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Pancytopenia and Diabetic Ketoacidosis due to Low Dose Methotrexate in Chronic Renal Failure Patient

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Abstract: Methotrexate is an antiinflammatory and immunosuppressive agent and it is used as antineoplastic and in the treatment of rheumatic diseases. On the other hand, significant side effects such as myelosuppression, stomatitis, hepatotoxicity and pulmonary toxicity can be seen. In our patient with type 1 diabetes, Chronic Renal Failure and Rheumatoid Arthritis; pancytopenia and diabetic ketoacidosis appeared due to methotrexate use and, were treated with appropriate treatment.
Keywords: Pancytopenia, Diabetic Ketoacidosis, Methotrexate, Chronic Renal Failure.

INTRODUCTION

Methotrexate (MTX) is an antimetabolite agent with antiinflammatory, anti-neoplastic and immunosuppressive effects. It is also used in the treatment of rheumatoid arthritis (RA) frequently. Important side effects of MTX are myelosuppression, stomatitis, hepatotoxicity and pulmonary toxicity. MTX and its metabolites are excreted from the kidneys through glomerular filtration and tubular secretion. MTX use is not recommended in patients with GFR <10 ml/ min. Despite dialysis treatments, toxicity due to MTX has been reported [1-3]. Diabetic ketoacidosis (DKA) is one of the most serious acute complications of diabetes mellitus (DM) resulting in absolute or partial insulin deficiency. Infections are the most common cause of DKA [4,5].

CASE PRESENTATION

A 42-year-old woman with type 1 DM for 30 years, who was under hemodialysis program for 6 months due to chronic renal failure due to diabetic renal disease, applied to our hospital due to fatigue, anorexia, high fever and mouth sores. About 2 months ago MTX 5 mg/ week and methylprednisolone 4 mg/ day treatments were started in another center with diagnosis of RA. In recent days due to fatigue, fever and oral lesions she hindered nutrition and insulin treatment. In physical examination consciousness was blurred and cooperation was disordered. The skin and mucous membranes were dehydrated and had aphthous lesions and candida plaques in the mouth. There was a sharp smell of acetone in the patient's breath. Tachycardia, tachypnea, 39 ^{o}C fever, 110/ min heart rate, 100/60 mmHg TA and 36/ min respiration rate were observed in the physical examination. In labaratory evaluation; 18% hematocrit, 42% platelet, 375 gr/ dl plasma glucose level, ketonemia, ketonuria, 7.22 pH, 11 mEq/ l HCO^{-}_{3}, 21 mmHg pCO_2, 2000/ mm^3 peripheral blood leukocyte, peripheral blood smear consistent with pancytopenia were observed. In addition with isotonic saline infusion; vancomycin, piperacillin-tazobactam and flucanazole therapies were started for neutropenic fever. Folinic acid infusion was started and granulocyte colony stimulating factor was administered 2 times at a dose of 5 mcg/kg/day. The patient's hemodialysis program was continued daily for the first 3 days, then 3 times a week. On the 2nd day of hospitalization DKA and, on the 3rd day pansitopenia were improved.

DISCUSSION

Diabetic ketoacidosis is a frequent metabolic complication of both type 1 and type 2 DM with high morbidity and mortality. The most common precipitating factor for DKA is insulin treatment non-adherence in type 1 DM, whereas infections in type 2 DM [4,5].

In patients using MTX; chronic renal failure (CRF), advanced age, low folic acid level, hypoalbuminemia and nephrotoxic agents facilitates the occurrence of toxic effects. In patients under dialysis treatment, even low dose use of MTX can cause severe pancytopenia. Therefore, MTX should not be used in these patientsand in case of toxicity, the drug should be discontinued and folinic acid should be started rapidly and frequent dialysis should be performed [1-3].

In our case with type 1 DM, CRF and RA; low-dose MTX use caused pancytopenia, associated infections and also feeding insufficiency led to DKA. Clinical and laboratory parameters of the patient were significantly improved with fluid replacement, antibiotherapy, folinic acid infusion, granulocyte colony stimulating factor application and hemodialysis treatments.

Clinicians should always have high caution and suspicion regarding the use of drugs in patients with DM, CRF and the posology and toxicity profiles of the agents used and; keep in mind that early and appropriate treatment may be life-saving.

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