REITER'S SYNDROME—TREATMENT WITH METHOTREXATE

BY S.M. Chu

SYNOPSIS

REITER'S SYNDROME may progress to permanent disability. No specific treatment is at present available. Its similarity to psoriasis has prompted the successful use of methotrexate in its treatment. In this report, the favourable response of another patient to methotrexate is described. The cutaneous lesions improved more remarkably than the arthritis though the latter underwent complete remission with the addition of indomethacin. The value of methotrexate in suppressing visceral complications of Reiter's Syndrome is not known.

INTRODUCTION

REITER'S SYNDROME (RS) is manifested by urethritis, together with arthritis, conjunctivitis and cutaneous lesions, notably circinate balanitis and keratoderma blennorrhagicum. The disease affects young men predominantly. Though it may arise following a lower genito-urinary tract infection after sexual intercourse, the aetiology is still unknown. Gonorrhoea neisseria, Mycoplasma and T. vaginalis have not been proven to have any aetiological relationship to it. The syndrome may also follow bacillary dysentery or non-specific diarrhoea. Grimble (1963) demonstrated the presence of autoantibodies to antigen prepared from prostate gland in patients with RS and ankylosing spondylitis, suggesting an autoimmune cause. The majority of attacks of RS lasts about three months but recurrence is common (Farber *et al*, 1967). Iritis, painful deformities of the feet and atypical spondylitis may result. Visceral involvement develops in a few of these patients. Aortic incompetence is due to elastic tissue disruption and hence loss of support for the aortic ring (Gsonka *et al*, 1969, Paulus *et al*, 1972). The aortic incompetence murmur is heard on the average about fifteen years from the onset of the syndrome. Recurrent facial nerve palsies, meningoencephalitis, pleurisy and pneumonitis are other described uncommon features. RS should not therefore be regarded as a condition which heals spontaneously without giving rise to permanent disability.

There is no specific therapy for RS. Tetracycline, aspirin and corticosteroids are usually ineffective though response to indomethacin is more favourable. Methotrexate has also been used with success in selected patients particularly those with crippling and incapacitating arthritis (Farber *et al*, 1967, Topp *et al*, 1971). In this report, the patient had severe incapacitating arthritis which did not respond to the more conventional methods of treatment but showed marked improvement after treatment with methotrexate.

DR. S.M. CHU, M.B., B.S. (Mal.), M.R.C.P. (UK), Dip. Derm. (Lond.), Lecturer.
Department of Medicine, University of Malaya, Kuala Lumpur.

CASE REPORT

A 17 year old Chinese boy developed dysuria associated with a yellowish urethral discharge in September 1972, 2 weeks after a sexual exposure. This stopped within 4 days after treatment by his general practitioner. Two weeks later he developed an intermittent fever together with swelling, redness and pain over both wrists and elbows simultaneously. This was followed subsequently by swelling and pain over both knees and ankles. He was unable to walk and was admitted to a local hospital a week later where he was treated with prednisolone 45 mgs daily. The relevant laboratory findings then were a leukocyte count of 26,000 and an erythrocyte sedimentation rate of 65 mm in the first hour. The rheumatoid factor and the LE cell test were negative. Blood uric acid was 4.0 mg/100 ml, ASOT 100 units and the Kahn test was negative. About two months following the onset of symptoms, whilst he was still hospitalised, he developed conjunctivitis and soreness of the tongue, with superficial ulceration of the buccal mucosa. This was followed by the stimultaneous appearance of initially pustular lesions over both palms and soles, later on becoming erythematous and covered with scales and crusts. The keratoderma blennorrhagicum were seen as circular or confluent plagues over the body particularly the front and back of the trunk and the scalp. Circinate balanitis on the glans penis were also seen. At this stage he became depressed and was transferred to the University Hospital on 19th December 1972.

Examination at the time of admission to the University Hospital showed the patient to be thin, ill-looking and mildly cushingoid. He was febrile with a temperature of 39°C. Acute conjunctivitis was present. The tongue and buccal mucosa showed superficial ulcerations. Hyperkeratotic scaly plagues as described above were seen on the scalp, trunk and the limbs. Those over the palms and soles were

papulo-pustular and crusted and extended to involve the nail folds of the thumb and fingers (Figs. 1 and 2). The left elbow, both wrists, knees and ankles were diffusely swollen, warm and tender with marked limitation of movements. There was definite muscle wasting over the thigh and calf muscles. The small joints of the hands were not affected. No abnormality of the cardiovascular system was detected. Laboratory tests showed a haemoglobin of 15.4 gm, leukocyte count 18,000 and an erythrocyte sedimentation rate of 128 mm in the first hour.

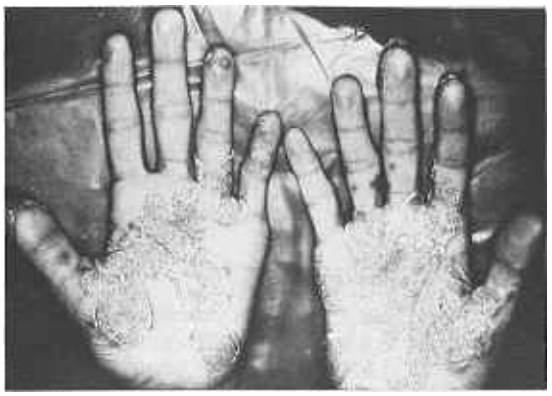

Fig. 1. Shows the hyperkeratotic, scaly lesions of keratoderma blennorrhagicum of palms. (Before methotrexate treatment).

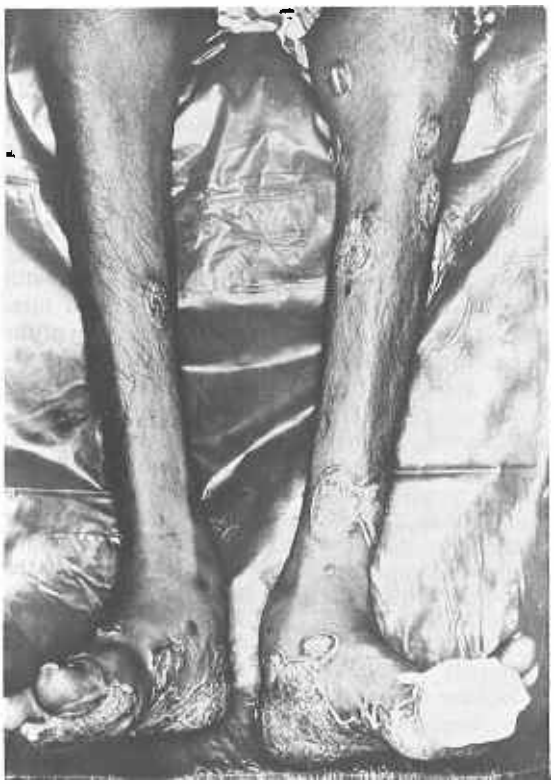

Fig. 2. Keratoderma blennorrhagicum of soles. Note the swelling of the knees and ankle joints. (Before methotrexate treatment).

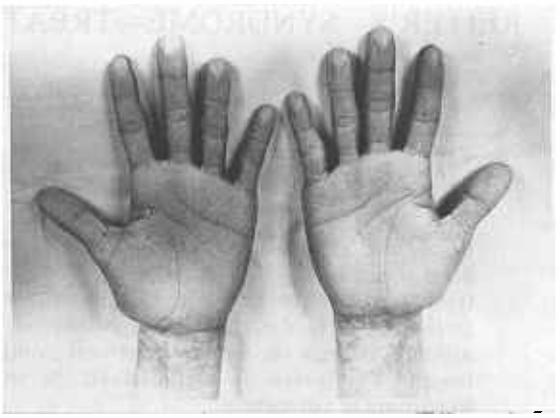

Fig. 3. After treatment with methotrexate (palms).

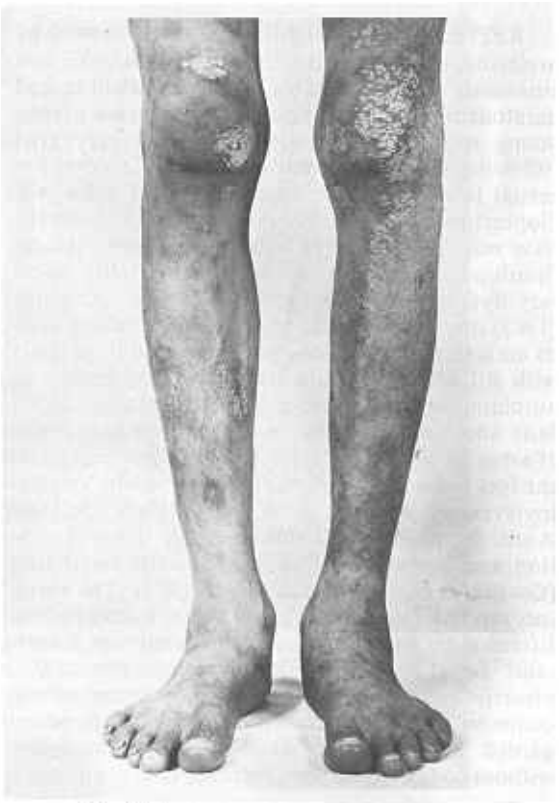

Fig. 4. After treatment with methotrexate (legs.)

Urinalysis showed 10 wbc/ul but culture of the urine was negative. The VDRL test was negative. X-rays of the knees, ankles and elbows were normal. A skin biopsy showed parakeratosis and irregular acanthosis with clubbed reteridges. Spongiform pustules were found in the upper epidermis. The papillae were oedematous and dilated and prominent papillary capillary loops were seen. The upper squamous cells showed intracytoplasmic vacuolation and pyknosis of nuclei.

He was treated with aspirin on admission but no benefit was obtained over the next three days. Because his condition was getting alarmingly more severe it was decided to put him on methotrexate. Hence he was started on oral methotrexate in 25 mg weekly doses on 22nd December 1972, in addition to aspirin. A week later the conjunctivitis subsided and the skin lesions were settling. The arthritis, however, persisted and after about three weeks since treatment with methotrexate, indomethacin was given in place of aspirin. By 27th January 1973, after four courses of methotrexate the arthritis subsided and the patient was gradually ambulated. It was noted at this stage that the keratoderma blennorrhagicum lesions, though under control, tended to reappear towards the latter part of the week after each weekly dose and the nails became progressively more dystrophic. By the tenth course of treatment the arthritis completely subsided and remained so even after indomethacin was stopped. By the 22nd course, virtually all signs of RS disappeared, the skin lesions remained suppressed and the dystrophic nails were being replaced by normal ones. A repeat skin biopsy showed focal parakeratosis and acanthosis but spongiform pustules and dermal cellular infiltrates were absent. Initial attempts were made to stop methotrexate therapy but his rashes, though minor, recurred when a period of cessation exceeded three weeks. He was thence put on methotrexate 17.5 mg fortnightly and this was gradually tailed off completely; the skin lesions since then having been easily controlled by topical coal tar ointment. He is now back to full employment as a truck attendant. To date, follow-up of the patient with regular blood counts, liver function tests and liver biopsies showed no toxic effects from methotrexate.

DISCUSSION

Perry and Mayne (1965) had suggested that because of the overlap of clinical and histological features with psoriasis, RS may possibly be a variant of psoriasis. Such a similarity has led to the use of folic acid antagonists in the treatment of RS. Mullins, *et al* (1966) had success with five of six patients and found that methotrexate was beneficial especially in patients with cutaneous manifestations of keratoderma blennorrhagicum though joint manifestations were recalcitrant. It is difficult to evaluate the therapeutic effects of methotrexate therapy as RS tends to undergo spontaneous remission. Hence the indication for use of this drug in this disease is less well defined. This patient is young and one would be rather hesitant to use methotrexate; but he did not show improvement despite the use of aspirin and steroids. In the presence of such disabling arthritis, the best available alternative was to put him on this folic acid antagonist. The response of the cutaneous lesions was rapid but the arthritis responded only after indomethacin was added though no exacerbation occurred after it was taken off. Mullins had the same experience with two of his patients. The patient is now very well and back to full employment, engaging in fairly heavy manual work. There is little doubt that methotrexate is responsible for his remission.

The long term effect of methotrexate therapy is well known, notably liver fibrosis and cirrhosis. In one study it was found that patients given frequent small doses were more prone to develop these after short periods of treatment than those given intermittent large doses (Dahl *et al*, 1972). In another study, Podurgiel *et al* (1973) found that they occurred significantly in patients given methotrexate at a frequency of more than twelve days of each month rather than the actual total dose per month. They feel that the drug may be safely given in weekly dosage for up to four years. Whether methotrexate can prevent subsequent development of visceral complications in RS is not established. One of the patients with aortic incompetence described by Paulus (1972) had been treated with methotrexate several years after the onset of symptoms. The possibility that damage may have occurred in the early phase of the disease in his patient cannot be ruled out. However, until proper long term follow-up studies are carried out this aspect of treatment with methotrexate remains unknown.

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