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Pancytopenia with Kaposi's Varicelliform Eruption and Oral Erosions in a Patient of Psoriasis Receiving Long Term Methotrexate for Psoriasis: A Rare Case Report

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ABSTRACT:
Methotrexate is an oral folic acid antagonist used in treatment of many dermatological diseases. It has varied side effects which may occur due to increased binding of drug to dihydrofolate reductase enzyme owing to its increased plasma concentration which may occur either due to drug overdose or drug interactions. Some of these adverse effects like pancytopenia are life threatening hence care should be taken while prescribing these drugs. Here we present an interesting case of methotrexate toxicity culminating in pancytopenia with KVE which occurred due to interaction with NSAIDs used concomitantly.

Key words: Methotrexate toxicity, Pancytopenia, KVE

I. INTRODUCTION:

Methotrexate is a folate antagonist which has varied applications in dermatology being used for various conditions ranging from psoriasis to atopic dermatitis, morphea, lupus erythematosus and many other dermatosis[1]. The adverse effects of this drug includes from trivial side effects of abdominal pain, nausea and vomiting to more dreaded side effects of pancytopenia, hepatic dysfunction, mucocutaneous ulcerations and severe infections. With the increased application of methotrexate in dermatology day by day many adverse effects have been observed by frequent use of this drug in dermatology. We present a case of methotrexate toxicity in a patient receiving methotrexate since 10 years for psoriasis and presented with pancytopenia, oral and cutaneous erosions and erythema multiforme like lesions.

II. CASE REPORT:

A 47 year old female patient presented to our hospital in emergency department with complaint of fever, skin rash, oral ulcers and diarrhoea since five days. On asking history she has been taking treatment for psoriasis since last 10 years and on methotrexate for last 10 years. She has been taking methotrexate regularly as directed by his dermatologist and dose was adjusted depending upon clinical course of disease. Since last 3 months she was on methotrexate 7.5 mg/week taking it cyclically every Saturday and Sunday 2.5 mg tablet 12 hourly. She was on tablet folic acid 5mg per day 5 days a week except for Saturday and Sunday. Before 2 weeks she suffered severe body ache and joint pain for which she was given injection diclofenac 50 mg intramusculary stat followed by oral diclofenac twice daily for 5 days by a general practitioner. After it she gradually developed abdominal pain, nausea, vomiting, fever, odynophagia, dysphagia and oral ulcers. Since last 5 days she started developing skin rashes which first appeared on face and gradually progressed to develop same on trunk, bilateral upper and lower limbs.

On clinical examination, she had multiple erosions with crusting and few vesicular lesions on face, trunk and extremities with painful erosions in oral cavity involving lips, soft and hard palate,and posterior pharyngeal wall. Along with it there were macular purpura on face, trunk and limbs with few erosions were present on face and trunk(images 1,2,3). on general examinationtemperature was 101.2 degreeF and blood pressure was 100/70 mm of mercury. Facial oedema was present but there was no signs of jaundice, clubbing or cyanosis. Respiratory, gastrointestinal and neurological examinations were normal.

On the basis of above findings primary diagnosis was made of methotrexate toxicity with Kaposi's varicelliform eruptions (KVE) and blood investigations including complete blood count, hepatic and liver function tests, urine analysis, serology for HIV, HbSAg, and syphilis were sent along with chest x-ray and abdominal ultrasound.

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Blood level of methotrexate was also ordered. Skin and bone marrow biopsy was not performed owing to risk of bleeding due to low platelet counts. The investigational reports were as shown in below cited table.

Table- 1

Name of the test	Result
CBC	Hb: 8.1 Tc: 2100 Platelets: 12000
Hepatic function test	WNL
Renal function test	S. creatinine : 2.1 Blood urea: WNL
Urine analysis	WNL
Serology	HIV: NR HbSAg: NR RPR: NR
Blood culture	Negative
Chest X-Ray	WNL
Abdominal ultrasound	WNL
Blood methotrexate level	<0.01 meq/litre
HSV 1 HSV 2	IgG: positive IgM:WNL IgG:WNL IgM:WNL

WNL: within normal limits

Patient was started on injection folinic acid(leucovorin) 50 mg every 6 hourly and granulocyte-monocyte colony stimulating factor (GM-CSF) 300 microgram per day. A broad spectrum antibiotic, fluid support and neutropenic care was also started. The platelets and total counts continued to fall on day 2 with PC reaching 8000 and TC 1100. Patient was given 2 pint of platelet concentrates. There after patient started showing improvement with TC increased to 1600 on day 3 and 2200 on day 4 and fever was subsided but PC didn't showed much improvement just increasing to 28000 on day 4. Renal functions also improved with creatinine decreased to 1.2 on day 4 and patient was started on injection acyclovir based on HSV 1 IgG report in dose of 500 mg three times a day intravenously. Later on GM-CSF was stopped and patient was continued on leucovorin. Platelets gradually started increasing and cutaneous lesions also started healing with KVE lesions started drying up with skin peeling and cutaneous and oral erosions were started healing. Patient was able to take liquid food from day 4 onwards and was started on soft semi-solid food on day 6. Platelets increased to 92000 on day 6 and came normal on day 9 of 162000. Patient was discharged on day 10.

Pictures:

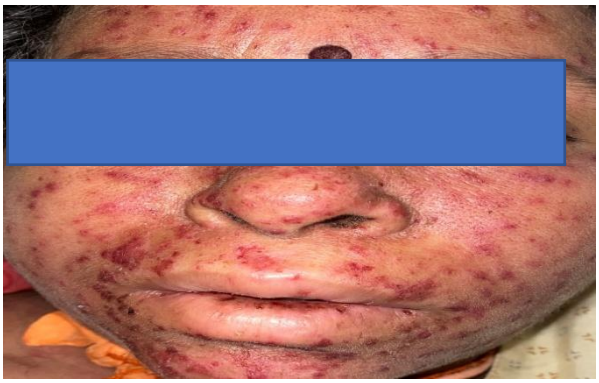

Image 1: erosions and crusted lesions on face

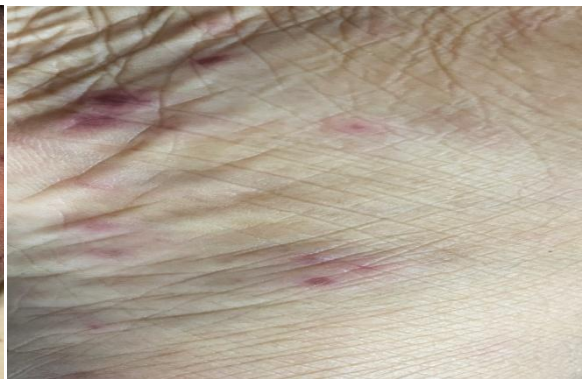

Image 2:Erosions on foot

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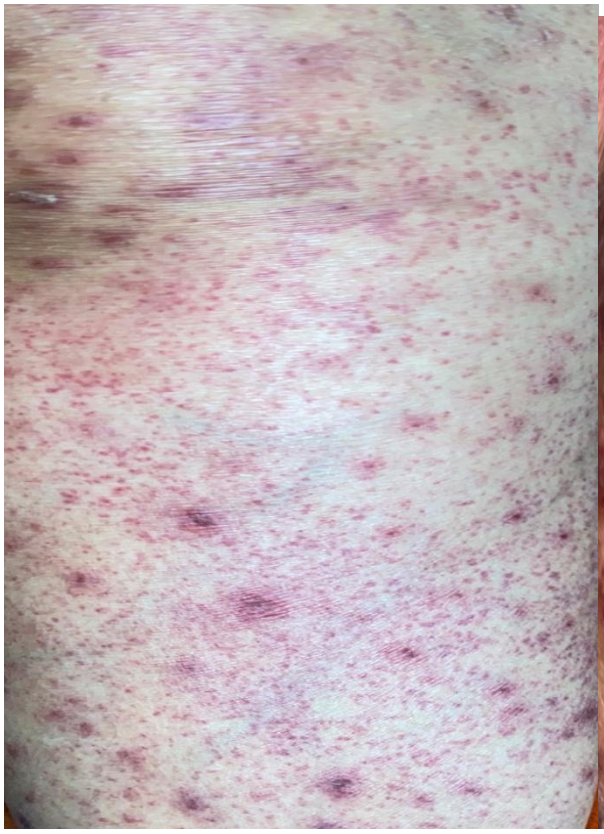

Image 3: KVE lesions on leg with multiple purpura

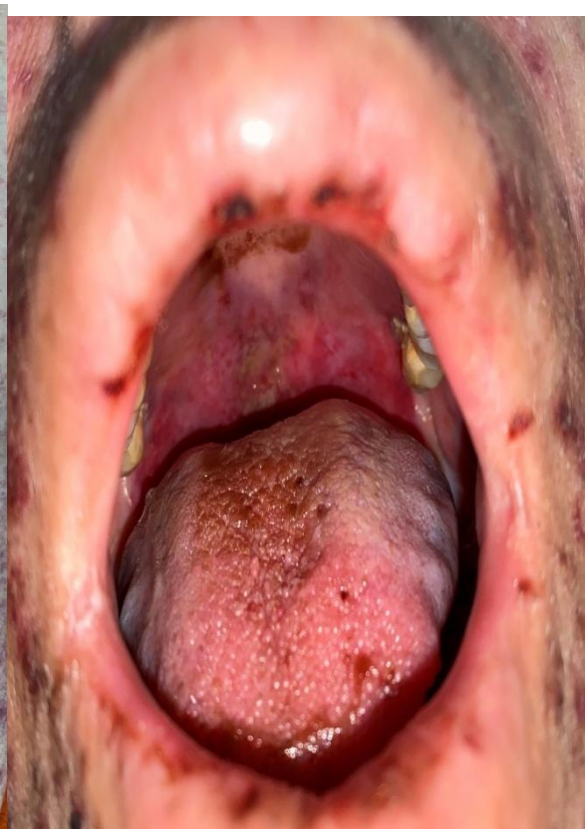

Image 4:Oral mucosal erosions

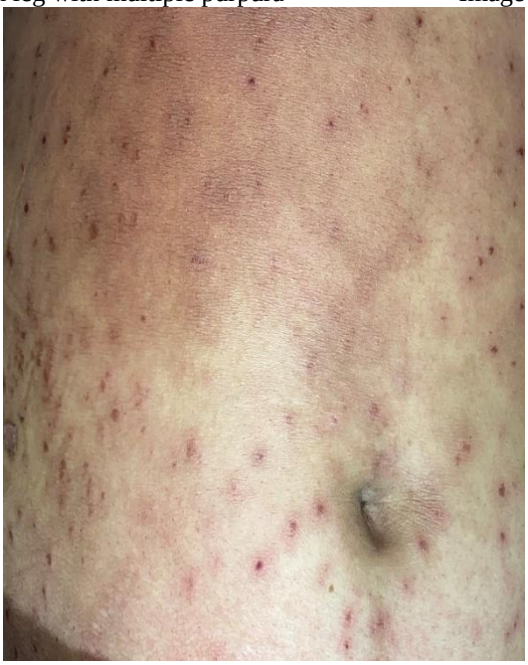

Image 5: Erosions with crusting with KVE lesions on abdomen

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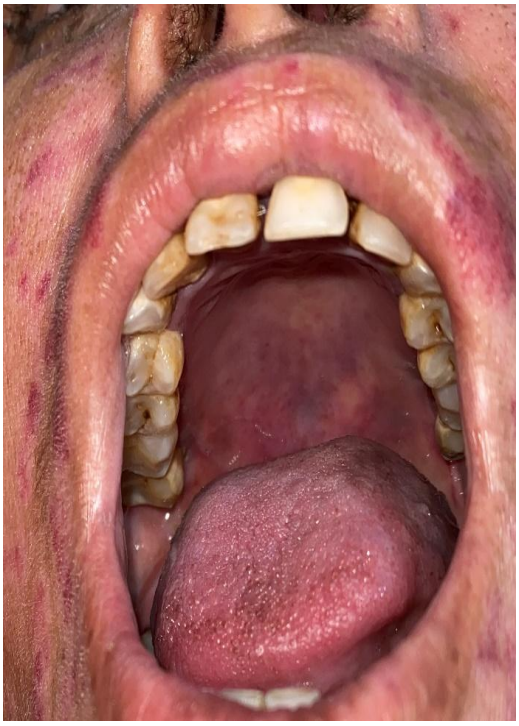

Image 6: Healed oral erosions on day 5

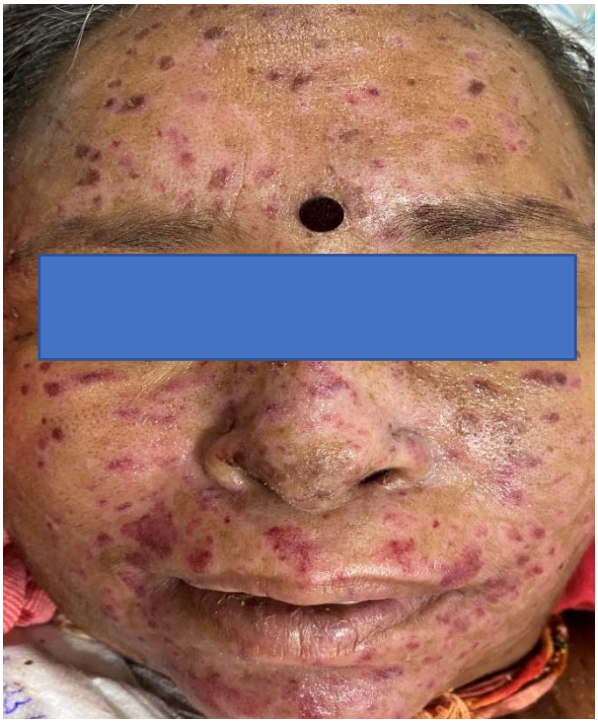

Image 7: Peeling of skin showing signs of healing on face lesions day 5

Image 7: Peeling of skin on foot lesions day 9

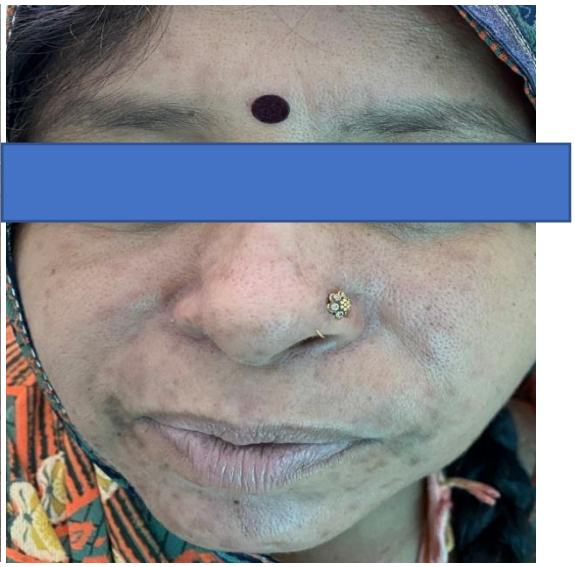

Image 8:Complete healing of face lesions with few post inflammatory hyperpigmentation Day 20

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III. DISCUSSION:

Methotrexate used in dermatology practice is much safer as compared to those used for malignancy or in rheumatology due to its weekly dosing schedule and lesser dose used as compared to other diseases[2,3]. Certain risk factors which can precipitate methotrexate toxicity includes higher doses of it, concomitant use of drugs like co-trimoxazole and NSAIDS[4,5,6], renal dysfunction, elderly age and no use of folinic acid for prevention of toxicity[7]. Our patient was on methotrexate since long but was taking it on low dose and was also supplemented by folic acid. The underlying factors which precipitated the methotrexate toxicity could be use of NSAID (diclofenac in our case) and renal dysfunction.In our case patient was not having any renal dysfunction previously but as seen with NSAIDs they can cause transient renal dysfunction by alteration in renal prostaglandin synthesis[8]. Also NSAID increases plasma methotrexate concentration by displacing it from its protein binding site and interfering with its renal excretion[9]. This could be the probable reason for acute methotrexate toxicity in our patient who was taking methotrexate in low dose since long. Also as seen in this patient KVE was probably due to reactivation of HSV virus owing to suppressed immunity by methotrexate induced pancytopenia leading to KVE like lesions.

IV. CONCLUSION:

This case is presented due to its interesting feature of toxicity occurring in a patient chronically taking a drug since long but developed drug toxicity due to drug interactions. Hence care should be taken to avoid possible interacting drugs in all the patients who have been taking such kind of therapy since long.

Conflict of interest:
Nil

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