Hepatic vascular lesions associated with dacarbazine treatment

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Abstract

Dacarbazine is widely used in the treatment of melanoma. Transient abnormalities of liver function tests are well-recognised side effects of the drug, but acute liver failure due to vascular occlusion in patients receiving single-agent chemotherapy with dacarbazine has been noted only rarely. Two cases are reported in which hepatic vascular lesions developed during treatment with dacarbazine and were confirmed at necropsy.

Hepatic vascular occlusion due to treatment with dacarbazine may be less rare than was previously thought. Greater caution may be needed when dacarbazine is prescribed, particularly as an adjuvant agent in stage I and II disease.

Introduction

Dacarbazine (dimethyl-triazeno-imidazole-carboxamide) has been widely used in the treatment of stage III melanoma and in trials of adjuvant chemotherapy in patients with stage I and II disease with a poor prognosis. We report two cases in which hepatic vascular lesions occurred during dacarbazine treatment.

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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). Haematotoxylin and eosin × 180 (original magnification).

Discussion

Transient abnormalities of liver function tests are recognised side effects of dacarbazine treatment. 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. 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 amitryptiline incriminate dacarbazine. A synergistic adverse drug reaction cannot, however, be excluded. The eosinophilia in case 1, which suggested 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 (J S Goodall, Miles Laboratories, personal communication). We suggest that this complication of dacarbazine treatment may not be as rare as was previously thought. 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.

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References


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Retinal vasculitis in rheumatoid arthritis

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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