

Pulmonary Disease Complicating Intermittent Methotrexate Therapy of Psoriasis

Jesper Verdich and Alice Lykke Christensen¹

*Department of Dermatology and Venereology and
¹Department of Thoracic Medicine,
 University Hospital, Odense, Denmark*

Received March 28, 1979

Abstract. A patient with psoriasis was treated with methotrexate (MTX) orally once a week. Bilateral pulmonary infiltrations, hilar- and peripheral adenopathy with granulomas, cough, fever and dyspnoea developed after 10 months of treatment. Similar symptoms in patients receiving MTX have been described by others. The clinical symptoms cleared after MTX was withdrawn. However, the radiographic changes persisted long after the symptoms had resolved. The possibility of sarcoidosis incidentally developing during the MTX treatment is discussed.

Key words: Psoriasis; Methotrexate; Pulmonary disease

Since Clarysse et al. in 1969 described pulmonary disease in seven patients treated with methotrexate (MTX) for acute lymphoblastic leukaemia (3), there has been an increasing number of case reports describing pulmonary disease in patients receiving MTX (1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13).

The present report describes pulmonary infiltrations, hilar-, paratracheal- and peripheral adenopathy developing in a psoriatic treated intermittently with MTX.

CASE REPORT

The patient is a 43-year-old Caucasian male suffering from psoriasis since the age of three. No previous history of pulmonary disease. From January 1977 he was treated with MTX 15 mg perorally once a week. Standard laboratory values were found normal before treatment commenced. X-ray of the chest was normal in 1974 and had not been checked subsequently.

There was a slow clinical response. In April 1977 the MTX dosage was reduced to 7.5 mg weekly because of a rise in serum glutamic oxaloacetic transaminase (GOT) and lactic dehydrogenase (LDH) levels. However, in August 1977 the dosage was increased to 10 mg weekly because the values of GOT and LDH had now normalized.

In September 1977 the patient developed a non-productive cough 1-2 days after the weekly dose of MTX. The symptoms subsided in a few days but recurred after the next dose.

A month later the patient developed fever in addition to the cough. The symptoms subsided slowly. X-ray of the chest now showed enlargement of the hilar lymph nodes. A control X-ray a month later showed unchanged hilar adenopathy and in addition small nodular infiltrations of the lungs (Fig. 1). MTX was withdrawn a month later. The patient's complaints were tiredness and malaise. A total dose of 370 mg of MTX had been given over a period of 10 months.

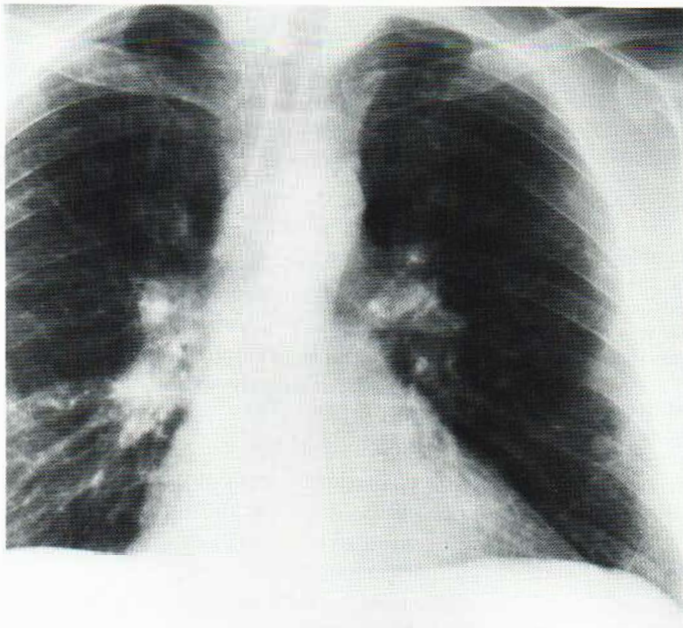


Fig. 1. Chest X-ray showing bilateral hilar lymphadenopathy and nodular infiltration of the lungs.

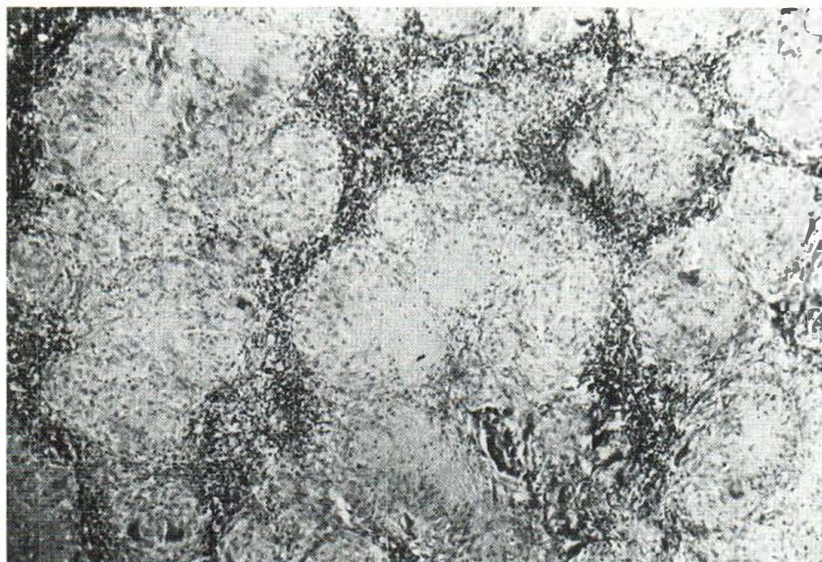


Fig. 2. Cervical gland biopsy showing marked epithelioid cell granulomas (van Gieson stain, $\times 45$).

A few days after MTX was withdrawn the patient developed cough, pyrexia (40°C) and resting dyspnoea. In the next few days enlargement of the cervical and inguinal glands was observed. A week later the patient was admitted to the department of thoracic medicine. On admission the body temperature was 37.3°C , auscultation of the lungs normal and enlarged cervical and inguinal glands were present. Chest X-ray was the same as that taken 6 weeks previously.

Pertinent laboratory values, including white blood cell count, differential blood count, hemoglobin, alkaline phosphatase and creatinine levels, were all normal. No eosinophilia was found. Arterial blood gas values were normal.

Biopsy of a cervical gland showed granuloma formation with epithelioid cells (Fig. 2). Biopsies of a paratracheal gland and the lung showed similar changes. The histological findings were compatible with those seen in sarcoidosis.

The general condition of the patient was only slightly affected.

The peripheral adenopathy showed considerable regression during the first weeks. The radiographic changes persisted and after 3 weeks, treatment with prednisolone 30 mg daily was started. A week later the dose was reduced with $2\frac{1}{2}$ mg weekly. The treatment had no significant effect on the radiographic changes.

Cultures of the sputum for fungi and acid-fast bacteria were negative. Mantoux was negative. No tumour cells were found in sputum. Antinuclear antibody test was negative. Serum titre studies for toxoplasmosis, yersinia and brucellosis gave negative results. LE cell test was negative. Pulmonary function test: Vital capacity 6700 ml (normal 5200 ml), forced expiratory volume 3700 ml (normal 3940 ml). X-ray of the chest in the following months showed slight regression of the hilar adenopathy but no change of the nodular infiltrations of the lungs.

DISCUSSION

Our case differs from previously published cases by the severe peripheral adenopathy with epithelioid cell granulomas and the persistent nodular infiltrations of the lungs. Biopsies of glands and lung showed changes compatible with sarcoidosis. None of the tests performed gave any suspicion of malignancy or infection. The patient received a total dose of 370 mg of MTX during a period of 10 months.

Compared with previously published cases, the pulmonary changes and the peripheral adenopathy in our patient may have been induced by the MTX. That sarcoidosis incidentally developed during the treatment is a possibility.

Lung biopsy has shown granuloma formation in the cases presented by Filip et al. (4), Clarysse et al. (3) and Rawbone et al. (7). In other cases lung biopsies have shown acute and chronic bronchiolitis and pneumonitis (6), mixed interstitial and exudative pneumonitis (8) and pneumonitis (12). Eosinophilia has been present in some cases (5, 6) absent in others (4, 6).

X-ray of the chest in our case showed nodular infiltrations of the lungs, in contrast to findings in most other cases, in which the infiltrations were more diffuse and extensive (3, 4, 7). As in other cases, our patient had cough, fever and malaise. His clinical symptoms were mild, with rapid improvement after MTX was withdrawn. Auscultation of

the lungs has been found normal in other cases too (6, 11).

In most of the published cases, the pulmonary changes developed in patients receiving MTX for acute lymphoblastic leukaemia (1, 3, 7, 8, 9, 10) or other grave diseases (2, 6, 11, 12, 13).

On reviewing the literature, only 2 cases of pulmonary disease developing in patients receiving MTX for psoriasis have been found (4, 5).

The case presented by Filip et al. (4) showed hilar- and paratracheal adenopathy and palpable cervical glands. Biopsy of a gland showed reactive hyperplasia. A biopsy of the lung showed a diffuse interstitial lymphocytic infiltrate, giant cells and non-caseating granulomas. Biopsy of paratracheal glands was not performed. The patient presented by From (5) had eosinophilia and life-threatening pneumonitis but no adenopathy. Biopsies of lung or glands were not performed.

In view of the common use of MTX for treatment of psoriasis, we found it of interest to present another case of pulmonary changes and adenopathy developing during intermittent treatment with MTX.

REFERENCES

1. Acute Leukemia Group B: Acute lymphocytic leukemia in children. Maintenance therapy with methotrexate administered intermittently. *JAMA* 207: 923, 1969.
2. Bhat, K. S. S., Andarson, K. R. & Stewart, R. D. H.: Lung disease associated with methotrexate therapy. *Aust NZ J Med* 4: 277, 1974.
3. Clarysse, A. M., Cathey, W. J. Cartwright, G. E. & Wintrobe, M. M.: Pulmonary disease complicating intermittent therapy with methotrexate. *JAMA* 209: 1861, 1969.
4. Filip, D. J., Logue, G. L., Harle, T. S. & Farrar, W. H.: Pulmonary and hepatic complications of methotrexate therapy of psoriasis. *JAMA* 216: 881, 1971.
5. From, E.: Methotrexate pneumonitis in a psoriatic. *Br J Dermatol* 93: 107, 1975.
6. Goldmann, G. C. & Moschella, S. L.: Severe pneumonitis occurring during methotrexate therapy. *Arch Dermatol* 103: 194, 1971.
7. Rawbone, R. G., Shaw, M. T., Jackson, J. G. & Bagshawe, K. D.: Complication of methotrexate-maintained remission in lymphoblastic leukaemia. *Br Med J* iv: 467, 1971.
8. Robbins, K. M., Gribetz, I., Strauss, L., Leonidas, J. C. & Sanders, M.: Pneumonitis in acute lymphatic leukemia during methotrexate therapy. *Pediatr* 82: 84, 1973.
9. Robertson, J. H.: Pneumonia and methotrexate. *Br Med J* ii: 156, 1970.
10. Schwartz, I. R. & Kajani, M. K.: Methotrexate therapy and pulmonary disease. *JAMA* 210: 1924, 1969.
11. Stutz, F. H., Douglass, C. T. & Blom, J.: Nonbacterial pneumonitis with multidrug antineoplastic therapy in breast carcinoma. *Can Med Assoc J* 108: 710, 1973.
12. Toyama, M. W., Reges, C. N., Lawton, B. R. & Sautter, R. D.: Open lung biopsy in infants and children. *Arch Surg* 103: 195, 1971.
13. Whitcomb, M. E., Schwartz, M. I. & Thorney, D. C.: Methotrexate pneumonitis: Case report and review of the literature. *Thorax* 27: 636, 1972.