Dose of Methotrexate the Association with Methotrexate Induced Rheumatoid Nodulosis

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To the editor

Methotrexate induced rheumatoid nodulosis (MIRN) is rarely seen side effect associated with treatment of methotrexate. This side effect tends to multiply and mostly develops at the extremity of distal parts. İmmunopathogenetic mechanisms are the most blamed factor pathogenesis of MIRN [1]. However pathogenesis is the unclear and very complex. We present a case when the dose of methotrexate was changed, MIRN was developed or overlooked.

Case report 1: 59 years old female patient was admitted to complaint with multiple swelling on the second finger of the right hand. Her history had that methotrexate (10 mg/week) was continued for rheumatoid arthritis for 23 years. After one, year, rheumatoid nodulosis was developed on the second finger of the right hand. But rheumatoid nodulosis was stable until now. Her new admission, dose of methotrexate was increased 15 mg/week because of increased of rheumatoid arthritis activities. Although, activities of disease have been controlled, numbers and size of rheumatoid nodules were increased. Physical examination revealed multiple nodules that size of <5mm and number of six on bilateral elbow joints (Figure 1). Pathological examination of nodules showed according to rheumatoid nodulosis. Laboratory examination and thorax comptozied tomography was normal. Over there, when the dose of methotrexate was again decreased 10 mg/week, size of nodules was gradually decreased.

Case report 2: 65 years old female patient was admitted to complain with swelling of elbows and feet. Her history methotrexate was started for rheumatoid arthritis before one year. After than 8 months, joint pain was reduced, but her swelling of elbows and feet were developed. Physical examination was detected multiple nodules on both the elbow extensor, first finger and the fifth finger metatarsafalangial joint of the both feet (Figure 2). Biopsy was showed rheumatoid nodules. Methotrexate was stopped, and leflunomide and hdroxiclorocnie was started. After two months,her rheumatoid nodulosis partially recovered. Laboratory examination and thorax computerized tomography were normal.

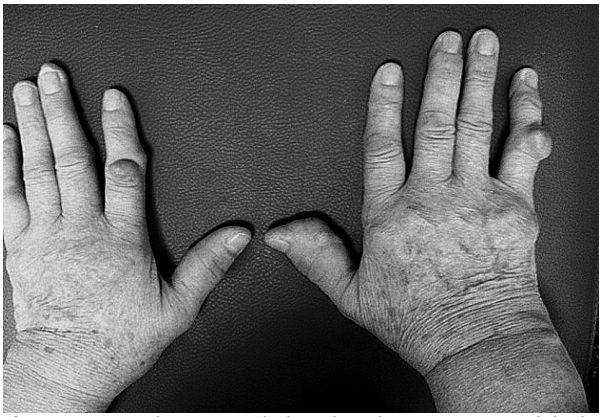

Figure 1. Methotrexate induced subcutaneous nodulosis show bilateral fingers.

MIRN is the uncommon side effects of methotrexate. Sometimes this side effect can lead to stopping treatment of methotrexate, and that can lead to mortality [2]. MIRN develops usually on the fingers of the distal part. However, MIRN can show other region such as lung, pericardium, larynx, tendons and penis [3]. Several factors including immunologic factors, genetic factors include CD4 expression, HLA DQ–DR activation and elevated T helper/suppression ratio, the presence of HLA DRB014101 allele and A2756G polymorphism of the methionine synthase reductase [4]. However, there has insufficient knowledge about dose of methotrexate effects on MIRN.

The dose and duration of methotrexate have been unknown about developing MIRN. Numerous reports mainly as a case report showed that MIRN developed in the course of low dose use of methotrexate. Only study demonstrated that investigation to dose and duration of methotrexate.

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Agarval V et al showed that no association of MIRN with cumulative dose and duration of methotrexate therapy and other factors such as gender, rheumatoid factor positivity, disease duration [5].

Our present case showed low dose methotrexate associated with multiple MIRN. When the methotrexate dose was increased, the number and size of MIRN were increased. In contrast to this, when methotrexate dose was decreased, we showed the size and number MIRN were decreased. The Naranjo probability scale was detected 10, in our cases. We think that a dose of methotrexate is an important factor in MIRN.

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