CASE REPORT: MINOCYCLINE-INDUCED LUPUS

P Premchand, Registrar, JP Halsey, Consultant Rheumatologist
Royal Lancaster Infirmary

INTRODUCTION

Minocycline hydrochloride is a semisynthetic tetracycline used for a variety of infections and is the most widely prescribed systemic antibiotic for *acne vulgaris*. Several adverse effects have been reported including nausea, blood eosinophilia, transient vestibular symptoms, photosensitivity, hyperpigmentation, rashes, fever, hypersensitivity pneumonitis and hepatitis⁽¹⁾. Eleven cases of minocycline-induced lupus have been reported previously^(1,2). In this paper we describe two patients who presented to the rheumatology department of the Royal Lancaster Infirmary with a lupus-like syndrome associated with minocycline therapy.

CASE REPORT I

A nineteen-year-old female student was referred to the rheumatology clinic in June 1995 with a six-week history of polyarthralgia and general malaise. She had prolonged morning stiffness, headache and difficulty concentrating and revising for her forthcoming exams. She had no associated eye, skin, bowel or urinary symptoms and there was no history of a preceding infection. There was no relevant medical or family history. She had been taking minocycline 50mg twice daily for the previous twelve months for acne.

On examination there was no lymphadenopathy and no mucocutaneous lesions. Although there was no definite synovitis there was tenderness affecting wrists, metacarpophalangeal joints, index and middle finger proximal interphalangeal joints, the right knee, ankles and metatarsophalangeal joints. Examination was otherwise unremarkable.

Investigations revealed an ESR of 10mm/hr, haemoglobin 13.1gm/dl, wcc $5.1 \times 10^9/L$, platelets $238 \times 10^9/L$ and c-reactive protein <6.52 mg/l. IgM and IgG antinuclear antibodies were elevated to titres of 1:140 and 1:40 respectively. DNA-related antibody was weakly positive. Urine analysis was negative and renal function normal.

She was started on Oruvail and paracetamol and advised to stop minocycline. All her symptoms disappeared within two weeks of stopping minocycline treatment.

When reviewed in September 1995 she was asymptomatic and there was no residual joint tenderness on examination. Repeat serology revealed negative DNA-related antibody and IgG antinuclear antibody and reduced titre of IgM antinuclear antibody (1:40). ESR and c-reactive protein remained normal.

On final review in March 1996 she was well and had had no recurrence of polyarthralgia, headache or general malaise. Her mild acne had not required further treatment.

CASE REPORT II

A thirty-six-year-old trainee nurse was referred to the rheumatology clinic in September 1996. She originally started taking minocycline 50mg twice daily in 1994 for facial acne, but discontinued treatment after a year due to reports she had read in the national press of adverse reactions to minocycline. Although she was prescribed an alternative tetracycline she discontinued this after two months as she felt unwell and had general aching. Due to flare-up of her acne she restarted minocycline and after taking one 50mg tablet she developed severe myalgia and painful swollen hands and feet. She was hardly able to move or even get out of bed. There was no associated skin rash, pleurisy, Raynaud's phenomenon or hair loss and she had not had any recent infection.

Her general practitioner (GP) promptly stopped the minocycline and started her on anti-inflammatories and analgesics. Her symptoms persisted for a further three weeks and investigations revealed an ESR of 65mm/hr and IgG and IgM antinuclear antibodies raised to the titres of 1:640 and 1:80 respectively. Haemoglobin was 13.3 gm/dl and DNA-related antibodies positive. There was no renal impairment.

She was started on prednisolone by her GP because of her severe symptoms and she responded very quickly. When she was seen in the clinic a week later she was asymptomatic and did not have any signs of synovitis or inflammation.

She was finally reviewed in January 1997 and remained asymptomatic and was not on any treatment. Her ESR had fallen to 26mm/hr, IgM antibody negative, IgG antibody had fallen to 1:160 and DNA-related antibody only weakly positive.

DISCUSSION

We describe two cases of young female patients who were prescribed minocycline for acne, who developed arthralgia or arthritis accompanied by myalgia and malaise. In the first case the onset was abrupt with symptoms becoming increasingly severe over the course of six weeks. She had been asymptomatic prior to starting minocycline therapy and did not develop any other features of systemic lupus erythematosus such as rash, renal or neurological impairment.

Both cases improved after stopping minocycline but in the second case symptoms were sufficiently severe to warrant treatment with a short course of prednisolone. In conjunction with clinical symptoms both patients had an elevated ESR and were antinuclear factor and DNA-related antibody positive. On stopping minocycline, DNA-related antibody became negative in the first case and reduced to weakly

positive levels in the second. Both sera were negative for antihistone antibodies.

Both patients received minocycline 100mg per day and did not exceed the recommended dose. There are no specific guidelines in the British National Formulary or ABPI regarding the duration of treatment. In the second case severe symptoms appeared on taking a single tablet of minocycline after an interval of twelve months. Similar flare-up of symptoms has been described following rechallenge with minocycline in three previous cases⁽³⁾.

It is a matter of speculation why patients who have been receiving continuous minocycline therapy for several years suddenly develop arthralgia and lupus-like syndrome. The possibility of a simple viral arthropathy is unlikely due to the rapid resolution of symptoms and the blood test abnormalities on stopping the drug. There is a recent report of minocycline-induced arthritis associated with fever, livedo reticularis and pANCA⁽³⁾. Two fatalities have been reported in patients taking minocycline for acne, one from severe hepatitis and the other from pancytopenia⁽⁴⁾.

Minocycline is understandably a popular treatment for acne as compliance is likely to be better with a once- or twice-daily regimen. By reporting these cases we hope to raise awareness of this type of drug-induced lupus syndrome

associated with minocycline. A high index of suspicion of this condition should exist if patients receiving minocycline develop arthralgia or arthritis.

In view of the severity of these potential side effects the use of minocycline for acne should be considered carefully, and other safer and less expensive drugs may be more appropriate.

REFERENCES

- 1 Gough A, Chapman S, Wagstaff K, Emery P, Elias E Minocycline-induced autoimmune hepatitis and systemic lupus erythematosus-like syndrome. *Br Med J* 1996;312:169-72
- 2 Byrne PAC, Williams BD, Pritchard MH Minocycline-related lupus. *Br J Rheumatol* 1994;33:674-76
- 3 Elkayam O, Yaron M, Capsi D Minocycline-induced arthritis associated with fever, livedo reticularis and pANCA. *Ann Rheum Dis* 1996;55:769-71
- 4 Davies MG, Kersey PJW Acute hepatitis and exfoliative dermatitis associated with minocycline. *Br Med J* 1989;298:1523-24

Forthcoming Publication

The Minutes of Lancaster Medical Book Club

Edited by G H Anderson

As mentioned in the January 1997 edition of the journal, the Lancaster Medical Book Club is in the process of publishing a book containing a record of its history and minutes, along with biographical details of some of its early members and other items of historical interest and association with the club. In addition there is information regarding the activities of the club once it became more of a social society in the 1960s with the introduction of formal postgraduate medical education.

Dr Graham Anderson has spent many hours compiling this work and the document is currently back in the hands of the publisher for a second draft. It is hoped that during the course of the summer the book will be ready for distribution. This has been a 'novel' experience for the club and not inexpensive. There have been several benefactors, but ultimately the financial balance will be helped by purchases from members at a price of about £10 per hard back copy (plus p&p). It is hoped that there will be widespread interest in, and uptake of, this publication.