Methotrexate-Induced Accelerated Nodulosis in Seropositive Rheumatoid Arthritis

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A 57 year old gentleman presented with multiple nodular swellings over dorsal aspects of hands (Figure 1), forearms (Figure 2), posterior superior iliac spine and over back (Figure 2) for last two weeks. He was diagnosed with seropositive rheumatoid arthritis (RA) 6 months back and was put on weekly subcutaneous methotrexate (MTX) and oral sulphasalazine. The patient did not notice any nodule during the time when RA was diagnosed.

Clinical examination revealed multiple non-tender subcutaneous nodules over the aforesaid regions. The nodules were firm in consistency and not fixed to the skin or underlying bones. Histopathology of the excision biopsy specimen of one of the nodules revealed central area of necrosis surrounded by palisading fibroblasts, perivascular collections of chronic inflammatory cells and multiple giant cells consistent with rheumatoid nodule. MTX was stopped and he was put on azathioprine with complete resolution of nodules within the next six weeks. The causality analysis for MTX and the nodules was suggestive of adverse drug events [Probable/likely on WHO-UMC causality assessment scale and probable (total score 7) on Naranjo probability scale].

Accelerated nodulosis is a rare complication of MTX therapy used to treat patients with RA.1 MTX nodulosis has also been described in patients with psoriasis and other inflammatory arthritides, however, interestingly enough this unique phenomenon has not been described in patients receiving MTX for treatment of different dermatological and malignant diseases. This unusual side effect of MTX therapy has been documented previously and almost identical case has been reported from Italy in a 62 year old man.2

The pathophysiology of accelerated nodulosis despite effective and durable suppression of synovial inflammation by MTX in RA is yet unsettled, but different pathologic mechanisms and differential MTX susceptibility have been proposed. Controversy surrounds the management of patients who develop accelerated nodulosis while receiving MTX and different drugs (Colchicine, Azathioprine, D-penicillamine, Hydroxychloroquin) have been tried with favorable outcomes. Awareness of this clinical entity is important for early diagnosis and treatment as MTX is being widely used as the first line agent in RA and related arthritides.

References


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