

CASE REPORT ON METHOTREXATE-INDUCED ANGIOEDEMA, PANCYTOPENIA, AND STEVENS-JOHNSON SYNDROME

JAYASUTHA J*, ROSHINI KV, SINDHUBHARATHI A, VISHNU VANDANA G, SREE AAKASH K

Department of Pharmacy Practice, SRM College of Pharmacy, SRM University, Chennai, Tamil Nadu, India. Email: jayasutha15@gmail.com

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ABSTRACT

A 52-year-old female patient was presented with the complaints of swelling of lips, difficulty in breathing, difficulty in swallowing of food, itching, and facial puffiness and also showed the history of a skin lesion in the neck, forearm, and genitalia. Medical history of the patient showed that she had been prescribed with methotrexate for rheumatoid arthritis. Within 10 days of treatment, the patient developed above mentioned signs and symptoms. Further upon patient's systemic and physical examinations were done and then a diagnosis of pancytopenia, angioedema, and Stevens-Johnson syndrome were made. According to Naranjo adverse drug reaction causality assessment scale, the association of angioedema, pancytopenia, and Stevens-Johnson syndrome due to methotrexate was probable. Methotrexate was withdrawn from the patient, and the patient was treated with methotrexate antagonist Leucovorin for 3 days with a frequency of thrice daily and injection Avil (Pheniramine maleate) with a frequency of twice daily which resolved the complications of the patient.

Keywords: Methotrexate, Angioedema, Pancytopenia, Stevens-Johnson syndrome.

INTRODUCTION

Methotrexate is the most common disease-modifying antirheumatic drug (DMARD) employed in treating rheumatoid arthritis. It is prescribed as monotherapy and combination with other DMARD. Methotrexate is an analog of folic acid and interferes with folic acid metabolism by competing with it for the active site of dihydrofolate reductase [1]. In methotrexate treated rheumatoid arthritis patients, the prevalence of hematological toxicity including leukopenia, thrombocytopenia, and pancytopenia were estimated to be 3% [2]. A recent review of the literature on health sciences shows less case reports of methotrexate-induced angioedema and pancytopenia. However, there have been considerable studies on Stevens-Johnson syndrome. Stevens-Johnson syndrome is a severe, sometimes fatal form of involvement of skin, and mucous membrane. It is a hypersensitivity reaction to certain drugs such as sulfonamides, penicillin, and barbiturates. The occurrence of angioedema, pancytopenia, and Stevens-Johnson syndrome together in a patient was found to be rare. But in this case report, the chain of events such as angioedema, pancytopenia, and Stevens-Johnson syndrome due to methotrexate was found to be present.

CASE REPORT

A 52-year-old female patient was admitted with the complaints of swelling of lips, difficulty in breathing and swallowing since a week. The patient had past medical history of rheumatoid arthritis and also showed the history of the skin lesion in the neck, forearm, and genitalia since a week. History of presenting illness shows that the patient developed swelling of lips followed by skin lesions. Lesions were progressively increasing for past 1 week with hoarseness of voice. Her past medication history included hydroxychloroquine 200 mg and methotrexate 10 mg. The patient was consuming methotrexate with a frequency of thrice a day where the correct frequency was once a week. Fig. 1 shows swelling of lips with skin lesions of the patient.

Her physical examination is evident for multiple lesions all over the body. Laboratory investigations such as complete blood count and liver function test were recommended to the patient. Her laboratory values showed a decreased platelet count of 776/cumm, hemoglobin of 8.2 g/dl, and total red blood count of 3.3 million/cumm. Liver function test values showed abnormality in the liver enzymes. The hematological report of the patient showed the presence of pancytopenia. As a clinical pharmacist, it is important to be aware of these complications and adverse drug reactions



Fig. 1: Swelling of lips with skin lesions of the patient

(ADR) for the safe and effective treatment of the patient.

Naranjo ADR causality assessment scale was used to assess the association of angioedema, pancytopenia, and Stevens-Johnson syndrome with drug and its result shows that it was probable with a score of 6 due to methotrexate. The patient was immediately started on injection Leucovorin 15 mg (antagonist to methotrexate) with a frequency of thrice daily and injection Avil (pheniramine maleate) with a frequency of twice daily. Blood transfusion was done to the patient. The patient conditions were improved significantly, and symptoms were found to be resolved.

DISCUSSION

Stevens-Johnson syndrome involves the skin, mucous membrane of the mouth, conjunctiva, genital and perianal area. It is a form of erythema multiforme involving oral and other membranes occurring mostly due to the ingestion of sulfa drugs [3]. It affects individuals of any age and is associated with infections such as herpes simplex, mycoplasma infections, histoplasmosis, and coccidiomycosis. Affected individuals present with an array of multiforme lesions including macules, papules, and bullae [4,5]. Typical toxicity of methotrexate can be predicted

by the timing of drug administration. The toxic nature is observed as mucositis which occurs as an earlier effect which is followed by myelosuppression and sequel of pancytopenia occurring later after methotrexate administration [6]. It is advised that routine blood count to be performed 4-8 weeks. Concomitant administration of folic acid 1-3 mg/day decreases the toxicities including mucositis, hematologic abnormalities without interfering with clinical efficacy [7,8]. In the present case, methotrexate administration was stopped to the patient owing to abnormal complete blood count, skin lesions, and facial pharyngeal edema. This case is rare due to an unfortunate chain of events. In this case, the causation can be proposed due to over dosage of methotrexate by believing that it will cure rheumatoid arthritis. The clinical pharmacist should play an important role in providing counseling to the patient regarding medication-taking behavior and the importance of taking proper dose of the drug.

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