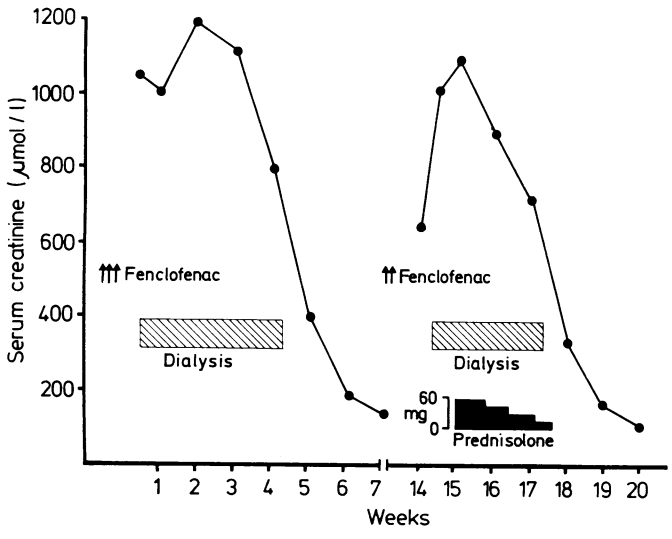
and the patient returned to Britain 10 days later in established acute renal failure. Open renal biopsy was performed as the patient had bilateral unilocular renal cysts which had been diagnosed previously. Histological examination showed normal glomeruli, interstitial oedema, and a mononuclear cell infiltrate with tubular necrosis and evidence of subsequent regeneration. Electron microscopy of three glomeruli showed diffuse foot process fusion. Diagnosis was of a tubulointerstitial nephritis. Subsequent questioning did not elicit any further drug exposure, and the patient began intermittent peritoneal dialysis. There was spontaneous recovery of renal function 21 days later, and at discharge the plasma creatinine concentration was 141 μmol/l (1·6 mg/100 ml).

Four months later the patient was readmitted in acute oliguric renal failure. Six days previously he had ingested six tablets of fenclofenac over 36 hours for vague shoulder pain. The drug had been prescribed many months before. Three days before admission he had felt feverish and noted a rash, decreasing urinary volume, and ankle swelling. On direct questioning he admitted taking several fenclofenac tablets before the first episode of acute renal failure. Examination showed evidence of fluid retention and a vasculitic rash on the lower legs. Plasma creatinine concentration was 1167 μmol/l (13·2 mg/100 ml) and an absolute eosinophil count $1{\cdot}2 \times 10^9$/l. A 24 hour collection of urine measured 460 ml and contained 21·6 g protein/litre. Renal biopsy showed severe tubulointerstitial nephritis with a dense infiltrate of lymphocytes, plasma cells, and eosinophils and with extensive tubular necrosis. Skin biopsy disclosed perivascular infiltration with mononuclear cells consistent with vasculitis. The patient began intermittent peritoneal dialysis and prednisolone 60 mg daily (fig). Renal function returned to normal after 22 days.

Comment

Allergic interstitial nephritis is a well described, though infrequent, complication of treatment with many non-steroidal anti-inflammatory drugs. In many instances the association is based on few anecdotes and mnay of the patients were receiving multiple drug regimens.[3] The description of allergic interstitial nephritis with the nephrotic syndrome and glomerular foot process fusion as a complication of propionic acid derivatives, notably fenoprofen, seems to be a specific entity.[4 5] The histological picture in our patient was remarkably similar, and the occurrence of an identical syndrome on inadvertent rechallenge provides convincing evidence that fenclofenac was indeed implicated. It is also of interest that steroid treatment did not appear to hasten resolution (fig), though the clinical picture of eosinophilia and vasculitic rash seemed to suggest a role for steroids.



Changes in plasma creatinine concentration in relation to fenclofenac ingestion, dialysis, and treatment with corticosteroids.

Conversion: SI to traditional units—Creatinine: 1 μmol/l ≈ 0·01 mg/100 ml.

MJR is supported by a grant from the Wellcome Trust.

1 Wendland ML, Wagoner RD, Hollay KE. Renal failure associated with fenoprofen. *Mayo Clin Proc* 1980;**55**:103-7.
2 Kimberley RP, Bowden RE, Keiser HR, Plotz PH. Reduction of renal function by new non-steroidal anti-inflammatory drugs. *Am J Med* 1978;**64**:804-7.
3 Ooi BS, Jao W, Feist MR, Mancilla R, Pollack VE. Acute interstitial nephritis. A clinical and pathologic study based on renal biopsies. *Am J Med* 1975;**59**:614-29.
4 Brezin JH, Katz SM, Schwartz AB, Chinitz JL. Reversible renal failure and nephrotic syndrome associated with non-steroidal anti-inflammatory drugs. *N Engl J Med* 1979;**301**:1271-3.
5 Finkelstein A, Fraley DS, Stachura I, Feldman HA, Gandy DR, Bourke E. Fenoprofen nephropathy: lipoid nephrosis and interstitial nephritis, a possible T-lymphocyte disorder. *Am J Med* 1982;**72**:81-7.

(*Accepted 8 January 1985*)

Department of Nephrology and Transplantation, The Royal Free Hospital, London NW3 2QG

M J RAFTERY, MRCP, Wellcome research fellow
P FORMAN, MRCP, senior house officer
K FARRINGTON, MD, MRCP, senior registrar
P SWENY, MD, MRCP, senior lecturer
J F MOORHEAD, FRCP, director and consultant physician

Correspondence to: Dr M J Raftery.

Acute disseminated encephalomyelitis as a complication of treatment with gold

Toxic reactions to chrysotherapy are well known. Neurological complications, however, are less well recognised. We describe a case of acute disseminated encephalomyelitis associated with treatment with gold.

Case report

A 39 year old woman presented with typical features of rheumatoid arthritis. She was initially treated with adrenocorticotrophic hormone and later penicillamine, which was withdrawn when she developed mouth ulcers. Five weeks before admission to hospital she suffered an exacerbation, which was not controlled by anti-inflammatory drugs. Injections of gold were started with a test dose of 5 mg intramuscularly, followed by doses of 10 mg, 20 mg, 50 mg, and 50 mg at weekly intervals. Six hours after each injection she developed backache, wheezing, and an erythematous rash on the back of her hands, which persisted until the following day. One week after the last injection she woke with diplopia, dysarthria, and unsteadiness of gait. She had no personal or family history of allergy. On admission she was taking azapropazone 600 mg twice daily and mianserin 10 mg at night.

On examination she showed an inappropriate affect, labile emotions, and a poor memory. She was dysarthric. Her fundi were normal. She had internuclear ophthalmoplegia but no nystagmus. She showed generally reduced tone, with pyramidal weakness in her right arm. Cerebellar signs were present in both arms and legs, and she had truncal ataxia. Reflexes were brisk and symmetrical, with extensor plantars bilaterally. Sensation was normal. The spleen was palpable 2 cm below the costal margin. There was no evidence of active arthritis or a rash. Haemoglobin concentration was 10·9 g/dl; white cell count $6{\cdot}6 \times 10^9$/l, eosinophils 50%; erythrocyte sedimentation rate 24 mm in the first hour; and autoantibody, Venereal Disease Research Laboratory, and *Treponema pallidum* haemagglutination tests and blood cultures all negative. Immunoglobulin concentrations were normal. Cerebrospinal fluid contained 0·84 g protein/l with no pleocytosis and a normal ratio of IgG to albumin concentrations. Radiographs of the chest, skull, and cervical spine were normal. Radiographs of the hands were compatible with rheumatoid arthritis. Electroencephalography showed generalised abnormality suggesting encephalitis. Visual evoked responses showed bilateral delay. A computed tomogram of the head was normal.

Acute disseminated encephalomyelitis secondary to treatment with gold was diagnosed provisionally. She was treated with oral prednisolone 45 mg daily and physiotherapy. Her mental state and cerebellar signs improved, as did the pyramidal weakness in her right arm. Her eosinophilia resolved. She was discharged taking a decreasing dose of steroids. Eighteen weeks after discharge she was still dysarthric with an ataxic gait and bilateral extensor plantar response, but electroencephalography showed substantial improvement as did her visual evoked responses.

Comment

We presumed that this was a case of gold toxicity and not the first presentation of multiple sclerosis because of the interval between the onset of treatment with gold and presentation (five weeks), the eosinophilia, and the normal ratio of IgG to albumin concentrations in the cerebrospinal fluid. The only reported neurological complication of treatment with mianserin is drowsiness; none has been reported for azapropazone.

Adverse reactions develop in roughly one third of patients treated with gold, the proportion varying from 5% to 80% in several reported series.[1] Eosinophilia occurs in roughly 5% of patients and has been directly correlated with the development of gold toxicity.[2] Vasomotor reactions to gold are not uncommon, but whether they indicate the development of more serious gold toxicity is unknown. Neurological complications, including peripheral neuropathy, myokymia, and a syndrome like the Guillain-Barré syndrome,[3] have received little attention even in major textbooks of rheumatology.[4] Encephalopathy has been reported: McAuley *et al* described a patient who recovered fully one month after treatment with gold was stopped.[5]

The severity of the illness in our patient, with residual neurological deficit nearly five months afterwards, shows the serious side effects that may occur during chrysotherapy.

1 Freyburg RH, Ziff M, Baum J. Gold therapy for rheumatoid arthritis. In: Hollander JL, McCarty DJ, eds. *Arthritis and allied conditions*. 8th ed. Philadelphia: Lea and Febiger, 1972:455-82.
2 Davis P, Hughes GRV. The significance of eosinophilia during gold treatment. *Arthritis Rheum* 1974;**17**:964-8.
3 Schlumpf U, Meyer M, Ulrich J, Friede RL. Neurological complications induced by gold treatment. *Arthritis Rheum* 1983;**26**:825-31.
4 Copeman WSC. In: Scott JT, ed. *Copeman's textbook of the rheumatic diseases*. Edinburgh: Churchill Livingstone, 1978.
5 McAuley DLF, Lecky BRF, Earl CJ. Gold encephalopathy. *J Neurol Neurosurg Psychiatry* 1977;**40**:1021-2.

(*Accepted 10 January 1985*)

Heath Road Wing, Ipswich Hospital, Ipswich, Suffolk IP4 5PD
M COHEN, BSC, MRCP, medical registrar
C P DAY, MA, MB, house physician
J L DAY, MD, FRCP, consultant physician

Correspondence to: Dr M Cohen, Royal Alexandra Hospital for Sick Children, Brighton BN1 3JN.

Nephrotic syndrome during treatment with interferon

Interferon has activity against multiple myeloma.[1] In a trial of lymphoblastoid interferon A (Wellferon) given by ambulatory intravenous infusion for myeloma a patient with renal damage developed a nephrotic syndrome.

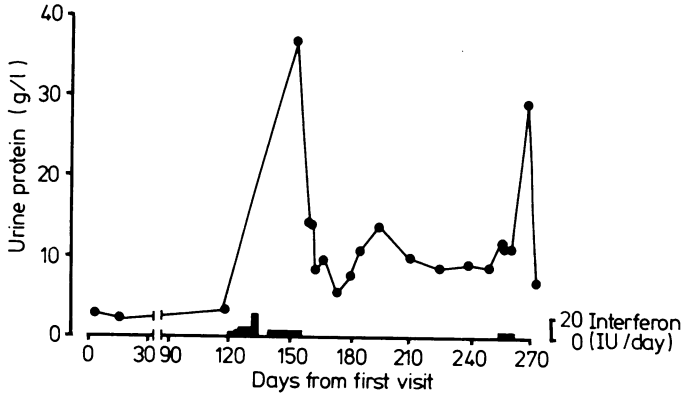
Case report

A 42 year old white woman presented with an IgGL myeloma in February 1980. Serum urea and creatinine concentrations were normal, but her urine contained Bence Jones protein. She received oral melphalan, but the condition did not improve.

She was referred to us in June 1983 suffering from back pain. She was kyphotic. Investigations showed extensive lytic bone disease and heavy infiltration of bone marrow with myeloma cells. Serum urea and creatinine concentrations were normal, and her creatinine clearance was 82 ml/min. The serum contained 45 g IgGL paraprotein/l. Urine contained 6 g protein/l with a trace of Bence Jones protein and a prominent leak of paraprotein. There was severe immune suppression, with a serum IgA concentration of $< 0{\cdot}1$ g/l. Intravenous cyclophosphamide produced transient benefit, but the disease progressed and in November she was admitted for a trial of interferon given by continuous intravenous infusion.

The figure shows the interferon dosage and urinary protein excretion. The urine volume was consistently about two litres daily. The maximum urinary protein concentration, 34 days after the start of interferon, was 37 g/l, with non-selective proteinuria including 14 g albumin/l, 11 g paraprotein/l, and 2 g lambda light chain/l. The electrophoretic patterns of serum and urinary protein were almost identical, indicating an almost complete leak. Her glomerular filtration rate was 44 ml/min. Her serum albumin concentration fell to 17 g/l and she developed bilateral ankle oedema. The serum creatinine concentration remained unchanged. Ultrasonography of the kidneys yielded normal results. There were no autoantibodies. Concentrations of C3 and C4 were slightly reduced, possibly owing to loss of protein in the urine. Tests for immune complexes (C1q binding and the platelet aggregation test) yielded negative results.

Interferon was stopped and the urinary protein concentration fell rapidly. Serum myeloma protein concentration had fallen during treatment, and this led us to try a further course of interferon three months later (figure). Her proteinuria immediately deteriorated but again fell rapidly when interferon was withdrawn. On this occasion the serum creatinine concentration rose from 138 μmol/l (1·6 mg/100 ml) before treatment to 181 μmol/l (2·0 mg/100 ml) during treatment and returned to 140 μmol/l (1·6 mg/100 ml) after interferon had been withdrawn.



Dosage of interferon given and urinary protein excretion.

Comment

In this case a nephrotic syndrome developed during treatment with interferon in a patient whose kidneys had been damaged by myeloma. The abnormality decreased when interferon was withdrawn but recurred when interferon was reintroduced. Although the nephrosis was rapidly reversed once interferon was stopped, evidence of renal damage remained.

Averbuch *et al* described a case in which intermittent intramuscular recombinant leucocyte interferon A produced both a nephrotic syndrome and renal failure in a patient with mycosis fungoides.[2] A renal biopsy specimen showed acute interstitial nephritis. Sherwin *et al* did not detect any evidence of a nephrotic syndrome in patients treated with leucocyte interferon A.[3] Kramer *et al* described three cases in which interferon was given as an antiviral agent after renal transplantation.[4]

We suggest that careful observation of all patients who are treated with interferon is necessary to avoid renal failure. Our observations suggest that the development of proteinuria, or an increase in its severity, may be the first indication of this complication and that regular testing for urinary protein is essential during treatment with interferon.

1 Mellstedt H, Ahre A, Bjorkholm M, *et al*. Human leucocyte interferon in the treatment of multiple myeloma. In: Maeyer E, Schellekens E, eds. *Biology of the interferon system*. Amsterdam: Elsevier, 1983:519-25.
2 Averbuch SD, Austin HA, Sherwin SA, Antonovynch T, Bunn PA, Longo DL. Acute interstitial nephritis with the nephrotic syndrome following recombinant leukocyte interferon therapy for mycosis fungoides. *N Engl J Med* 1984;**310**:32-5.
3 Sherwin SA, Knost JA, Fein S, *et al*. A multiple-dose phase I trial of recombinant leukocyte A interferon in cancer patients. *JAMA* 1982;**248**:2461-6.
4 Kramer P, Ten Kate FWJ, Bijnen AB, Jeekel J, Weimar W. Recombinant leucocyte interferon A induces steroid-resistant acute vascular rejection episodes in renal transplant recipients. *Lancet* 1984;i:989-90.

(*Accepted 28 January 1985*)

Royal Marsden Hospital, Sutton, Surrey SM2 5PT
P SELBY, MD, MRCP, lecturer in medicine
J KOHN, FRCPATH, professor of clinical pathology
J RAYMOND, BSC, scientific officer, department of clinical pathology
I JUDSON, MRCP, clinical fellow, department of medicine
T McELWAIN, FRCP, professor of medicine

Correspondence to: Dr P Selby.