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Pancytopenıa Induced By Low Dose Methotrexate

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Özet

Metotreksat antineoplastik hastalıkların ve romatoid artrit gibi kronik inflamatuvar hastalıkların tedavisinde kullanılan folik asid antagonistidir. Metotreksat pansitopeni gibi şiddetli yan etkiler yapabilir. Bu istenmeyen yan etkiler genelde yüksek doz metotreksat tedavisinde ortaya çıkar. Düşük doz metotreksat kullanımına bağlı gelişen pansitopenihayatı tehdit edicidir. Romotoid artrit tedavi için düşük doz metotreksat kullanımı sonrasında pamsitopeni gelişen 71 yaşında kadın hastayı sunmayı amaçladık.

Anahtar Kelimeler: Romatoid artrit, Metotreksat, Pansitopeni

Abstract

Methotrexate is an folic acid antagonist used in the treatment of neoplastic diseases and chronic inflammatory diseases such as rheumatoid arhritis because of its anti-inflammatory and immunosuppressive effect. Metotrexate has several severe side-effects such as pancytopenia. This undesirable side effects usually occurs with high dose methotrexate usage. Low dose methotrexate induced pancytopenia is rare but life-threatening complication. We want to present a 71 year old female patient who had pancytopenia after low dose methotrexate treatment for romatoid arthritis

Keywords: *Rheumatoid arhritis, Methotrexate, Pancytopenia*

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Introduction

Methotrexate is an folic acid antagonist used in the treatment of neoplastic diseases and chronic inflammatory diseases such as rheumatoid arhritis (RA) because of its anti-inflammatory and immunosuppressive effect. Metotrexate has several severe side-effects such as bone marrow suppression, nausea, stomatitis, hepatic and pulmonary toxicity[1]. This undesirable side effects usually occurs with high dose methotrexate usage. Low dose MTX induced pancytopenia is rare but life-threatening complication. Pancytopenia occurs more frequently in the presence of dehydration, high mean corpuscular volume level, advanced age, infection, hypoalbuminemia, renal failure, low folate levels and lack of concomitant administration of folic acid[2]. We want to present a 71 year old female patient who had pancytopenia after the methotrexate treatment for romatoid arthritis.

Case

71 year old female patient was admitted to emergency department with complaints of anorexia, fever and fatigue. There was romatoid arthritis (5 years), type 2 diabetes mellitus (10 years), hypertension (10 years) in her medical history. We learned that the patient was received subcutaneous methotrexate 7.5 mg weekly for three weeks. She was using folic acid 10 mg per oral daily. Fever was 39.5 °C, Blood Pressure was 130/80 mmHg, pulse was110/min in his physical examination. Diagnosis in the emergency department were pancytopenia, acute kidney injury and urinary tract infection. Laboratory results in the admission are presented in the table1. The patient was admitted to internal medicine clinic. In peripheral blood smear examination hypochromic normocytic anemia, 4-5 platelet groups, a few mature lymphocytes and no atypical cells were detected. No organomegali or lymphadenopaty was detected in the abdominal ultrasonography. Urine culture was taken and ceftriaxone 1 gr was started. The diagnoses of methotrexate ınduced pancytopenia, urinary tract infection and acute renal failure were established. Intravenous hydration was started and urine was monitorized. Acute renal failure was completely improved after three days of hydration. Intravenous folinic acid 30 mg was started for rescue of methotrexate. The folinic acid treatment was continued for three days but there was no response in the hemogram. Filgrastim 48 million units was initiated in the fourth day of admission. Neutropenia and trombocytopenia were completely improved. Hemoglobin was increased up to 9 g/dL. The laboratory results in the sixth day of admission were presented in the table 1.

Table 1 : Laboratory Results

Parameter	Admission	6th days of admission
White Blood Cell (n/uL)	2030	7250
Neutrophil (n/uL)	1152 (56%)	5006 (69%)
Lymphocyte (10^3/Ul):	686 (33,8%)	1030 (14.6%)
Trombocyte (10^3/Ul) :	89000	319.000
Hemoglobin (g/dL)	6.9	9
Hgb (g/dL) :	6.9	9,0
Albumine (g/dL) :	2,5	3.0
Creatinine (mg/dL) :	3,5	0,9
Urine Analysis	+3 Leucocyte esteraz	-

Discussion

Romatoid arthritis is a chronic, progressive, auto-immune, inflammatory disease characterised by synovial cell proliferation and destruction in the joints[3]. Methotrexate which is selective competetive inhibitor of the enzyme dihydrofolate reductase, is one of the first choice of drug in the treatment of romatoid arthritis. The most common adverse effects include: hepatotoxicity, ulcerative stomatitis, low white blood cell count and thus predisposition to infection, nausea, abdominal pain, fatigue, fever, dizziness, acute pneumonitis, rarely pulmonary fibrosis and kidney failure[4]. Pancytopenia is a rare but severe side effect of methotrexate. Ohosone et al. reported 4 (1,4%) pancytopenia cases at the end of a 33,2 month long term follow-up of 284 patients during MTX treatment[2]. In another study, Nakazaki et al. reported only one (0,002%) pancytopenia case at the end of a 60 month long-term follow-up of 420 patients treated with MTX[5]. Gutierrez-Urena et al. found pancytopenia ratio 1-2% in RA patients taking MTX treatment[6].

The mechanism of development of methotrexate induced pancytopenia is not clearly known. It is commonly seen in some patients having several risk factors such as dehydration, high MCV level, hypoalbuminemia, daily MTX intake instead of weekly, renal failure, low folic acid level, lack of concomi-

tant folic acid supplementation, advanced age, infection and polypharmacy[1,2,4]. In our case; advanced age of the patient, acute renal failure and infection could facilitate the development of pancytopenia. We could not identify the reason of acute renal failure. It could occur due to methotrexate or urinary tract infection or nausea.

Folinic acid is administered at the appropriate time following methotrexate as part of a total chemotherapeutic plan, where it may "rescue" bone marrow and gastrointestinal mucosa cells from methotrexate. No apparent effect is seen on pre-existing methotrexate-induced nephrotoxicity[4]. Intravenous calcium folinat 30 mg was started for rescue treatment of methotrexate. The folinic acid treatment was continued for three days. Filgrastim is a granulocyte colony-stimulating factor (G-CSF) analog used to stimulate the proliferation and differentiation of granulocytes; it is a pharmaceutical analog of naturally occurring G-CSF[8]. Filgrastim 48 million units was initiated in the fourth day of admission.

Methotrexate is an effective agent in the treatment of romatoid arthritis. Pancytopenia is a rare but life-threatening side effect of methotrexate and it can occurs in the low dosage. In the presence of the risk factors such as dehydration, high MCV level, hypoalbuminemia, renal failure, advanced age, infection and polypharmacy; clinician have to be very carrefull about side effect. In this risk group, other treatment options should be considered.

Confilict of Interest
None declared.

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