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Methotrexate-induced pleural effusion in a patient with systemic lupus erythematosus: a possible and rare adverse event

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BACKGROUND

MTX is useful for treatment of Systemic lupus erythematosus (SLE). Despite that, MTX has side effects that can mimic SLE`s manifestations. We present a case of probable MTX-induced pleural effusion (PE), associated with interstitial pneumonitis (IP), in a lupus patient.

CASE REPORT

45-year-old woman with SLE since 2015 (discoid lesions, lymphopenia, thrombocytopenia, ANA, anti-dsDNA, anti-Sm, and hypocomplementemia). In July 2017, as she presented hand arthritis and active cutaneous lupus, MTX was started at a dose of 15mg/week, increased to 20mg/week two months later. After eight months, she presented dyspnoea (mMRC 2) and cough, with normal chest x-Ray, followed by hospital admission due to possible erythema nodosum in legs and associated cutaneous infection. MTX was promptly suspended and prednisone dose was increased. She had complete resolution of cutaneous and respiratory manifestations. However, the actual cause of respiratory symptoms was not identified, since chest CT and spirometry were not done during the acute phase of symptoms. She remained well controlled with prednisone (5mg/day) and azathioprine (3 mg/Kg/day). In February 2019, she presented recurrence of arthritis, and MTX was restarted (20mg/week). After one month, arthritis had disappeared but dyspnoea and dry cough relapsed and worsened progressively. At physical examination she had features of pleural effusion, confirmed by x-Ray. MTX was immediately discontinued and prednisone dose was increased (0.8mg/Kg/day). Chest CT showed a moderate-sized left PE, ground glass opacity and interlobular septal thickening in superior and inferior right lung, suggestive of IP, and mild pericardial effusion. Pleuroscopy revealed scattered nodules implants in parietal pleura. Effusion analysis showed a neutrophilic exudate. Usual bacterial and fungal cultures were negative, as well as molecular tests for M. tuberculosis. Pleural biopsy showed chronic moderate and unspecific pleuritis, with mononuclear infiltrate, and no evidence of neoplasm. After thoracocentesis and MTX withdrawal, she became asymptomatic with no other evidence of lupus activity.

CONCLUSION

The incidence of pulmonary MTX-toxicity is 1% to 7%, less than 0.01% presents PE. Once there are no diagnostic criteria for MTX lung toxicity, some features suggested this diagnosis in this case: first episode of non-diagnosed cause of dyspnoea, associated with erythema nodosum, which resolved with the withdrawal of MTX; recurrence of respiratory manifestations (PE and IP) after restarted the drug; pleuroscopy compatible to hypersensitivity pleurisy; complete resolution of symptoms after a second

withdrawal of MTX, without recurrence and any evidence of lupus activity; and lack of any other plausible cause of PE.