CME LIVE OPEN ACCESS

International Journal of Nursing Care

Case Report

Fixed Drug Eruption in a Patient with COVID-19 Infection: A Case Report

Mahsa Rekabi[1], Jamal Mirzaei[2], Vahab Rekabi[3] and Sepideh Darougar[4*]

[1]*Pediatric Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[2]*Infectious diseases Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[3]*Fellowship of Molecular Pathology and Cytogenetics, Tehran, Iran*

[4]*Department of Pediatrics, Faculty of Medicine, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran*

Corresponding Author: Sepideh Darougar, MD Department of Pediatrics, Faculty of Medicine, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Received: 2023 Dec 01 **Accepted:** 2023 Dec 21 **Published:** 2024 Jan 03

Abstract

Background: More than 30 different cutaneous drug reaction patterns, ranging from mild dermatitis to extensively affected skin, are reported, among which fixed drug eruption is the third most common involvement pattern. Fixed drug eruption is an immunological reaction characterized by lesions recurring at the same location every single time after exposure to a causative substance.

Case Report: A healthy 26-year-old male patient developed red erythematous itching macules on his lips, hands and genitalia 15 days following COVID-19 infection in May 2022. With the passage of time, they turned to bullous lesions, which were then ulcerated. He did not have any history of previous allergic disorders. The only medication used by the patient during the course of the disease was acetaminophen, which he was used to consuming regularly at the times of pain and fever without the appearance of any signs, symptoms or skin lesions. Two months later, the eruption recurred on exactly the same sites after taking a 500mg naproxen tablet. Laboratory tests were all within normal limits. A diagnosis of fixed drug eruption was suspected and a skin biopsy specimen from the involved area was indicative of the aforementioned diagnosis.

Conclusion: Considering the widespread use of acetaminophen and NSAIDs, it seems important to be aware of the adverse reactions of drugs. Actually, in a case such as our patient, who had already tolerated acetaminophen safely prior to COVID-19 infection, the triggering effect of viral infection in inducing skin lesions may become more prominent.

Keywords: Fixed Drug Eruption, Acetaminophen, Naproxen, COVID-19.

1. Introduction

Drug-induced cutaneous adverse reactions, which are observed in multi-medicated patients, encompass a heterogeneous challenging diagnostic field [1]. Currently, more than 30 different cutaneous drug reaction patterns, ranging from mild dermatitis to extensively affected skin, are reported, among which fixed drug eruption is the third most common involvement pattern [1]. Infection with certain viruses is a patient-related factor, which is linked with an increased risk of developing immunologic reactions to drugs [2].

Fixed drug eruption is an immunological reaction characterized by lesions recurring at the same location every single time after exposure to a causative substance [3]. In the majority of the patients, antimicrobials (80.6%) and non-steroidal anti-inflammatory agents (20.8%) are the most common implicated medications in the development of the disease [3]. With acetaminophen as the most common causative drug for FDE [4]. The drug that results in an acute reaction may be often reported in the past medical history of the patient as an offending agent [5]. Lips, hands, legs, face, genitalia and oral mucosa are the most common affected sites [6]. FDE occurs in both sexes and all age range groups, although the majority of cases fall between 20 and 40. Interestingly, fixed drug eruptions do not appear spontaneously or after an infection [3]. The lesions appear approximately 30 min to

8 h after ingestion of the drug. The differential diagnosis includes HSV infection, autoimmune bullous diseases, erythema multiform, Bechet's disease and erosive lichen planus, all with similar clinical appearances.

Immunologically, intraepidermal CD8+ T cells are involved in epithelial damage [7]. Activation of these cells along with cytokines and /or adhesion molecule-mediated recruitment of CD4+ T cells, and neutrophils may contribute to tissue damage in FDE lesions. CD8+ T cells with an effector-memory phenotype are detected in dermo epidermal junction. Upon rechallenge and activation of CD8+ T cells, interferon-gamma and cytotoxic granules are released, which contribute to tissue damage [8, 9].

Patients without a suggestive medication history should be asked about the types of the consumed foods [10]. Lactose is confirmed by oral challenge as one of the implicated substances [11].
This study is a report of a patient with histopathologic examination of a punch biopsy specimen indicating fixed drug eruption after COVID-19 infection. Two months later, the eruption recurred on exactly the same sites after taking a 500mg naproxene tablet.

Laboratory tests including CBC, ESR, CRP, ANA, RF, pANCA, and cANCA were all within normal limits. A diagnosis of fixed drug eruption was suspected and a skin biopsy specimen from the involved area was indicative of the aforementioned diagnosis.

Case Report

A healthy 26-year-old male patient developed red erythematous itching macules on his lips, hands and genitalia 15 days following COVID-19 infection in May 2022 (Figures 1).

Figure 1: Fixed drug eruption on lips and tongue.

Figure 2: Fixed drug eruption on penis

Figure 3: Fixed drug eruption on the ulnar side of the hand, between thumb and ring finger.

After some time, they turned to bullous lesions, which were then ulcerated. He did not have any history of previous allergic disorders. The only medication used by the patient during the course of the disease was acetaminophen, which he was used to consuming regularly at the times of pain and fever without the appearance of any signs, symptoms or skin lesions. With time, the lesions faded, but a violet pigmentation remained. Two months later, the eruption recurred on exactly the same sites after taking a 500mg naproxen tablet. Laboratory tests including CBC, ESR, CRP, ANA, RF, pANCA, and cANCA were all within normal limits. A diagnosis of fixed

drug eruption was suspected and a skin biopsy specimen from the involved area was indicative of the aforementioned diagnosis. He was successfully treated with topical hydrocortisone, eucerin cream, and cetirizine. The resolution of the lesions was noticed a few days later after the initiation of the treatment, but residual pigmented macules persisted.

2. Discussion

Drug-induced cutaneous reactions encompass a wide spectrum of clinical manifestations induced by a drug or its metabolites [1]. This is a report of a young man with fixed drug eruptions developing simultaneously with covid-19 infection.

As the lack of information on the causative drugs in skin allergies increases the patients' anxiety about future consumption of medications, determining the definite diagnosis and the offending drug is of paramount importance to avoid future exposures.

Since oral provocation tests are not always safe, the diagnosis of FDE was initially suggested by a careful history, and the typical characteristic appearance of the lesions in this patient [12]. Then, the diagnosis was confirmed by skin biopsy and histopathologic examination. His drug history was re-evaluated in accordance with the histopathologic findings and in consideration with the fact that FDE does not occur spontaneously nor along with infections [3]. The only medication he had used before these eruptions was acetaminophen due to high fever and body pain.

Acetaminophen is a readily available over-the-counter antipyretic with a widespread use, particularly in patients with COVID-19 infection because of its low risk of adverse reactions. Although the patient in this study had frequently used acetaminophen as an analgesic medication prior to COVID-19 infection, this was the first time he reacted this way. As it was previously shown that infection with certain viruses may be associated with an enhanced risk of development of immunologic reactions to drugs, we attributed this reaction to the concurrent COVID-19 infection playing as a trigger for the development of FDE [2]. Acetaminophen is known as one of the most common etiologic agents of fixed drug eruptions in the literature [11].

Another noteworthy finding of this case report was the recurrence of the lesions after taking another medication (naproxen). While there are reports of FDE due to selective hypersensitivity to naproxen with tolerance to other NSAIDs, the patient in the current study showed a rare reaction as one type of lesion appeared twice at the same site upon consuming two different substances at two separate occasions [13].

Considering the widespread use of acetaminophen, NSAIDs and antibiotics, it seems important to be aware of the systemic and local adverse reactions of drugs. Actually, in such cases as our patient, who had already tolerated acetaminophen safely prior to COVID-19 infection, the triggering effect of viral infection in inducing skin lesions may become more prominent.

Consent for Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

References

1. Del Pozzo-Magaña, B. R., Liy-Wong, C. (2022). Drugs and the skin: A concise review of cutaneous adverse drug reactions. British Journal of Clinical Pharmacology.
2. Warrington, R., Silviu-Dan, F. (2011). Drug allergy. Allergy, Asthma & Clinical Immunology, 7(1), 1-8.
3. Jhaj, R., Chaudhary, D., Asati, D., Sadasivam, B. (2018). Fixed-drug eruptions: What can we learn from a case series?. Indian journal of dermatology, 63(4), 332.
4. Jung, J. W., Cho, S. H., Kim, K. H., Min, K. U., Kang, H. R. (2014). Clinical features of fixed drug eruption at a tertiary hospital in Korea. Allergy, Asthma & Immunology Research, 6(5), 415-420.
5. Palla, S., Anand, G. S., Sethuraman, V. (2022). Oral fixed drug eruptions to mefenamic acid–adverse drug reaction to over the counter medication taken for menstrual pain. Medicine and Pharmacy Reports, 95(3), 348.
6. Prabhu, M. M., Prabhu, S., Mishra, P., Palaian, S. (2005). Cellulitis-like fixed drug eruption attributed to paracetamol (acetaminophen). Dermatology Online Journal, 11(3).
7. Mizukawa, Y., Yamazaki, Y., Shiohara, T. (2008). In vivo dynamics of intraepidermal CD8+ T cells and CD4+ T cells during the evolution of fixed drug eruption. British Journal of Dermatology, 158(6), 1230-1238.
8. Komatsu, T., Moriya, N., Shiohara, T. (1996). T cell receptor (TCR) repertoire and function of human epidermal T cells: restricted TCR Vα-Vβ genes are utilized by T cells residing in the lesional epidermis in fixed drug eruption. Clinical & Experimental Immunology, 104(2), 343-350.
9. Mizukawa, Y., Yamazaki, Y., Teraki, Y., Hayakawa, J., Hayakawa, K., et al. (2002). Direct evidence for interferon-γ production by effector-memory-type intraepidermal T cells residing at an effector site of immunopathology in fixed drug eruption. The American journal of pathology, 161(4), 1337-1347.
10. Anderson, H. J., Lee, J. B. (2021). A review of fixed drug eruption with a special focus on generalized bullous fixed drug eruption. Medicina, 57(9), 925.
11. Anderson, H. J., Lee, J. B. (2021). A review of fixed drug eruption with a special focus on generalized bullous fixed drug eruption. Medicina, 57(9), 925.
12. Bilgili, S. G., Calka, O., Karadag, A. S., Akdeniz, N. E. C. M. E. T. T. İ. N., Kosem, M. (2012). Nonsteroidal anti-inflammatory drugs-induced generalized fixed drug eruption: two cases. Human & experimental toxicology, 31(2), 197-200.
13. Aouam, K., Fadhel, N. B., Fredj, N. B., Chaabane, A., Belhadjali, H., et al. (2014). Non steroidal anti-inflammatory drugs-induced fixed drug eruptions: A case series. Clinical and Translational Allergy, 4(Suppl 3), P82.