1er Congrès Franco-Tunisien de gériatrie
Congrès National de la Société Tunisienne de Gériatrie
3ème Journée de Gériatrie du Sud
26 - 27 Octobre 2019 Djerba

PANCYTOPENIA AFTER POISONING BY METHOTREXATE (ABOUT A CASE)

Hsine H 1 , Jdira S 1 , Sghaier S 2 , Salah S 2 , Hachaichi I 3 , Ghodbene Z 2 ;Rejeb I 1
1- Regional hospital of Gabes, ER departement
2- District hospital of Oudhref
3- Ghanouche Hospital

Introduction :

Methotrexate (MTX) is an inhibitor of dihydrofolate reductase, used in high doses in the treatment of tumoral pathologies, but also at low doses in rheumatology. It is generally well tolerated. We report the case of hematological intoxication with methotrexate

Clinical vignette: vignette : A 79-year-old female patient with a history of high blood pressure, stroke, slowed non-anticoagulated atrial fibrillation, and rheumatoid arthritis with Methotrexate **10mg** / week. The history of the disease dates back to about ten days when the patient presented a table of gastroenteritis without fever and anorexia. The patient was treated symptomatically. In front of theappearance of edema of the lower limbs with swelling of the knees, his Rheumatologist prescribe **15mg** of Methotrexate instead of 10mg on 21/09/2018 with improvement of edema and autonomy according to his family. The patient consults the 27/09/2018 a General Practitioner who objectified a fever to **39°C**, a blood pressure to **100/60** with signs of dehydration and a haemorrhagic cutaneous syndrome from where it was addressed to us.

At the exam :

* Febrile dehydrated patient with Erosive perioral lesions
* Blood pressure **at 80/60**

Biology has shown: pancytopenia with leukocytes at **1300**, hemoglobin at **8.4** and thrombocytopenia **91000** ; compared to a recent assessment that was correct: Leucocyte,**5000**, Hemoglobin **11** and **320000** platelets.

The patient had a filling and a slowing of tachycardia with an improvement in blood pressure at **100/60**. She was hospitalized in the department of general medicine for exploration where she was put under follicum and antibiotic active on digestive germs .The evolution was marked by the
correction of pancytopenia after 5 days of stopping MTX.

Discussion :

Methotrexate (MTX) is one of the most widely used drugs in rheumatology. Frequently observed adverse events of MTX include nausea, vomiting, diarrhea and elevated transaminases but the hematological toxicities remain rare. In MTX-treated RA patients as in our case, the prevalence of hematological toxicity is estimated to be around 3%[1]. Pancytopenia has been reported in 1,0–1.4% of cases [2,3],but despite the rarity of this complication pancytopenia is potentially fatal and it's associated with significant mortality goes from 17% to 44% [2,4,5]. The antifolic effect of methotrexate has always been mentioned as the main mechanism of toxicity in general and hematologically in particular. This action has as its main consequence the blocking of cell proliferation . Numerous risk factors have been associated with increased risk of MTX-induced pancytopenia, including renal dysfunction, hypo-albuminemia, low folate levels, concomitant infection, advanced age, concomitant use of more than five drugs, and lack of folate supplementation [6] .The principal mechanism of elimination of MTX is through kidneys , so even mild to moderate renal dysfunction can predispose to severe pancytopenia [2]. In our case the patient presented a diarrhea few days before her rheumatologist increases the doses of MTX, and whether the diarrhea was a manifestation of neutropenia or led to hypovolemia and renal injury the clinician should had exercised particular vigilance .

Conclusion: Methotrexate is widely used in many disciplines. Although its therapeutic effects are obvious, its narrow therapeutic index and the potentially fatal consequences in case of overdose indicate a good control of its pharmacology as well as an education of the patients.

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