|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
NLM (National Library of Medicine ID: 101738825)
Index Copernicus Value 2019: 79.34
Case Report Volume 5, Issue 2; February: 2021; Page No. 231-234

PARACETAMOL-INDUCED FIXED DRUG ERUPTION: A CASE SERIES

Dr. Priyanka Sharma[3], Dr. Dinesh Kumar Yadav[2], Dr. Nidhi Sanwalka[3]

[1]Consultant, Department of Dermatology, Rukmani Devi Beni Prasad Jaipuria Hospital, Jaipur
[2]Postgraduate resident, Department of Medicine, Rukmani Devi Beni Prasad Jaipuria Hospital, Jaipur
[3]Postgraduate resident, Department of Medicine, Rukmani Devi Beni Prasad Jaipuria Hospital, Jaipur

Article Info: Received 20 January 2021; Accepted 26 February 2021
DOI: https://doi.org/10.32553/ijmbs.v5i2.1767
Corresponding author: Dr. Nidhi sanwalka
Conflict of interest: No conflict of interest.

Abstract
We are reporting three cases of patients who came to dermatology outdoor department, with a complain of painful blistering eruption affecting the various body parts with no systemic symptoms after taking paracetamol drug. In cases applying Naranjo's algorithm, a casuality score of 7,6,7 were obtained. Paracetamol was characterized as a probable cause of this fixed drug eruption in all the cases. Clinicians should be aware of this rare side effect of paracetamol, which is a widely used NSAID.
Keywords: Paracetamol, Fixed drug eruption, bullae, eruption

Introduction

Fixed drug eruptions accounts for 20-43% of cutaneous adverse drug reactions (CADR) in India.[1,2] An adverse drug reaction is a harmful or unpleasant reaction, resulting from the use of medicinal products, which predicts hazard from future administration and warrants alteration or prevention of drug or withdrawal of that medicinal product. Cutaneous drug reaction is the most common among drug eruption.[3] Fixed drug eruption (FDE) is most common in India in cutaneous drug reaction.[4,5] Analgesics and antibiotics are common drugs that causes CADR.[4] Most common areas involved are genitalia, extremities, sacrum and perianal areas. Mucosa especially lips can also be involved. After healing hyperpigmention is normally seen at the affected area. Exact pathogenesis is obscure but it has been said that intraepidermal CD8+ T cells which persist at the previous site of injury mediates and are directly involve in the epidermal injury and causing localized cutaneous changes.[6,7]
Here we are reporting three cases of fixed drug eruption by a very common drug which is paracetamol.

Case report

A 37-year-old woman presented to outdoor department of Dermatology with painful blistering eruption affecting the medial side of arms. Day before she had taken paracetamol as she was suffering from fever. She was a known case of autoimmune hepatitis. Within few hours of ingestion of drugs she developed itching and burning sensation over medial side of left arms.
On physical examination the patient was afebrile and had jaundice. Cutaneous examination revealed multiple bullae, few were present with haemorrhagic component over medial side of left arm. Nikolsky's sign was negative (figure 1). Laboratory investigations revealed total white blood count 26.64/cu mm, with absolute eosinophil count of 50/cu mm serum creatine was normal. Liver function tests revealed total bilirubin 2.32 mg/dl with direct bilirubin as 1.66 mg/dl. SGOT and SGPT were 42U/L and 20 U/L respectively. Antinuclear antibody was weakly positive. Patient refused oral provocation test. From one of the intact bulla a regular biopsy was done. Formalin fixed Sample was sent to Department of Pathology for histopathological examination. On histopathological examination, at and above the basal layer foci of basal cell vacuolation , lymphocytic exocytosis and many necrotic keratinocytes were revealed in epidermis. There was moderate perivascular infiltrates of neutrophils, eosinophils, histiocytes and lymphocytes. No basement membrane thickening, dermal mucin deposits or fungal organisms were seen. A diagnosis of bullous fixed drug eruption to paracetamol was made.
The patient was treated with IV and topical steroids and antibiotics. On follow up, lesions of arms were resolved but hyperpigmentation was seen at the site of lesion. She was advised to avoid paracetamol and always carry a drug alert card with her to avoid such condition in future.

Figure 1: multiple bullae were noted on medial aspect of left arm.

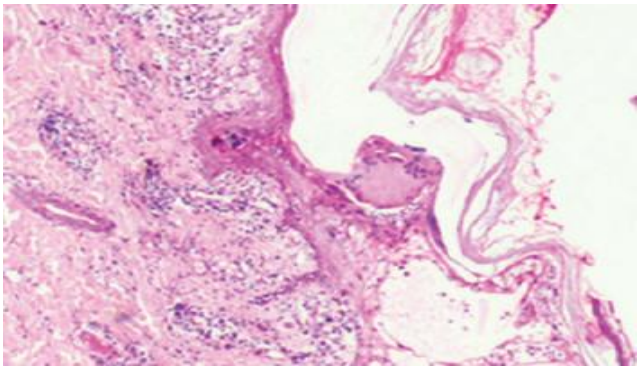

Figure 2: Photomicrograph showing keratinocytes, basal cell vacuolation and lichenoid infiltrate seen in superficial dermis (H&Ex400)

CASE 2

A 15 year old male presented in outdoor department of dermatology with complaints of painful bullae and plaques all over the body. He had history of fever for one day 15 days back and had taken paracetamol for fever reduction and on the same day he developed itching and formation of bullae which later developed into plaque all over the body. He had similar history 4 years back when he took paracetamol for fever reduction but had mild symptoms.
On physical examination patient was afebrile. Cutaneous examination reveled multiple bullae on knee joint and anterior side of left leg and multiple plaques on anterior chest wall, back, face , arms, and legs (**figure 3,4**). Laboratory investigations showed hemoglobin- 8.7g/dl, total leukocyte count-6200, ESR- 35mm/Hr, toral eosinophil count- 200, IGe- 2612. CRP was raised (56). Anti nuclear antibody was mildly positive. All other lab investigations were normal. Punch biopsy was not done in this patient as patient did not give consent.

Figure 3,4 : multiple bullae and plaque on hands and leg
For the present bullae and plaque patient was given topical steroids. His lesions improved over few weeks, but leaving post inflammatory hyperpigmentation.

CASE 3
A 30-year-old healthy female presented with erythematous rash of skin on back and papules on the neck from the past 2 weeks. She had a history of fever 3 weeks back, for which she had received paracetamol. There was no history of any other drug intake. A day after taking paracetamol, she developed reddish lesions around trunk. A similar episode of skin lesion was present on the same site 2 years back with intake of paracetamol. On examination, the female had few well-defined discrete, erythematous rash on the back (**figure 5**) and papules on neck (**figure 6**). Systemic examination was normal. Complete hemogram and biochemistry profile was normal. Skin biopsy was not done as the patient did not give consent. Given the history of recurrent lesions occurring at the same site after ingestion of paracetamol and clinical presentation diagnosis of FDE due to paracetamol was considered.
Patient was started on topical steroid cream and her lesions improved over 3 weeks.

Figure 5, 6: rash on back and papule on neck

Discussion

Brocq coined the term 'fixed drug eruption' (erytheme pigmentefixe) in 1894. Fixed drug eruption occurs within 30 minutes to 12 hours after the intake of causative drug. It is a skin lesion characterized by red, round to oval macule with edematous plaque that appears at the same site. It is usually solitary in the initial attack but with multiple exposure, the number of involved site ad lesion increases. The lesions are usually painful, oval to round erythematous plaques and become violaceous 1-2 days later. After 1-2 week, healing occurs resulting in crusting and scaling at the site, followed by hyperpigmentation.

Paracetamol is a very common non-steroidal anti-inflammatory drugs (NSAIDs) with a reliable safety profile. Cutaneous adverse drug reaction due to this drug is very rare and usually of fixed type. Fixed drug eruption has various variant, they are, linear, bullous, urtecarial, generalized, pigmenting, wandering, psoriasiform, nonpigmenting, erythema dyschromicum perstans like, oral and vulvitis.[8,9,10,11]

There are many drugs which causes fixed drug eruprion, they are, sulphonamides (cotrimoxazole), tetracyclines, penicillin, erythromycin, clarithromycin, rifampicin, NSAIDs, barbiturates, banzodiazepines, fluconazole,

cetrizine, lamotrigine, omeprazole, lansoprazole, ACE inhibitors, and hormonal preparations.

In literature only a few cases of fixed drug eruption has been reported due to paracetamol.[6,12,13] Naranjo's algorithm was applied for casuality score in all three cases and a score of 7,6 and 7 were obtained (table 1).[14] Thus this was categorized as a probable reaction to paracetamol.

Table 1: Naranjo adverse drug reaction probability scale

Question	Yes	No	Do not know
1. Are there previous conclusive reports on this reaction?	+1	0	0
2. Did the adverse event appear after the suspected drug was administered?	+2	−1	0
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
4. Did the adverse event reappear when the drug was readministered?	+2	−1	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	−1	+2	0
6. Did the reaction reappear when a placebo was given?	−1	+1	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0

Adapted from Naranjo CA *et al.* A method for estimating the probability of adverse drug reactions Clin Pharmacol Ther 1981;30:239-45

Peak age for FDE is 21-30 years, although it may vary. Ratio of male: female is generally equal. Genetic predisposition occurs in cases who have family history of diabetes mellitus, atopy and drug allergy.[15,16,17,18]
Other differential diagnosis of bullous lesions are bullous lupus erythematosus, bullous pemphigoid, linear IgA bullous dermatosis and blistering disorder. Oral rechallenge can be dangerous but is the most reliable technique to identify the causative agent. To avoid this danger, a relatively safe method 'patch test' over the affected site can be done. Lymphocyte transformation tests gives poor results in FDE.[19] Only treatment of FDE is the discontinuation of the culprit drug.

Conclusion

Paracetamol is a widely used drug. Clinician should be highly suspicious and vigilant about the possible adverse reaction of this drug. Identification of the offending drug is challenging when the patient is on multidrug therapy. Drug alert card is a helpful tool for patient to avoid FDE by the offending drug in future. We report these cases, to draw attention towards a rare side-effect of paracetamol.

References

1. Patel TK, Thakkar SH, Sharma D. Cutaneous adverse drug reactions in Indian population: A systematic review. Indian Dermatol Online J 2014;5 Suppl 2:S76-86.
2. Padmavathi S, Manimekalai K, Ambujam S. Causality, severity and preventability assessment of adverse cutaneous drug reaction: A prospective observational study in a tertiary care hospital. J Clin Diagn Res 2013;7:2765-7.
3. Breathnach SM. Adverse Cutaneous reactions to drugs. Clin Med 2002; 2: 15-9.
4. Hiware S, Shrivastava M, Mishra D, Mukhi J, Puppalwar G. Evaluation of Cutaneous Drug Reactions in Patients Visiting Out Patient Departments of Indira Gandhi Government Medical College and Hospital (IGGMC and H), Nagpur. Indian J Dermatol 2013 Jan-Feb; 58(1): 18-21.
5. Balaji O, Amita D, Patil N. Rabeprazole-induced fixed drug eruption: a rare case report. Asian j Pharm clin Res,2017;10(5):13-14.
6. Agarwala MK, Mukhopadhyay S, SekharMR, Peter CV. Bullous fixed drug eruption probably induced by paracetamol. Indian J Dermatol.2016 Jan-Feb;61(1):121.
7. Mizukawa Y, Yamazaki Y, Shiohara T. *In vivo* dynamics of intraepidermal CD8+ T cells and CD4+ T cells during the evolution of fixed drug eruption. Br J Dermatol 2008;158:1230-8.
8. Korkij W, Soltani K. Fixed drug eruption. A brief review. Arch Dermatol 1984;120:520-4.
9. Mizukawa Y, Shiohara T. Fixed drug eruption presenting as erythema dyschromicum perstans: A flare without taking any medications. Dermatology 1998;197:383-5.
10. Özkaya E. Oral mucosal fixed drug eruption: Characteristics and differential diagnosis. J Am Acad Dermatol 2013;69:e51-8.
11. Sigal-Nahum M, Konqui A, Gaulier A, Sigal S. Linear fixed drug eruption. Br J Dermatol 1988;118:849-51.
12. Guin JD, Baker GF. Chronic fixed drug eruption caused by acetaminophen. Cutis 1988;41:106-8.
13. Ayala F, Nino M, Ayala F, Balato N. Bullous fixed drug eruption induced by paracetamol: Report of a case. Dermatitis 2006;17:160
14. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.

15. Akira Kawada, Masattaro Hiruma, Koukichi Morimoto.Fixed drug eruption induced by ciprofloxacin followed by ofloxacin.Contact dermatitis;1994;31(3):182-183.
16. Hazano S, Kume A, Higashi N. A case of fixed drug eruption from ofloxacin.Hifu;1991;33:229-31.
17. Kitagawa K, Fukuda T, Yamazaki Y. A case of fixed drug eruption from oflaxacin. Rinsho Derma; 1991;33:1472-3.
18. Jonathan L,HagerMD, Mohsin R Mir MD, Sylvia Hsu MD. Fluoroquinolone induced generalized fixeddrug eruption.Dermatology J;15(12):8.
19. Shiohara T. Fixed drug eruption: Pathogenesis and diagnostic tests. Curr Opin Allergy Clin Immunol 2009;9:316-21.