Asian Journal of Healthy and Science
p-ISSN: 2980-4302
e-ISSN: 2980-4310
Vol. 3 No. 7 July, 2024

Dimenhydrinate-induced Fixed Drug Eruption in Adult Woman: A Case Report

Qanita Khairunnisa[1*], Erni Setiyawati[2]
[1,2]Wiradadi Husada Hospital, Banyumas, Central Java, Indonesia
Email: drqanitanisa@gmail.com

Abstract

Dimenhydrinate is an H1 antihistamine of the ethanolamine class used to prevent and treat motion sickness due to its significant anticholinergic, antiserotoninergic, and sedative properties. Drug reactions to dimenhydrinate are rare, with only three reported cases of fixed drug eruption (FDE) following its ingestion recorded in the MEDLINE database from 2000 to April 2024. This case report presents a 40-year-old housewife who arrived at the emergency room with severe pain in both legs and multiple plaques on her back and upper arms after taking a second dose of 50 mg dimenhydrinate for nausea and abdominal pain. Approximately one month prior, she experienced a similar but less severe reaction after taking the same drug. Examination revealed well-demarcated dark purple plaques, 4-5 cm in diameter, with no itching or pain. The patient was diagnosed with FDE based on clinical findings. The lesions improved after one week of intravenous methylprednisolone (62.5 mg daily) during hospitalization, along with discontinuation of dimenhydrinate. This case highlights the importance of recognizing rare drug reactions like FDE in patients using common medications and underscores the need for prompt diagnosis and treatment.

Keyword: Dimenhydrinate, Fixed Drug Eruption, Motion Sickness.

INTRODUCTION

Fixed drug eruption (FDE) is a distinct form of skin reaction to medication. The phrase "fixed drug eruption" was created by Brocq in 1894, following its initial description by Bourns in 1889 (Anderson & Lee, 2021; Patel et al., 2020). Brocq describe it as the presence of swollen plaques that appeared to be round or oval in shape. These plaques fluctuated in size, ranging from the size of a coin to the size of a palm. Additionally, they reappeared on different areas of the body (Hannah J. Anderson, 2021). These lesions usually manifest between 30 minutes and 8 hours after the ingestion of the suspected medication. The typical areas affected include the hands, feet, genitalia, and perianal region (Aditi Maitra, 2017). It reappears in the same spots within 48 hours after being exposed again to the drug causing the reaction (Antoine Salloum, 2020). After the eruption faded, the affected areas still exhibited a range of pigmentation that varied in both colour and size.

Drug-induced dermatitis is a prevalent condition in the field of dermatology. According to reports, drug eruption makes up around 2%–5% of all skin illnesses (Blum & Burgin, 2021; Del Pozzo-Magaña & Liy-Wong, 2022). FDE can manifest in individuals of all age groups, encompassing children, the elderly, and particularly adults in the age range of 35 to 60, with

the majority falling within the middle-aged category. The majority of people can achieve a cure by promptly discontinuing the offending medicine and receiving anti-allergic therapy (Jingzhan Zhang, 2021) (Hannah J. Anderson, 2021).

Dimenhydrinate is an H1 antihistamine of the ethanolamine that is utilised to prevent and treat motion sickness due to important anticholinergic, antiserotoninergic and sedative properties (Isidora Paffumi, 2012). Dimenhydrinate is composed of a diphenhydramine component and is occasionally referred to as the "chlorotheophylline salt of diphenhydramine" (Elizabeth J Scharman, 2006). There have been only 3 reported occurrences of FDE (fixed drug eruption) following the ingestion of dimenhydrinate, according to the MEDLINE database from 2000 to April 2024. Here we are reporting one more case of FDE due to dimenhydrinate consumption.

RESULTS AND DISCUSSION

Case Presentation

A 40-year-old woman, worked as a housewife, presented to the emergency room with a complaint of severe pain in both legs accompanied by complaints of several plaques spreading in the back and upper arms after taking the second dose of 50 mg dimenhydrinate tablets given by the primary healthcare facility for her nausea and abdominal pain complaints. The patient reported the onset of the skin reaction, characterized by multiple dark plaques that begin with an erythematous patch that progressively intensifies in shade and size over time, 2 hours after ingesting the medication. She did not report experiencing fever, itching, or discomfort in the skin lesions. Previously, about a month ago, the patient consulted a dermatologist and described suffering the exact same condition after taking the same drug, dimenhydrinate. At that time, the patient only experienced a single plaque on the back, without any itching or pain and was given topical corticosteroid and was instructed to stop taking all previously prescribed drugs. Over time, as she stopped the medication, the stains gradually diminished, resulting in hyperpigmented lesion.

At the present time, alongside the intense discomfort in her legs, the patient admitted herself to the emergency hospital seeking assistance. The patient claims to have no history of illness or allergies. Patient says no family member has ever experienced the same. During the general physical examination, the patient was found to be in good overall health, with normal vital signs. Upon further examination, a lesion consisting of well-demarcated multiple dark purple plaques, measuring approximately 4-5 cm in diameter, was observed in the back and both upper arms **(Figure 1**). The patient reported no itching or pain. The patient was diagnosed with Fixed Drug Eruption (FDE) based on the results of subjective and objective examinations. Based on the laboratory findings of complete blood count, all measurements fall within the expected range. Subsequently, the patient was diagnosed with pedis cellulitis and underwent concurrent skin reaction therapy at the hospital. The lesion improved after one week of intravenous methylprednisolone 62,5 mg administration once a day during the hospitalised period with discontinuated of dimenhydrinate (**Figure 2**).

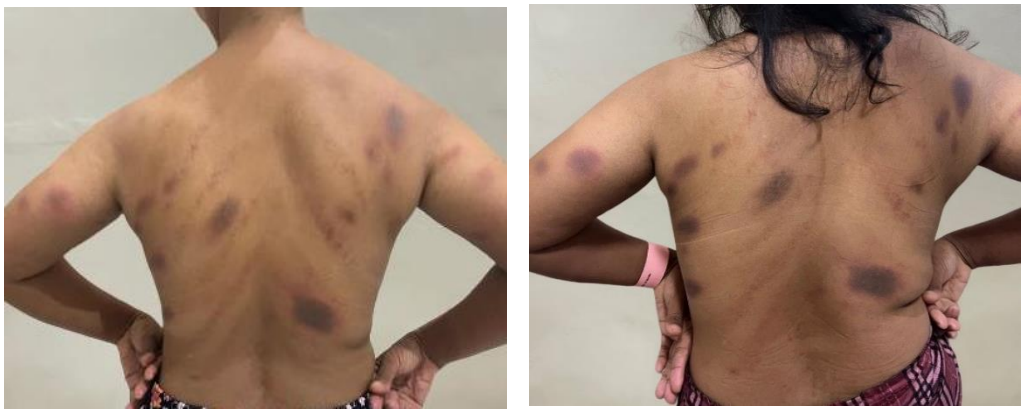

Figure 1. Multiple darkened patches, measuring around 4-5 cm in diameter, with a well-defined border, located on the back and both upper arms prior to treatment.

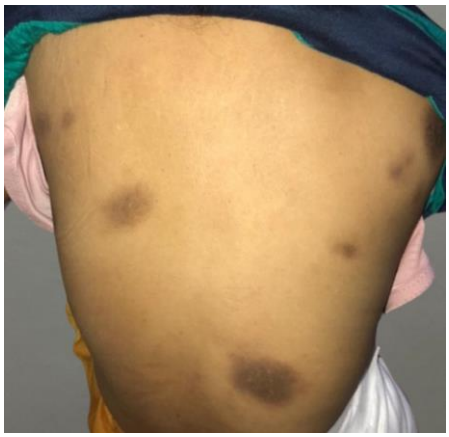

Figure 2. Improvement of the lesion after one week of treatment with intravenous 62,5 mg methylprednisolone once a day at the hospital.

Discussion

FDEs are characterised by the reoccurrence of lesions in the same areas of the skin or mucous membranes after repeated exposure to the responsible substance and heal with persistent hyperpigmentation (Rahman, 2014) (Hyun Jong Lee, 2011). It commonly manifests as circular or elliptical, well-defined, red to bluish-purple, slightly raised patches that can vary in size from a few millimetres to more than 10 centimetres in diameter. Through recurrent assaults, the dimensions and/or quantity of the lesions may escalate (Hyun Jong Lee, 2011). The phenomenon of site preference in FDE remains unresolved. A study found that the distribution of lesions varied based on sex. Specifically, 89% of women had limb involvement, particularly on the hands and feet, whereas 90% of men had lesions on the genitals (Hannah J. Anderson, 2021). This statement is in line with the results we observed in this case, as the patient has a lesion in both upper arms and back.

There are numerous types of medications that can be FDE causative agents. The medications that most typically induce FDE are nonsteroidal anti-inflammatory drugs (NSAIDs), followed by antibiotics, antipsychotics, and herbal compounds. In our patient, dimenhydrinate is believed to be the cause. FDEs to dimenhydrinate are rare. In the last two

decades, only 3 cases of FDE caused by dimenhydrinate have been collected from the MEDLINE database. Dimenhydrinate consists of diphenhydramine salt and 8-chlorotheophylline. Classified as an H1 antihistamine in the ethanolamine group, it possesses significant anticholinergic, antiserotoninergic, and sedative effects. Considering the frequency of usage, adverse effects are uncommon, with sedation being the most prevalent, it is employed in a range of conditions including vertigo, motion sickness, nausea, vomiting, and cold sensations (B Rodríguez-Jiménez, 2009) (B Saenz de San Pedro, 2000).

FDE refers to a type IVc reaction where cytotoxic T lymphocytes have the main function (Isidora Paffumi, 2012). It is believed that CD8+ memory T cells, located in the basal layer of the epidermis of inactive FDE lesions, are responsible for mediating FDE. The CD8+ T lymphocytes present in the epidermis of the damaged skin are the primary cells accountable for inducing harm to the epidermis. Within 24 hours of consuming a medication that causes harm, these CD8+ T cells move towards the upper layer of the skin, produce cytokines like interferon-gamma and TNF-alpha, and transform into natural killer cells. These cells express the cell surface molecule CD56, as well as the cytotoxic molecules granzyme B and perforin. CD8+ T lymphocytes persist in the inactive (pigmented) FDE lesions and are present among the basal keratinocytes, even after the symptoms have resolved (Hannah J. Anderson, 2021) (Yuichi Teraki, 2003).

Typically, the causal medicines of FDE are identified through re-challenge, although patch tests may be a safer option. The re-challenge test is considered the most dependable approach for detecting causal medicines, despite its lack of complete reliability and potential hazards (Hyun Jong Lee, 2011). Due to the restricted resources available in our hospital, we are unable to conduct patch tests in our patient. Furthermore, due to the patient's repeated usage of dimenhydrinate resulting in consistent and localized skin reactions, there is a strong probability that dimenhydrinate is the cause, despite the little available evidence of patch test examination.

While occurrences of fixed drug eruption induced by dimenhydrinate are rare, it is crucial for healthcare professionals to identify cases of drug eruption where dimenhydrinate is implicated in the patient's consumption history. It is crucial to perform a thorough assessment in order to increase patients' awareness of their immunological condition. This measure is taken to prevent the ingestion of culprit drugs that can potentially lead to more severe and extensive skin eruptions, such as Steven Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN).

CONCLUSION

Dimenhydrinate is commonly used to prevent and cure symptoms such as nausea, vomiting, and dizziness that are caused by motion sickness. It is rarely reported to cause FDE. Although FDE instances are mostly not fatal, patients should be thoroughly warned about their allergic status to prevent a recurrence that could potentially result in more severe manifestations in the future.

BIBLIOGRAPHY

Antoine Salloum, D. N. (2020). Esomeprazole fixed drug eruption. *Contact Dermatitis*, 334-5.

Hannah J. Anderson, J. B. (2021). A Review of Fixed Drug Eruption with a Special Focus on Generalized Bullous Fixed Drug Eruption. *Medicina*.

Aditi Maitra, S. B. (2017). A Rare Case of Fixed Drug Eruption due to Ondansetron. *Iran J Med Sci*, 497-500.

Jingzhan Zhang, Z. L. (2021). Current Perspectives on Severe Drug Eruption. *Clin Rev Allergy Immunol*, 282–298.

Elizabeth J Scharman, A. R. (2006). Diphenhydramine and dimenhydrinate poisoning: an evidence-based consensus guideline for out-of-hospital management. *Clin Toxicol (Phila)*, 205-23.

Daniel J Hogan, M. E. (1989). Fixed drug eruption due to dimenhydrinate. *Journal of the American Academy of Dermatology*, 503-4.

B Rodríguez-Jiménez, J. D.-O.-G.-R. (2009). Dimenhydrinate-induced fixed drug eruption in a patient who tolerated other antihistamines. *J Investig Allergol Clin Immunol*, 334-5.

B Saenz de San Pedro, J. Q. (2000). Fixed drug eruption caused by dimenhydrinate. *Allergy*.

Özkaya, E. (2007). Fixed drug eruption: state of the art. *J Dtsch Dermatol Ges*, 181-8.

Rahman, M. H. (2014). Fixed drug eruption in Bangladeshi population: confirmed by provocative test. *International Journal of Dermatology*, 255-8.

Yuichi Teraki, T. S. (2003). IFN-gamma-producing effector CD8+ T cells and IL-10-producing regulatory CD4+ T cells in fixed drug eruption. *J Allergy Clin Immunol*, 609-15.

Hyun Jong Lee, H. S. (2011). Fixed Drug Eruption Due to Allopurinol: Positive Oral Provocation. *Ann Dermatology*, 402-3.

Isidora Paffumi, S. S. (2012). Urticaria caused by dimenhydrinate. *Allergologia et Immunopathologia*, 253-4.