sensitivity (for example, skin eruption), but eosinophil counts were not available. He died about 72 hours later. No other cytotoxic agents had been administered.

Necropsy disclosed no thrombi in major vessels but showed recent hepatic infarcts, and thrombi were seen in portal and hepatic vein branches on microscopy (figure). Metastases were present in the heart, lung, pancreas, and kidneys.

Recently formed thrombus (T) in hepatic vein branch (V). Haematoxylin and eosin $\times 180$ (original magnification).

Discussion

Transient abnormalities of liver function tests are recognised side effects of dacarbazine treatment.¹ To our knowledge acute liver failure due to vascular occlusion in patients receiving single-agent chemotherapy with dacarbazine has been reported in only one case.² Our patients showed broadly similar clinical, laboratory, and histological features. The temporal relation to

dacarbazine treatment, the absence of any other identifiable cause, and the histological dissimilarity to the rare hepatic lesions attributed to chlorpromazine and amitriptyline incriminate dacarbazine. A synergistic adverse drug reaction cannot, however, be excluded. The eosinophilia in case 1, which suggests a drug reaction, was transient and preceded clinical deterioration. Eosinophil counts during each course of treatment may therefore be valuable in the early detection of liver damage.

One of us (PJS) reviewed the histology of a further patient receiving dacarbazine in whom hepatic vein thrombosis had led to the Budd-Chiari syndrome. We are also aware of five other deaths after hepatic vascular occlusions in patients receiving dacarbazine as part of multiple-agent chemotherapy^{3,4} (J S Goodall, Miles Laboratories, personal communication). We suggest that this complication of dacarbazine treatment may not be as rare as was previously thought.² In view of this greater caution may be needed when considering the use of dacarbazine, especially as an adjuvant agent in stage I and II disease.

We thank Dr J D Everall for permission to publish the clinical details; Dr A Levene for access to postmortem material in case 1; the Ministry of Defence for permission to publish the details of case 2; and the late Dr J S Goodall of Miles Laboratories for his help.

References

- Johnson RO, Metter G, Wilson W, Hill G, Krementz E. Phase I evaluation of DTIC (NSC45388) and other studies in malignant melanoma in the central oncology group. *Cancer Treat Rep* 1976;**60**:183-7.
- Asbury RF, Rosenthal SN, Descalzi ME, *et al*. Hepatic veno-occlusive disease due to DTIC. *Cancer* 1980;**45**:2670-4.
- Lehrner LM, Enck RE. Hepatic vein thrombosis after chemotherapy for histiocytoma. *Ann Intern Med* 1978;**88**(4):575-6.
- Hoghton AN, Shafi N, Rickles FR. Acute hepatic vein thrombosis occurring during therapy for Hodgkin's disease. *Cancer* 1979;**44**:2324-9.

(Accepted 18 March 1981)

Retinal vasculitis in rheumatoid arthritis

M F R MARTIN, D G I SCOTT, C GILBERT, P A DIEPPE, D L EASTY

Abstract

A woman with exacerbation of severe rheumatoid arthritis developed lesions compatible with retinal vasculitis. Laboratory studies confirmed the diagnosis, and the rapid clinical improvement that accompanied a fall in circulating immune complexes suggested that the vasculitis was a direct consequence of the rheumatoid disease.

From these observations retinal vasculitis should probably be sought in any patient with rheumatoid disease

and the vasculitis added to the list of ocular complications of rheumatoid arthritis.

Introduction

We report a case of severe rheumatoid arthritis with high concentrations of circulating immune complexes, nailfold vasculitis, and transient lesions consistent with retinal vasculitis.

Case history

A 51-year-old white woman with a history of pulmonary tuberculosis developed rheumatoid arthritis in 1965; this was complicated by recurrent scleritis (1971, 1976), keratoconjunctivitis sicca (1976), sensory peripheral neuropathy (1971), and rheumatoid nodules. She presented in September 1979 with an exacerbation of the rheumatoid arthritis while taking penicillamine 500 mg and prednisolone 5 mg daily. She reported increased joint pain and stiffness, night sweats, weight loss, and diminished visual acuity. Examination showed active

Bristol Royal Infirmary, Bristol BS2 8HW

M F R MARTIN, MRCP, senior registrar

D G I SCOTT, MRCP, medical registrar

P A DIEPPE, MRCP, consultant rheumatologist

Bristol Eye Hospital, Bristol BS1 2LX

C GILBERT, FRCS, senior registrar

D L EASTY, FRCS, consultant ophthalmologist

synovitis, lymphadenopathy, nodules, a sensory neuropathy, scleritis, and extensive nailfold vasculitis.

Ophthalmological examination including rose bengal staining confirmed sicca syndrome, and bilateral active scleritis with scleral thinning was also noted. Also the right retina showed a background pigmentary disturbance and several large fresh soft white exudates randomly distributed over the posterior pole. No retinal changes were seen in the left eye. Her right visual acuity was 6/18. At an ophthalmic examination six months earlier both retinæ were normal and the right visual acuity 6/9.

Investigations showed haemoglobin concentration 14.5 g/dl, viscosity 2.23 mPa s (2.23 cP), rheumatoid factor titre 1/2560, and antinuclear factor titre 1/40. C₃ and C₄ values were normal, though there was evidence of high concentrations of circulating immune complexes: anticomplementary activity 1/32 (normal 1/2). C1q binding was 65% (normal 20%), platelet aggregation 1/512 (normal 1/16), and cryoglobulins positive. Chest radiography showed extensive old tuberculosis but results of sputum culture and microscopy were negative.

The patient was treated with bed rest, non-steroidal anti-inflammatory drugs, local hypromellose and cortisone eye drops. After two months there was a noticeable improvement, and by six months the retinal changes had disappeared and visual acuity had improved. Her systemic rheumatoid disease also became less active, she gained weight, and tests for circulating immune complexes became negative.

Discussion

Retinal vasculitis may complicate many systemic diseases,¹ including tuberculosis, sarcoidosis, Behçet's syndrome, and systemic lupus erythematosus. In a recent review² of 17 patients

with retinal vasculitis, immune complexes were found in the sera of 13 and rheumatoid factor was present in four.

Vasculitis complicating rheumatoid arthritis^{3,4} usually occurs in nodular disease, with high titres of classical IgM rheumatoid factor and raised concentrations of circulating immune complexes. Infarcts in nailfold capillaries are often seen and weight loss and general malaise are common. Our patient had all these features, including circulating immune complexes detected by four different assays. The timing of the retinal disease and the observed rapid clinical improvement that accompanied the fall in concentrations of circulating immune complexes suggest that the retinal changes were a direct consequence of her active rheumatoid disease.

We suggest that the retina should be examined for evidence of vasculitis in rheumatoid disease, and that vasculitis should be added to the list of ocular complications of rheumatoid arthritis.

References

- 1 Saunders MD. Retinal vasculitis: a review. *J R Soc Med* 1979;72:908-15.
- 2 Andrews BS, McIntosh J, Petts V, Penny R. Circulating immune complexes in retinal vasculitis. *Clin Exp Immunol* 1977;29:23-9.
- 3 Fauci AS, Haynes BF, Katz P. The spectrum of vasculitis. *Ann Intern Med* 1978;89:660-76.
- 4 Scott DGI, Tribe CR, Bacon PA. Systemic rheumatoid vasculitis: clinical and laboratory studies in 50 patients. *Medicine (Baltimore)* (in press).
- 5 Murray McGavin DD. Episcleritis and scleritis. In: Buchanan WW, Dick WC, eds. *Recent advances in rheumatology*. Vol 1. Part II. London: Churchill Livingstone, 1976:166-92.

(Accepted 14 April 1981)

Haloperidol secreted in breast milk

L J WHALLEY, P G BLAIN, J K PRIME

Abstract

A nursing mother was given haloperidol 5 mg twice daily for puerperal psychosis and continued to breast feed under hospital supervision. Despite considerable amounts of haloperidol being secreted in the breast milk (up to 23.5 µg/l), the infant was apparently not sedated, fed well, and continued to thrive.

The findings suggest that maternal ingestion of haloperidol for short periods has no deleterious effect on the infant's development.

Introduction

Mania occurring in the puerperium, though rare, can present important problems of management, particularly when the mother continues to breast feed. We report a case of puerperal psychosis treated with haloperidol in which substantial amounts of the drug were secreted in breast milk and ingested by the infant. There was no evidence, however, of any long-term effect on the infant's development.

MRC Brain Metabolism Unit, Thomas Clouston Clinic, Edinburgh EH10 5LG

L J WHALLEY, MD, MRCPsych, honorary consultant psychiatrist

Wolfson Unit of Clinical Pharmacology, Newcastle upon Tyne

P G BLAIN, MRCP, Wellcome research fellow

GP Practice, 38 Palmerston Place, Edinburgh EH12 5BJ

J K PRIME, RGN, SCM, health visitor

Case report

A mother delivered a live girl weighing 2660 g at 39 week's gestation after induction of labour with an intravenous infusion of oxytocin. Apgar scores were 9 at one and five minutes. Pregnancy had been uneventful and there was no history of psychiatric illness. The immediate postnatal period progressed normally; breast feeding was established and mother and child were well. On the 16th day the mother was found by the health visitor to be tense, anxious, and talking continuously. The general practitioner diagnosed puerperal psychosis and prescribed chlorpromazine 25 mg four times daily. There was no improvement, and on the 20th day mother and baby were admitted to hospital. The baby was progressing well and breast feeding was continued under supervision. The mother was deluded, euphoric, and overactive. Puerperal hypomania was diagnosed and treatment begun with oral haloperidol 5 mg twice daily.

Samples of the mother's plasma and breast milk and the baby's urine were collected on the first, sixth, seventh, and 21st days of treatment. Only one of the urine samples was suitable for assay. The concentration of haloperidol in these samples was measured by radioimmunoassay (sensitivity 0.5 µg/l). The table gives the results.

Four weeks after the birth mother was improving, though still very tense and anxious. The baby did not appear to be sedated and was feeding well. Haloperidol was stopped in the sixth week after birth and

Concentrations of haloperidol in mother's plasma and breast milk and in baby's urine (µg/l)

Day	Dose	Mother's plasma	Mother's milk	Baby's urine
1	None	0	0	0
6	5 mg twice daily	40	23.5	—
7	5 mg twice daily	26	18.0	—
21	None	4	3.25	1.5