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Ciprofloxacin induced Stevens Johnson syndrome: A case report on Dermatology department

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Abstract

Ciprofloxacin is a broad-spectrum quinolone antibiotic which is used to treat a wide variety of infections, especially those likely to be caused by Gram-negative bacteria. A 15-year-old female patient presented in medical outpatient department of dermatology with the chief complaints of increased frequency of urine. she was prescribed Ciprofloxacin 500 mg bid with Rantidine 150mg for her urinary tract infection. After 3-4 days, she reported back with some complaints and later diagnosed as SJS. As ciprofloxacin drug can induce various adverse reactions. Hence, close monitoring is necessary for the patients who are receiving this drug.

Keywords

ciprofloxacin; stevens-johnson syndrome; urinary tract infection; adverse drug reaction

Introduction

Ciprofloxacin is a 4th generation quinolone antibiotic and a broad spectrum antimicrobial agent. It has very few side effects and this drug is relatively safe [1]. Fluoroquinolones represent approximately 11% of antibiotics prescribed worldwide to treat outpatient infections such as urinary tract infections, lower respiratory tract infections, and bronchitis [2] Side effects occur in 10% of patients and are generally mild. Adverse reactions rarely require discontinuation of therapy. Common side effects include nausea, vomiting, diarrhoea, headache, dizziness, agitation, sleep disturbances and hypersensitivity reactions. Rarely, it has been associated with agranulocytosis, stevens Johnson syndrome, toxic epidermal necrolysis, photosensitivity reaction, renal damage and acute renal failure [3].

Stevens Johnson syndrome (SJS) is a severe hypersensitive reaction that can be precipitated by infection such as herpes simplex virus or mycoplasma, vaccination, systemic diseases, physical agents, foods and drugs [4,5]. The drugs that cause SJS commonly are anti-bacterial(sulfonamides), anticonvulsant (phenytoin, phenobarbital, carbamazepine), non-steroidal anti-inflammatory drugs (oxicam derivatives) and oxide inhibitors(allopurinol) [6,7]. SJS may present as a non specific febrile illness (malaise, headache, cough, rhinorrhea) with polymorphic lesions of skin and mucous membrane characterized by acute blisters and erosions [4]. Stevens-Johnson syndrome, otherwise known as erythema multiforme major, is thought to represent acontinuum of disease; the most benign type of

which iserythema multiforme, whereas toxic epidermal necrolysis is the most severe [8].

Case Report

A 15-year-old female patient presented in medical outpatient department of dermatology Rajiv Gandhi Institute of Medical Sciences (RIMS), with the chief complaints of increased frequency of urine. A urine complete examination which includes culture and sensitivity tests were done and the report concluded as UTI. So, she was prescribed with Ciprofloxacin 500 mg bid and Ranitidine 150mg. After 3-4 days, she reported back with complaints of 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 associated with fever. For these complaints, the patient was admitted and kept under isolation with all aseptic precautions. On local examination, multiple erythematous to hypopigmented macules and varying sized patches of 5cm × 6 cm and also Multiple vesicles and bullae of size varying from 3 cm ×4 cm to 6 cm × 3 cm were present and were present over face, neck, chest, back, abdomen and bilateral upper and lower limbs. Lesions were also present over both upper and lower lips which were surrounded by erythematous halo. Oral cavity showed multiple erosions present over bilateral over the face and all over the body, hard palate, In the nose, erythematous crusted lesions were present over the chest region. She was slight drowsy at the time of presentation. Other systemic examination including respiratory system, cardiovascular system, and abdomen was normal. Her hemoglobin was 12.7 gm/dl, and total leucocyte count was 12,700/mm3, Renal function test, liver function and serum electrolytes were within normal limits. No abnormality was detected in electrocardiogram. At first provisional diagnosis of SJS was made. But as the lesions subsequently extended to involve more than 60% body surface area, she was finally diagnosed as a case of SJS. For the treatment, standard regimen was followed and injection hydrocortisone, injection amoxiclav, injection ranitidine ,and for application Ointment betamethasone , beclomethasone dipropionateand fusidic acid cream, dologel MP (choline salicylate, benzalkonium chloride, lignocaine), relub (carboxymethylcellulose) eye drop, tobramycin eye drop, hypomellose eye drop were administered. Ciprofloxacin induced stevens johnson syndrome shown in (figure 01). After 7 days, she recovered maximum and discharged. The probability due to ciprofloxacin cannot be ruled out after applying Naranjo's scale of causality assessment of adverse drug reactions with a score of 4. WHO ADR assessing scale karch and lasagna results were shown in (TABLE 1).We also assessed the severity, predictability and preventability as a part of management through modified hart wig and Siegel severity scale, schomok and Thornton preventability scale.

ADR Management: Generally, management of ADR includes withdrawal/suspension, dose reduction of suspected drug and administration of supportive therapy. Here in this case report the suspected drug Ciprofloxacin was discontinued.

ADR Analysis:

Table 1: Causality assessment of suspected ADRs

Suspected drug And Reaction (ADR)	Naranjo's Scale	WHO- Probability Scale	Karch& Lasagnas Scale
Ciprofloxacin Induced Stevens Johnson syndrome	Possible	Probable	Probable

SEVERITY: Moderate level 4

PREDICTABILITY: Unpredictable

PREVENTABILITY: Probably preventable

Discussion

Ciprofloxacin is a well-known and widely used antibiotic for various infections. It induces various drug reactions ranging from an urticarial eruption to SJS. In a country where over the counter prescription is more abused, the exact magnitude of the usage is very tough to estimate. It has been associated with the following types of drug reactions (Table 2).

Stevens-Johnson syndrome spectrum is one of the severe drug induced cutaneous reaction. SJS is the milder form; the incidence of SJS is estimated to be 1 to 6 cases per million people per year. It is characterized by erythema with blisters and erosions of the skin with the degree of epidermal detachment of less than 10% of body surface area, fever and malaise, and erosions of mucous membranes [9].Before the appearance of mucocutaneous erosions, the initial symptoms include fever, conjunctivitis, pharyngitis and pruritus. Mucous membranes in the oral cavity, eyes, genitalia, and anus are commonly affected a few days before skin lesions appear. The initial lesions are poorly defined macules with dark centers. The lesions usually reach their greatest area of coverage in a few days, but they can manifest over a period of a few hours after [10]. Stevens-Johnson syndrome is an immune-complex–mediated hypersensitivity disorder that may be caused by many drugs, viral infections, and malignancies [11].The main feature of SJS is epidermal cell apoptosis, which may be mediated through keratinocyte Fas-FasL interaction or through cytotoxic T-cell release of perforin and granzyme B [10]. SJS clinical features are shown in (Table 3).

Table 2: Cutaneous adverse drug reactions (CADRs) caused by Ciprofloxacin

S.No.	Ciprofloxacin induced CADRs	S.No.	Ciprofloxacin induced CADRs
1	Bullous fixed drug eruption	6	Stevens-Johnson syndrome
2	Erythema multiforme	7	Dress
3	Vasculitis	8	Urticaria
4	Toxic epidermal necrolysis	9	Sweets syndrome
5	Bullous Pemphigoid		

Table 3: Clinical features of Stevens-Johnson syndrome

Clinical features	Stevens-Johnson syndrome
Incubation period	Few days to 1 month of drug intake
Prodromal symptoms	Severe flu like symptoms
Lesions	Bullae, flat atypical targets or purpuric macules
Distribution	Predominantly central
Skin	May be involved
Mucosa	Always involved
On rechallenge	No predilection for previously affected sites
On histopathology dermal melanophages	Lesser
Inflammatory infiltrate	Lymphohistiocytic infiltrate
Serum level of granulysin	Relatively higher
Systemic complications	Present
Sequelae	Ocular: Symphblepharon, trichiasis, xerosis

Re-challenging the patient to the suspected offending drug is the only known test to possibly recognize the causative agent, but that is unethical and not advisable. Therefore, certain causality assessment scales regarding drug reaction have been described like the Naranjo ADR probability scale and ALDEN algorithm [12,13].

Management of SJS depends upon the severity, in milder cases topical steroids and withdrawal of drug is enough but in severe cases fluid replacement, nutritional support, antibacterial therapy, ophthalmology consultation and early systemic corticosteroids are beneficial. A few studies have shown cyclosporine, plasmapheresis and IV immunoglobulin to be helpful [10].

Conclusion

Ciprofloxacin is widely prescribed by physician as well as also a popular common antibiotic OTC drug. Physician must suspect if such reaction occurs during therapy involving ciprofloxacin and should carefully evaluate drug-associated reaction. It is important that skin reactions are identified and documented in the patient record. Rapid recognition of adverse reactions are important, thereby specific action should be taken whether to withdraw the drug or to provide specific treatment which may leads to decrease in morbidity rate.