cm × 3 cm were present over face, neck, chest, back, abdomen and bilateral upper and lower limbs. Multiple vesicles and bullae of size varying from 0.2 cm × 0.2 cm to 1 cm × 4 cm were present over chest, back, bilateral upper and lower limbs. The lesions were surrounded by erythematous halo and ring. Crusted lesions were present over both upper and lower lips. Oral cavity showed multiple erosions of size 0.3 cm × 0.4 cm-1.5 cm × 2 cm present over bilateral buccal mucosa, hard palate, and tongue with erythematous floor. Ophthalmic examination showed congestion and profuse discharge in bilateral eye. In the nose**,** erythematous crusted lesions of size 0.2 cm × 0.3 cm were present over the nasal bridge whereas on palms and soles, erythema with multiple vesicles and bullae was present. 25-30% total body surface area was involved, and Pseudo Nikolsky's sign was positive.

On systemic examination, the patient was alert, and her pulse and blood pressure were within normal limits. She had no pallor, icterus, lymphadenopathy, clubbing, and pedal edema. No abnormality was detected in her cardiovascular, respiratory and central nervous system examination. On the day of admission, her hemoglobin was 13.7 g/dl, platelets, and total leukocyte counts were adequate. Renal function test and serum electrolytes were within normal limits. No abnormality was detected in electrocardiogram.

At first provisional diagnosis of TEN/SJS was made. But as the lesions subsequently extended to involve more than 30% body surface area, she was finally diagnosed as a case of TEN. For the treatment standard regimen was followed and injection hydrocortisone, injection amoxyclav, injection ranitidine were given. Capsule tetracycline, tablet iron, tablet B complex, and calcium carbonate, tablet betnesol were also given and for local application flusid-b (beclomethasone dipropionate and fusidic acid) cream, dologel MP (choline salicylate, benzalkonium chloride, lignocaine), relub (carboxymethylcellulose) eye drop, tobramycin eye drop, Lacrigel (hypomellose) eye drop, and Condy's gargles were given.

But the patient did not show any sign of recovery and died after 5 days of septicemia.

DISCUSSION

TEN is a rare, but potentially life-threatening condition characterized by an extensive detachment of the epidermis with subepidermal blisters formation and severe constitutional symptoms. It is predominantly induced as side effects of medication such as antimicrobials (50%), nonsteroidal anti-inflammatory drugs (22.41%), and anti-seizure drugs (18.96%).[7] Other etiologies include various infections, malignancy, vaccination,[8] and transplant of bone marrow.[9]

The average incidence of TEN is 0.4-1.3 per million per year.[10] Females appear to have a greater predilection for developing TEN than males pertaining to its immunological etiology.

In the literature, among fluoroquinolone sparfloxacin, moxifloxacin, norfloxacin, and levofloxacin are most commonly documented for causing TEN/SJS. Only a handful of cases have been reported where ciprofloxacin has been implicated. A fatal case of ciprofloxacin-induced TEN in a 50-year-old man treated for a bacterial infection of lower extremity venous stasis ulcers was reported in the west.[11] On literature search, one case of TEN and agranulocytosis because of ciprofloxacin has been reported from India[12] and patient was recovered completely after 2 months of treatment.

In this case, the patient was placed on ciprofloxacin 2 days prior to the onset of cutaneous signs and had not taken any other medication including over the counter drugs known to cause TEN. Causality assessment was done using Naranjo scale and WHO-Uppsala monitoring center causality assessment system. By Naranjo scale, the score was five, so causality was assigned as probable and also by WHO-UMC assessment the ADR was labeled as probably caused by ciprofloxacin.

CONCLUSION

Ciprofloxacin is one of the most commonly used antibiotics. The incidence of TEN as an ADR reported with this drug is very rare, but it is still occurring in the population. Hence, physicians need to be aware of this rare side effect not only

to avoid life-threatening reaction but if occurs it should be reported in order to generate further data regarding its incidence in the general population.

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