

## **Case Report**

### **Methotrexate induced sprue- like disease in a psoriatic patient: A rare case report**

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**Abstract:** “Drug – induced” or “medication- related” forms of enteropathy are known to result in alterations in small intestinal architecture and function causing “sprue- like” mucosal changes, diarrhoea and malabsorption. Many drugs are proved to induce these changes and these include chemotherapeutic agents like colchicine, vincristine, and immunosuppressants like methotrexate, azathioprine, mycophenolate mofetil [1]. Several cases of villous atrophy following use of immunosuppressants are reported. But, literature search revealed only two cases of intestinal villous atrophy secondary to methotrexate [2]. We present this third case of sprue- like syndrome secondary to methotrexate treatment in a psoriatic patient.

**Keywords:** methotrexate, sprue- like enteropathy

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#### **INTRODUCTION**

Many medications are known to cause sprue-like small intestinal mucosal inflammatory process. Alcohol, antibiotics, non-steroidal anti-inflammatory drugs, stathokinetic and chemotherapeutic agents and immunosuppressants may cause sprue- like small intestinal mucosal changes [1]. Several reports of villous atrophy following the use of immunosuppressants are available.[3] But, only two cases of intestinal villous atrophy secondary to use of methotrexate have been reported [2]. Ours could be third case of sprue- like enteropathy in a psoriatic patient following methotrexate treatment. We are reporting this case because of its rarity.

Methotrexate is an immunosuppressant and is a structural analogue of folic acid. It is exuberantly used in treatment of many autoimmune diseases and malignancies [4]. It damages the small intestinal mucosa by preventing crypt mitotic activity, inhibiting dihydrofolate reductase and thus impairing folic acid and D-xylose absorption [5]. These effects occur for several days, but can last for a day or more after cessation of treatment [1].

Mucositis is a common side effect in experimental studies but not many human cases are described [6]. Clinically it presents as weight- loss, diarrhoea, nausea and malaise [2]. The pathogenesis of methotrexate induced sprue- like mucositis is uncertain.

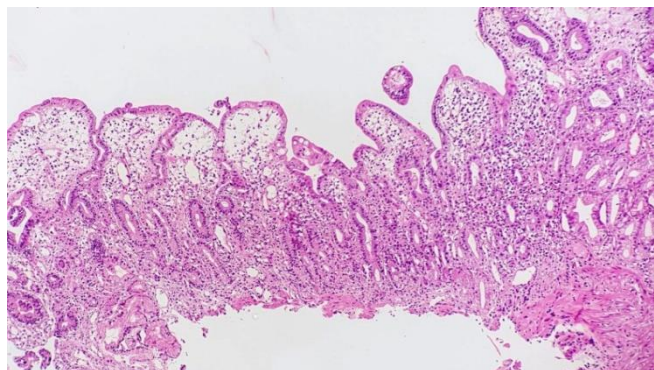
Two mechanisms accepted could be due to local antimetabolite toxicity and genetic predisposition [7].

#### **CASE REPORT**

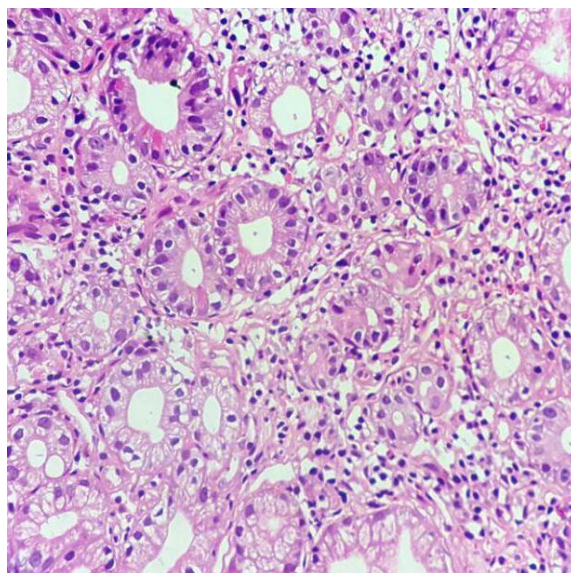
A 42 year old male presented with two days history of oral ulcers, dysphagia and loose stools. He was a known patient of psoriasis and was on treatment. Due to flaring of skin lesions he was started on methotrexate a week ago, following which he presented with the above symptoms. The blood investigations showed that patient was having pancytopenia with hemoglobin being 9.9g/dl. Total leucocyte count was  $1.9 \times 10^3$ /cumm and platelet count being  $55 \times 10^3$  cells/cumm. Clinically patient had inflamed soft palate mucosa with an ulcer. Endoscopy revealed a superficial ulcer at gastroesophageal junction, antral gastritis, mucosal inflammation with erosions and small ulcers at duodenal bulb and mucosa of second and third part of duodenum. Degenerative changes were evident on X-rays of bilateral knees. The duodenal biopsy was done from multiple sites and sent for histopathology.

Histopathology revealed atrophied duodenal villi, crypt distortion, increase in intraepithelial lymphocytes and dense lymphoplasmacytic infiltrate in lamina propria (fig 1, fig 2 & fig 3). With these findings and clinical correlation, diagnosis of methotrexate induced sprue- like disease was made. Methotrexate was withdrawn from treatment protocol and the patient was followed up. Endoscopy and hemogram were repeated after a month. Hemoglobin,

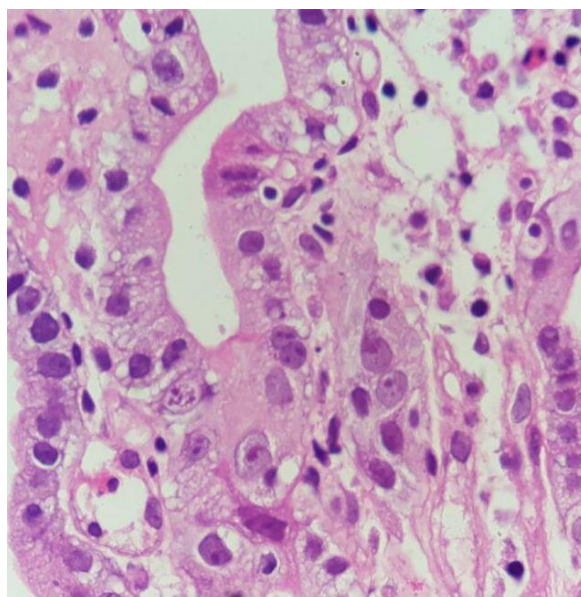
total leucocyte and platelet count had improved. changes.  
Histopathology of duodenal biopsy showed reparative



**Fig-1: showing villous atrophy and fusion, crypt distortion and dense lymphocytic infiltrate in lamina propia (H & E, 4x)**



**Fig-2: showing lymphocytic infiltrate in lamina propia and intraepithelial lymphocytes (H & E, 10x)**



**Fig-3: showing intraepithelial lymphocytes and reactive atypia of epithelial cells (H & E, 40x)**

## DISCUSSION

The most accepted recent hypothesis for methotrexate induced gastrointestinal mucositis consists of five phases- 1. Initiation, 2. Upregulation with generation of messenger signals, 3. Signal amplification, 4. Ulceration and 5. Healing. These phases leads to cell death resulting in villous atrophy and crypt ablation in small intestine. This in turn affects the activity of hydrolases, which are present at enterocyte brush border and are vital in carbohydrate metabolism [8].

There are many studies done on animals regarding methotrexate induced mucositis. A study by Aurigena Antunes de Araujo et.al showed that methotrexate treated rats had high levels of myeloperoxidase activity throughout the small intestine. Methotrexate induced alimentary toxicity is due to high rate of enterocyte proliferation and subsequent cell death that is induced by this pro-oxidant compound that depletes dihydrofolate pools. Thus, villous atrophy and crypt hyperplasia are seen in small intestine, which adversely affects hydrolase activity [9].

Another study by Giuseppe D' Argenio et.al proved that methotrexate treated rats showed biochemical and histological features similar to atrophic celiac disease. Pronounced effect was noted in duodenum and proximal jejunum and maximal damage was seen on day 3, followed by rapid recovery on day 7 [10].

This case was presented because of its rarity. Methotrexate induced sprue- like enteropathy has to be considered in patients treated with this immunosuppressant. This knowledge will help to reduce the morbidity and help to choose an alternative treatment which will be compliant with the patient.

## CONCLUSION

Several cases of villous atrophy following use of immunosuppressants are reported. But, literature search revealed only two cases of intestinal villous atrophy secondary to methotrexate. We present this third case of sprue- like syndrome secondary to methotrexate treatment in a psoriatic patient. This knowledge will help to reduce the morbidity and help to choose an alternative treatment which will be compliant with the patient.

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