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# Ciprofloxacin Induced Stevens-Johnson Syndrome

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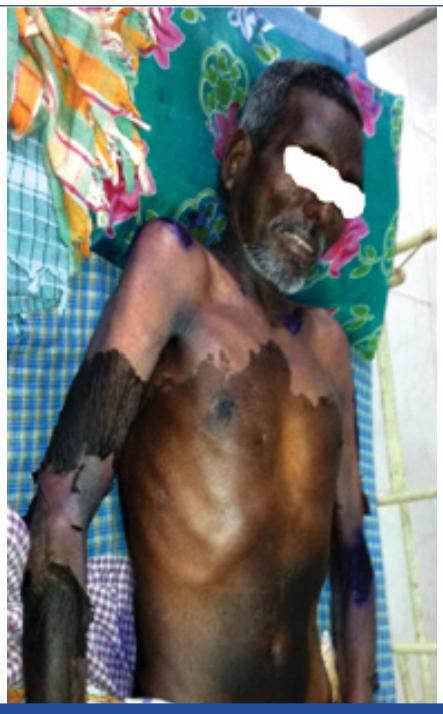
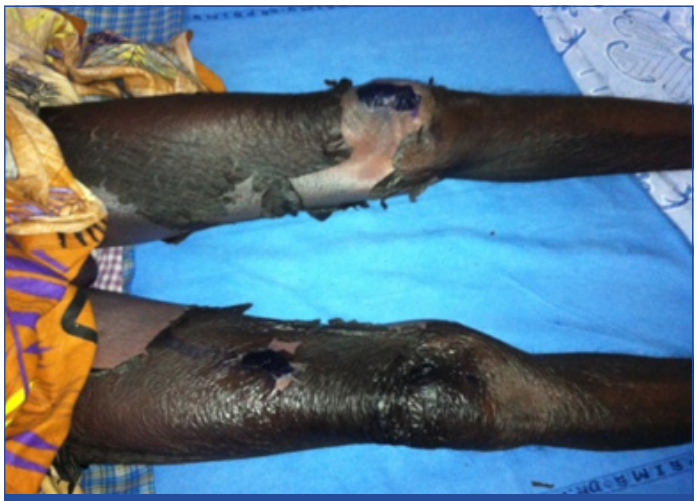
**Keywords:** Adverse drug reaction, Skin, Toxic epidermal necrolysis

A 65-year-old man was admitted to the hospital with high grade fever, loose stools and exfoliated hyperpigmented skin. His past history revealed that he had consulted a Registered Medical Practitioner (RMP) with the chief complaints of loose stools, vomiting and fever. He was then prescribed Ciprofloxacin 500 mg and Tinidazole 600 mg. Later, he observed hyper pigmented areas and some blebs over the skin, half an hour following administration of the same drug. Gradually, by the next morning, the pigmentation spread all over the body and the blebs increased in size. Then, he was rushed to a government hospital where he was administered Ringer Lactate (RL), Dextrose Normal Saline (DNS), IV CIFRAN (Ciprofloxacin), injection RANTAC (ranitidine), injection Diclofenac, injection Paracetamol, injection PIPTAZ (Pipercillin+Tazobactam) IV BD. Following administration of these drugs, he experienced painful exfoliation of skin [Table/Fig-1,2]. Due to administration of IV CIFRAN, the problem further aggravated. The causality assessment was carried out using Naranjo scale. The obtained causality score was 10. Causal relationship was found to be "Definite" as per Naranjo scale [Table/Fig-3]. Laboratory findings indicated that urine myoglobin was positive, LDH and SGOT were abnormally elevated whereas, serum creatinine and urea levels were moderately elevated [Table/Fig-4].

Hyperpigmented patches with exfoliated skin in the involved areas were left arm (9%), right arm (1%), right lower limb (2%), left lower limb (4%), back (1%), scrotum (1%), buttock (1%). Ulcer with serum discharge was positive, lips were dry and chapped, oral cavity white plaque positive on hard palate and glossitis positive. The total percentage of the skin involved was 19%. Nikolsky's sign was positive. The medical history and dermatological picture allowed us to make an initial diagnosis of SJS, likely triggered by the administration of ciprofloxacin.



**[Table/Fig-1]:** Hyperpigmented patches on chest.



**[Table/Fig-2]:** Exfoliated skin over lower limbs.

| | Question | Yes | No | Do Not Know | Score |
|---|---|---|---|---|---|
| 1. | Are there previous conclusive reports on this reaction? | +1 | 0 | 0 | 1 |
| 2. | Did the adverse event appear after the suspected drug was administered? | +2 | 0 | 0 | 2 |
| 3. | Did the adverse event improve when the drug was discontinued or a specific antagonist was administered? | +1 | 0 | 0 | 1 |
| 4. | Did the adverse event reappear when the drug was readministered? | +2 | 0 | 0 | 2 |
| 5. | Are there alternative causes that could on their own have caused the reaction? | 0 | +2 | 0 | 2 |
| 6. | Did the reaction reappear when a placebo was given? | 0 | 0 | 0 | 0 |
| 7. | Was the drug detected in blood or other fluids in concentrations known to be toxic? | 0 | 0 | 0 | 0 |
| 8. | Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 | 1 |
| 9. | Did the patient have a similar reaction to the same or similar drugs in any previous exposure? | +1 | 0 | 0 | 1 |
| 10. | Was the adverse event confirmed by any objective evidence? | 0 | 0 | 0 | 0 |
| | | Total Score: 10 | | | |
| | Causality of ADR is Definite as the total score exceeded 9 | | | | |

**[Table/Fig-3]:** Causality assessment of adverse drug reaction as per Naranjo scale.
If total score is ≥9, ADR considered as Definite; if total score is between 5 to 8; ADR considered as probable; if total score is between 1 to 4, it is considered as possible; if total score is ≤0; it is considered as doubtful.

| Parameters | Patient values | Reference values |
|---|---|---|
| Urine Myoglobin | Positive | - |
| Serum Creatinine | 1.9 | 0.6-1.5 (mg/dL) |
| Urea | 70 | 15-45 mg% |
| Haemoglobin | 10.9 | 13-18 (gm%) |
| ESR | 65 | 0-20 mm/1 hour |
| PCV | 30.5 | 35-45 % |
| LDH | 738 | 230-460 IU/L |
| SGOT | 100 | 0-42 IU/L |

**[Table/Fig-4]:** Laboratory findings of the patient with SJS.
*SJS - Stevens-Johnson Syndrome

There was a prompt resolution of the clinical status following the injection of Dexamethasone 0.5 mg one time a day, and topical therapy with a fusidic acid 2% + hydrocortisone acetate 1% based cream, three times per day, vitamin E cream on lips two times a day IV fluids of Normal Saline (NS) at a rate of 100 mL/hour were given. The patient was reviewed on daily basis and at the end of one week there was significant healing of the hyper pigmentation and the exfoliated skin.

Adverse Drug Reactions (ADRs) are one of the leading causes of morbidity and mortality. It has been estimated that approximately 2.9%-5.6% of all hospital admissions are caused by ADRs and as 35% of the hospitalised patients experience an ADR during their hospital stay [1]. SJS and TEN are one of the most serious, and rare ADRs. In SJS, less than 10 % of body surface area is involved and more than 30% in TEN [2]. The main feature of SJS and TEN is epidermal cell apoptosis, which may be mediated through keratinocyte Fas-FasL interaction or through cytotoxic T-cell release of perforin and granzyme [3]. Diagnosis majorly depends on the clinical presentation such as haemorrhagic erosions and erythematous macules along with histological analysis of skin biopsy showing typical full thickness epidermal necrolysis due to extensive keratinocyte apoptosis. It is important to identify the medication causing SJS and withdraw it immediately.

NSAIDs, Sulphadiazine, Sulfapyridine, Sulfamethoxazole, Sulfasalazine, Carbamazepine, Phenytoin, Phenobarbitone, Nevirapine, Lamotrigine are the drugs at high risk of causing SJS [4]. Based on causality assessment, ciprofloxacin was identified as the main culprit that has caused SJS in the indexed case. There were few recent evidences of Ciprofloxacin causing SJS in Indian population [5,6]. In this case, SJS symptoms were more aggravated by the repeated administration of the IV Ciprofloxacin. Treatment approach of SJS depends upon the severity, in milder cases topical steroids and withdrawal of the offending drug may suffice but in severe cases fluid replacement, antibacterial therapy, nutritional support, early systemic corticosteroids and ophthalmology consultation are beneficial. A few studies have shown cyclosporine, plasmapheresis and IV immunoglobulin to be helpful [7]. Steroid therapy should be initiated during initial stage (within 72 hours) and rapidly tapered off [8]. Dexamethasone 0.5 mg once daily remarkably improved the clinical status of the indexed patient. At times, early administration of high dose immunoglobulin along with corticosteroid therapy has also been recommended [9]. It is thus advised that Ciprofloxacin should be administered with the caution in patients with history of drug induced SJS.

Patient must be issued a medical allergic card that gives the information about the drugs that are allergic to the specific patient. Patients shall be educated to carry drug allergy cards for their subsequent visits to any hospital. Similarly, appropriate drug allergic history may help in preventing drug induced allergic reactions.

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