CLINICAL IMAGES

Methotrexate-induced nodulosis

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A 52-year-old woman with a seven-year history of seropositive rheumatoid arthritis treated with oral prednisolone (5 mg/d) and methotrexate (6 mg/wk) presented after two weeks of experiencing rapidly increasing tender eruptions on her fingers. Clinical examination showed multiple skin-coloured hard nodules of up to 15 mm in diameter on the finger pulps (Figure 1A). Skin biopsy specimens showed early granulomas containing neutrophilic infiltrates in the dermis and the subcutaneous fat. Her C-reactive protein level and erythrocyte sedimentation rate were normal, and a series of disease activity scores recorded in her file suggested that her rheumatoid arthritis activity had decreased and stabilized. We diagnosed methotrexate-induced accelerated nodulosis. Because her rheumatoid arthritis had been well controlled, methotrexate was continued and colchicine (1.5 mg/d) was added. Within two months, the cutaneous nodules decreased in number, size and tenderness, and the arthritis remained clinically and serologically inactive (Figure 1B). An assessment of causality for the nodulosis and methotrexate use gave a result of "probable" (score of 6) on the Naranjo Adverse Drug Reaction Probability Scale.[1]

The estimated incidence of methotrexate-induced accelerated nodulosis is 8%–11.6% among patients receiving the drug for rheumatoid arthritis.[2] Reported cases have shown that the time between the start of treatment and the occurrence of nodulosis varies from 3 months to 12 years, and the cumulative dose of methotrexate ranges from 90 to 7200 mg.[3] Histologic features are typically identical to those of a rheumatoid nodule.[3] Clinically, methotrexate-induced nodules are smaller than rheumatoid nodules, and they develop more rapidly in soft tissue and away from the joints, usually involving the fingers.[2] Methotrexate-induced nodulosis tends to occur while the arthritis is inactive during methotrexate treatment.[2,3] The primary treatment is cessation of the drug. However, additional treatment with colchicine, sulfasalazine, hydroxychloroquine or D-penicillamine has been shown to shrink the nodules, even if methotrexate is continued.[2,3]

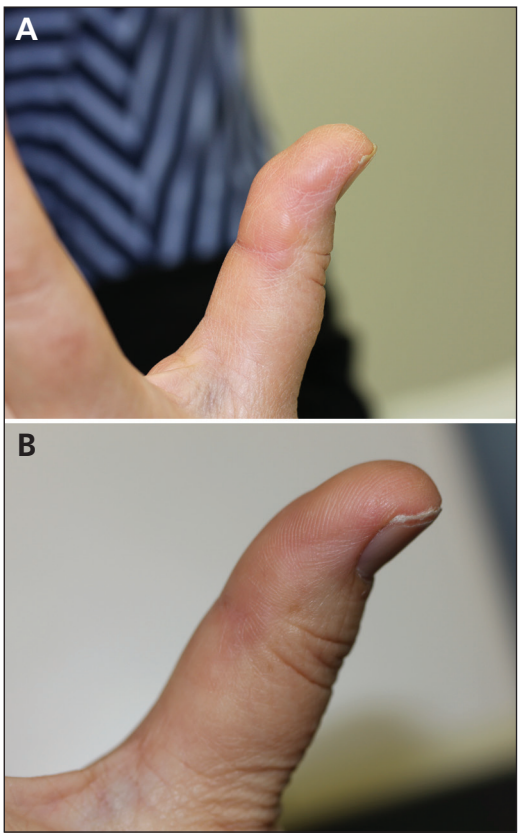

Figure 1: (A) Skin-coloured small, hard nodules on the left thumb pulp of a 52-year-old woman receiving methotrexate for rheumatoid arthritis. (B) The nodules decreased in size within two months after colchicine was added to her treatment.

References

1. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239-45.
2. Patatanian E, Thompson DF. A review of methotrexate-induced accelerated nodulosis. *Pharmacotherapy* 2002;22:1157-62.
3. Motegi S, Ishikawa O. Methotrexate-induced accelerated nodulosis in a patient with rheumatoid arthritis and scleroderma. *Acta Derm Venereol* 2014;94:357-8.

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