

# Ofloxacin Induced Cutaneous Reactions in Children

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## ABSTRACT

Cutaneous adverse effects to antimicrobials are a major health problem. Though majority of them are mild and self-limiting, severe variants like Steven Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN) are not uncommon. Ofloxacin, a fluoroquinolone widely used for the treatment of urinary tract infections, acute bacterial diarrheas, enteric fever, STDs and other soft tissue infections either as a single drug or in combination with other drugs. Earlier a case of mucocutaneous maculopapular rash with oral ofloxacin and was reported in an adult. In the present hospital set up there were few reports of such reactions to adults. Here we report three different variants of reactions associated with oral ofloxacin in children. Early detection of cutaneous lesions and immediate withdrawal of the offending drug can prevent progression of such reactions to their severe variants as well as morbidity and mortality.

**Keywords:** Children, Drug eruptions, Fluoroquinolones, Steven johnson syndrome

## CASE REPORT

### CASE- 1

A five-year-old female child weighing 16 kg had come to the paediatric OPD with upper respiratory tract infection for which she was prescribed Ofloxacin Hydrochloride syrup 5ml twice daily along with paracetamol syrup 5ml thrice daily. After a three day course, the patient came back with red coloured papules all over the body with severe itching. As soon as Ofloxacin was withdrawn the reactions subsided. Because she had improved from respiratory infection, no other antimicrobial was added, only calamine lotion for local application was advised. Following causality assessment the reaction was graded as 'probable' as per Naranjo's Scale and WHO-UMC causality assessment system.

### CASE- 2

A male child four-year-old age weighing 14 kg was prescribed Ofloxacin syrup 7.5 ml twice daily, along with paracetamol syrup 5 ml twice daily for enteric fever. Laboratory findings revealed Widal test positive, albuminuria and other haemogram findings in normal range. On clinical examination, pulse rate 92/minute, respiratory rate 20/min and blood pressure 100/76 mm of Hg was found. Two days after initiation of therapy multiple annular erythematous lesions of 2x2 mm size developed all over the body associated with itching [Table/Fig-1]. Ofloxacin was withdrawn immediately and substituted with Azithromycin syrup and paracetamol was continued. The skin reactions were treated with local application of calamine and oral



**[Table/Fig-1]:** Back of the child showing multiple erythematous lesions

hydroxyzine hydrochloride syrup. The reactions resolved 48 hours following change of treatment. Naranjo's causality assessment Scale describes the reaction to be probable.

### CASE - 3

A six-year-old female child was referred to the department of pediatrics for management of rash and papules all over the body and ulceration of buccal mucosa. Medical history revealed that such reactions developed following intake of ofloxacin syrup for three days which was prescribed by a local physician empirically for fever of nonspecific origin. Following 48 hours of medication, the patient developed erythema of eyelids with conjunctival congestion and buccal mucosal ulcerations. Also, painful red to black coloured erythematous maculopapular blisters rapidly appeared all over the body [Table/Fig-2]. On clinical examination her body temperature (axillary) was 101°F, pulse rate 108/minute, blood pressure 108/82



**[Table/Fig-2]:** Chest area of the child showing red to black coloured erythematous maculopapular blisters

mm of Hg. Naranjo's causality assessment Scale describes the reaction to be probable. The patient was treated promptly with I.V. Dexamethasone, chlorohexidine mouth wash, levocetizine and local treatment with calamine lotion. The patient was kept under observation under good nursing care, fluid electrolyte balance, strict asepsis and nutrition. Ten days following the treatment the reaction abated and general condition also improved.

## DISCUSSION

Permission from Institutional ethics committee and informed consent from the patient's parents for photographing was obtained before documentation of these cases. Naranjo's Scale and WHO-UMC causality assessment system are the most widely used and generally accepted methods for causality assessment, which were employed for causality assessment for the present cases.

Cutaneous drug eruptions are one of the most common types of adverse reaction to drug therapy, with an overall incidence rate of 1-5 % [1]. Ofloxacin is a widely prescribed antimicrobial agent for management of urinary tract infection, acute bacterial diarrheas, enteric fever, STDs and other soft tissue infections [2]. It's commonly reported side effects include fever, acute renal failure, agranulocytosis and other dermatological reactions. Earlier a case of mucocutaneous maculopapular rash with oral ofloxacin and was reported in an adult [3]. Here we describe three cases of oral Ofloxacin induced various cutaneous adverse reactions in children.

The fluoroquinolones as a class are generally well tolerated; most adverse effects are mild in severity, self-limiting and rarely result in treatment discontinuation [4]. The most commonly occurring effects are GI upset (nausea, vomiting, diarrhea, constipation and abdominal pain; less than 7% total). Less common effects may include central nervous system (CNS) events (less than 5%), blood disorders (approximately 5%), renal disturbances (approximately 4.5%), and skin hypersensitivity and photosensitivity effects (approximately 2%) [5]. Steven Johnson Syndrome associated with administration of Ofloxacin had been reported [6]. Of the above three cases, first case was of milder form where as in second and third case the reactions were severe. All the three cases reported such reactions following three days of initiation of Ofloxacin and had no known drug allergy previously. The severity of reaction was not dose and duration dependent but the recovery time varied according to the severity. Similar reactions have been documented with ciprofloxacin and levofloxacin (a L-racemic isomer of ofloxacin) also [7,8]. In our hospital setup, many other cases with such cutaneous reactions in adults went unreported where ofloxacin and ornidazole combination was prescribed for acute GI infection.

The lesions of SJS occur as a consequence of apoptosis of keratinocytes. This apoptosis is induced by pro-inflammatory cytokines TNF $\alpha$ , CD-40, IL-6 [9]. Genetic deficiency of an abnormal epoxide hydrolase enzyme may lead to excessive accumulation of

epoxide which initiates an immune reaction and cell damage [10]. Several recent studies have reported strong genetic associations between HLA alleles and susceptibility to drug hypersensitivity [10]. So, drug specific genetic screening tests may prevent such catastrophic diseases.

## CONCLUSION

Documentation of ADRs in clinical practice contributes to quality assurance in drug therapy, but is often under reported. Our case reminds physicians of the importance of drug reactions, their patterns, morphology and its severity. Prescribing medication, according to history and genetic tests, will decrease the prevalence of such adverse reactions. So, Ofloxacin should be avoided to people predisposed to SJS. Early detection of cutaneous lesions and immediate withdrawal of the offending drug can prevent progression of such reactions to their severe variants as well as morbidity and mortality. Finally as many numbers of these cases are being reported recently, drug manufacturers can incorporate possibility of such reactions to ofloxacin in their package inserts.

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