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Case Report

Paracetamol induced fixed drug eruption: a case report

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ABSTRACT

Fixed drug eruption (FDE) is a type of drug-induced skin reaction pattern that characteristically recurs at the same skin or mucosal site. Paracetamol is one of the common drugs prescribed as analgesic–antipyretic agent in all age group of patients. FDE is a well-reported, but uncommon side-effect of paracetamol, usually the classic, pigmenting type most commonly found in children and adolescents. We present a case of 52 years old male patient who developed FDE over the glans penis following paracetamol use.

Keywords: Skin eruptions, Acetaminophen

INTRODUCTION

Fixed drug eruption (FDE) is a cutaneous adverse drug reaction commonly seen in children and adolescents that is frequently misdiagnosed, leading to recurrent eruptions when the offending drug is readministered.[1] The diagnostic hallmark is its recurrence at previously affected sites. Paracetamol is a readily available over the counter (OTC) antipyretic. Despite its widespread use, adverse reactions are unusual at therapeutic dose. Its cutaneous adverse effects are rare, varying from transient pruritis or maculopapular rash to Stevens-Johnson syndrome and even fatal toxic epidermal necrolysis.[2] FDE to paracetamol is well-reported in children and adolescents but is rare in elderly and very few reports are available.[2,3] Here, we describe a case of 52 years old male patient who developed FDE over the glans penis following paracetamol use.

CASE REPORT

A 52 years old male patient was brought with a history of erythematous rash that started on back and gradually became generalized all over the body sparing palms, soles, and mucosal surfaces over a period of 5 days. Rashes were well-circumscribed, 5-7 cm in size with a burning sensation without itching and blebs or pustules formation. These rashes were associated with intermittent moderate grade fever without chills and rigors. There was no history of similar complaints in the past. Hence, the provisional diagnosis of generalized erythematous rash of allergic origin was made. After admission, patient was given tablet paracetamol 500 mg three times a day, tablet prednisolone 10 mg twice a day and tablet chlorpheniramine maleate 25 mg twice a day. This oral treatment was also supplemented with intravenous fluids. The same day, late in the evening patient accidently noticed erythematous, macular, multiple lesions with size varying between 1 and 2 mm over the glans penis after retracting the prepuce. There was no itching, scaling or burning over the glans. Immediately, withdrawal of paracetamol was initiated suspecting it to be the causative agent. Thereafter, erythema associated with the lesions over the glans started subsiding over next 2 days. On the 3rd day after withdrawal of tablet paracetamol, erythematous lesions over the glans completely evolved into hyperpigmented lesions in the phase of recovery. The probability of FDE due to paracetamol cannot be ruled out after applying Naranjo's

scale of causality assessment of adverse drug reactions with a score of six. Laboratory investigations such as hemoglobin, complete blood count, and blood sugar level were found to be within normal limits. Rest of the treatment was continued and the initial symptoms improved over next 5 days.

DISCUSSION

Drug eruptions have been found to contribute to 5-7% among all type of cutaneous drug reactions.[4,5] FDE is a cutaneous type of hypersensitivity reaction to drugs. Paracetamol-induced FDE is reported in literature in less than 1.5% of all cases of FDEs.[2] FDE is a hypersensitivity reaction mediated by T cells recognizing haptenated drug antigens presented by epidermal cells. It was recently shown that the most probable effecter cells in established FDE are cytotoxic CD8-positive T cells with natural killer cell-associated molecules resembling effecter cells found in toxic epidermal necrolysis. In fully evolved FDE that eventually resolves, high numbers of intraepidermal suppressor $CD4^+$, $CD25^+$, $Foxp3^+$ regulatory T cells counteract the cytotoxic cells and ameliorate the damage.[6]

FDEs are sharply marginated, round, erythematous to violaceous, 2-10 cm plaques occurring after ingestion of the drug. The lesions usually flare within 30 min to 8 hrs after drug intake; mean length of time from drug intake to the onset of symptoms is approximately 2 hrs.[7] The acute inflammation disappears within a few days, leaving circumscribed hyperpigmentation for months or even years.[8] FDEs characteristically recur in the same location after repeated ingestion of the drug. The antimicrobial drug combination trimethoprim-sulfamethoxazole has been reported as the most common cause of FDE.[7,9] Other causes include antimicrobials such as tetracyclines, erythromycin, tinidazole, ampicillin, griseofulvin, clindamycin, albendazole, non-steroidal anti-inflammatory drugs agents such as aspirin, ibuprofen, diclofenac sodium, piroxicam, paracetamol[1] and other drugs like barbiturates.[10]

There are previous reports establishing FDE producing potential of paracetamol.[6,8,11] However in this case, the patient suffered from FDE due to paracetamol for the first time in his life though there was history of taking paracetamol many times earlier without any such occurrence. We tried to find out the cause of this new onset FDE to paracetamol even though patient had received it many times in the past. Is this due to the concomitantly administered drug (pheniramine maleate, prednisolone)? We extensively searched the literature about the drug interactions among these three but couldn't find any satisfactory explanation for this. It is probably the gradual accumulation of memory T cells over a certain period responsible for such new onset FDEs occurring for the first time even though there was history of drug exposure many times in the past.

To conclude, in countries where many drugs are available OTC which can produce serious as well as non-serious adverse reactions, it becomes very difficult to identify the exact etiological agent when such a reaction occurs. Even previous history of uneventful administration of any commonly used OTC drug does not make it safe for future unadvised administration.

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