

## Case report

# Hepatocellular disease in the giant-cell arteritis/ polymyalgia rheumatica syndrome

ANTHONY S-Y. LEONG<sup>1</sup> AND MICHAEL H. ALP<sup>2</sup>

From the <sup>1</sup>Department of Histopathology and the <sup>2</sup>Gastroenterology Unit, Queen Elizabeth Hospital, Woodville, South Australia 5011, Australia

**SUMMARY** An elderly man developed temporal arteritis and polymyalgia rheumatica with co-existing biochemical abnormalities of liver function. Biopsy revealed hepatic changes which have not been previously reported. There was hepatocellular necrosis and inflammation together with a prominent hyperplasia of perisinusoidal lipocytes of Ito. Temporal artery biopsy confirmed the presence of granulomatous panarteritis. Corticosteroid therapy produced rapid resolution of symptoms and reversion of liver function tests to normal.

The association of giant cell (temporal) arteritis with polymyalgia rheumatica is well recognised.<sup>1</sup> Most workers now accept polymyalgia rheumatica as a clinical manifestation of giant cell arteritis,<sup>2,3</sup> and temporal arteritis has also been observed following treatment of polymyalgia rheumatica.<sup>4</sup>

Little is known about the systemic effects of giant cell arteritis. Lesions of the myocardium, kidneys, gastrointestinal tract, and nervous system have been attributed to underlying arteritis.<sup>5</sup> Changes in liver function tests have frequently been documented. These changes have been variable, with elevation of alkaline phosphatase being the most frequent abnormality.<sup>6,7</sup> The histology of liver biopsies from these patients has mainly been normal.<sup>2</sup> In some instances nonspecific fatty change was found,<sup>8</sup> and single granulomas were described in 2 cases.<sup>7,9</sup> We report a case of giant cell arteritis with hepatocellular necrosis and hyperplasia of perisinusoidal lipocytes of Ito, histological changes which hitherto have not been described in this syndrome.

### Case report

A 64-year-old man presented with a 3-month history of right-sided intermittent facial pain. His headache and facial pain became continuous and were asso-

ciated with night sweats, fever, weight loss, and anorexia. He gave no significant family history and had not been in contact with hepatitis. There was no history of excessive consumption of alcohol, vitamin A, or other drugs.

On examination he showed significant weight loss. The liver was palpable at 3 cm below the costal margin and was not tender. The spleen was not palpable and there was no lymphadenopathy. The temporal arteries were slightly thickened but not tender. Neurological and fundal examinations were normal.

The white cell count was  $13.9 \times 10^9/l$ , with a neutrophil leucocytosis. Erythrocyte sedimentation rate was 85 mm/h, blood urea 11 mmol/l, and there was mild hypoalbuminaemia without hypogammaglobulinaemia. Liver function tests showed a total bilirubin of 5  $\mu\text{mol/l}$ , aspartic transaminase 229 U/l, alkaline phosphatase 631 U/l. Screening for hepatitis B antigen and antibody was negative. Tests for antimitochondrial, antismooth muscle, and antinuclear factor antibodies were negative. Blood cultures grew no organisms, and brain scan, liver scan, and CAT scan of the abdomen were normal.

After admission to hospital he continued to have a high swinging fever. The liver function tests continued to show a persistent elevation of alkaline phosphatase but the aspartic transaminase level returned to normal. Viral and rickettsial agglutinins were not found. Loss of weight continued, and he developed generalised muscle aches and pains

Accepted for publication 7 January 1980  
Correspondence to Dr Anthony S-Y. Leong, Histopathology Department, Queen Elizabeth Hospital, Woodville, Adelaide, SA 5011, Australia.

involving mainly the shoulder girdle and to a less extent the thighs. There was no clinical evidence of arthritis. A liver biopsy was performed, and despite the absence of tenderness a segment of right temporal artery was removed for histological examination.

The temporal artery showed the classical changes of giant cell arteritis. There was a panarteritis with granulomatous inflammation of the media spilling over into the adventitia. Lymphocytes plasma cells, epithelioid histiocytes, and multinucleated giant cells were most prominent adjacent to a split internal elastic lamina, which displayed foci of dissolution. Phagocytosed fragments of elastica were seen in giant cells, and there was associated proliferation of the intima.

The liver biopsy was characterised by a spotty necrosis and inflammation which was most marked round portal tracts and central veins (Figs. 1 and 2). Scattered foci of hepatocyte dropout were also evident in the lobules. Mononuclear cells and

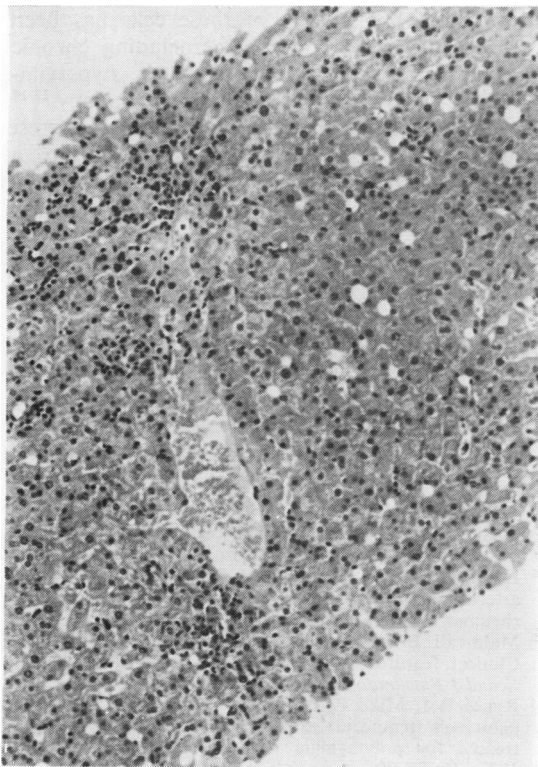


Fig. 1 Foci of hepatocyte drop-out with associated inflammatory cells are seen round a dilated central vein as well as within the lobules. Scattered perisinusoidal lipocytes are visible. (H & E,  $\times 125$ ).

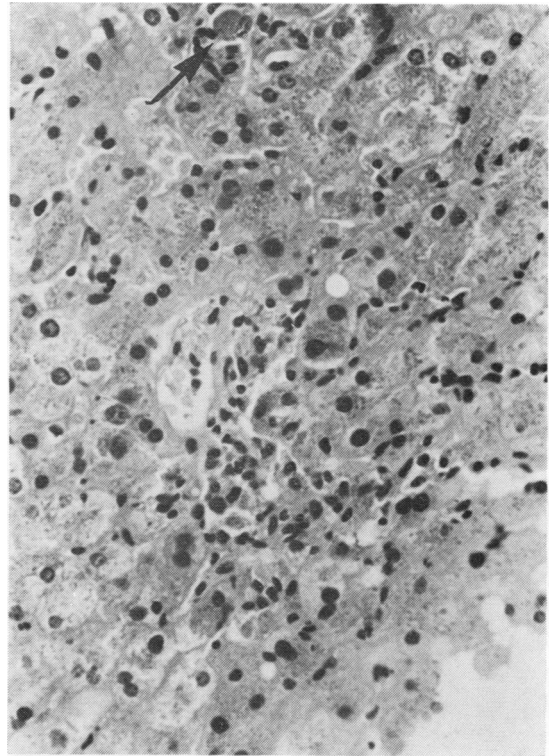


Fig. 2 Centrilobular foci of hepatocyte necrosis with an acidophilic body (arrow). Note the prominent cytoplasmic lipofuscin pigment in the liver cells. (H & E,  $\times 310$ ).

occasional polymorphs were present in these areas, and occasional acidophilic bodies were evident. There was mild disarray of hepatic cords, and hepatocytes were filled with lipofuscin pigment. Increased numbers of perisinusoidal lipid-filled Ito cells were present (Fig. 3). There was no significant fibrosis in the biopsy, and the orcein stain for hepatitis B surface antigen was negative. No granulomas were present, and all vessels in the biopsy were normal.

The patient was put on steroid therapy. There was excellent response to treatment, with cessation of symptoms and reversion of liver function tests to normal. He is at present maintained on prednisolone 7.5 mg and day and is symptom-free.

#### Discussion

Clinical manifestations of hepatic involvement in giant cell arteritis are well recognised but uncommon.<sup>10</sup> Hyperbilirubinaemia has not been an associated abnormality, and biochemical abnormalities

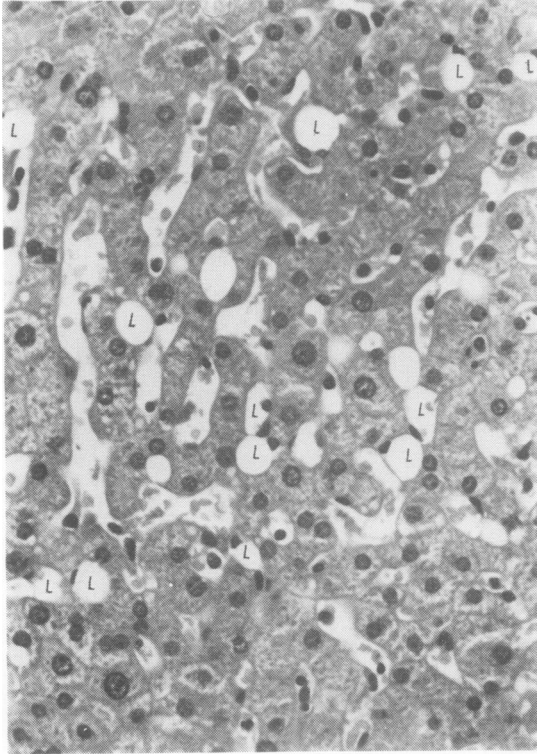


Fig. 3 Prominent hyperplasia of perisinusoidal lipocytes (L). (H & E,  $\times 310$ ).

of hepatic enzymes have been variable. Serum aspartate transaminase (SGOT) levels may be normal<sup>6</sup> or slightly elevated.<sup>7,9</sup> Serum alkaline phosphatase of liver origin appears to be the most consistently elevated enzyme, occurring in 62% of a series of 37 patients.<sup>6</sup> Hepatitis B surface antigen has not been found in association with this disease, nor has there been an association with any of the serological HLA antigens.<sup>5</sup> In all reported studies resolution of abnormal hepatic biochemical parameters was complete after adequate treatment with corticosteroids.

The histological changes observed in the liver of patients with giant cell arteritis are variable. Most reports have described the liver as normal or as showing nonspecific changes, and 2 recent papers have reported a single small granuloma in each of their patients.<sup>6,9</sup> von Knorring and Wasastjerna<sup>6</sup> described 2 patients with polymyalgia rheumatica in whom smears of liver aspirates stained for amino acid naphthylamidase activity revealed irregularly dilated bile canaliculi with increased enzyme activity. With corticosteroid therapy these changes reverted

to normal, and their significance remained obscure.

The present case represents one of the few reports in which necrosis of hepatocytes with accompanying portal and lobular inflammation has been observed. Immune complex deposition has been demonstrated in giant cell arteritis,<sup>11</sup> and it has been postulated that patchy deposition of circulating immune complexes in branches of the hepatic artery may be responsible for the liver abnormalities.<sup>7</sup> A careful search in our patient revealed no evidence of vascular inflammation in the liver biopsy. Furthermore, hepatic arteritis, such as that occurring in lupus erythematosus and polyarteritis nodosa, produces small infarcts and not foci of hepatocellular dropout. Bacon *et al.*<sup>12</sup> have reported a high incidence of hepatitis B antibodies in patients with polymyalgia rheumatica. They suggested that the vasculitis in polymyalgia rheumatica could be due to the deposition of immune complexes in which hepatitis B antibodies might be an important component. In our patient both hepatitis B antigen and antibody titres were consistently negative.

The presence of hyperplasia of fat cells of Ito is intriguing. Hyperplasia of these cells has been observed in several conditions, including chronic hepatitis, extrahepatic biliary cirrhosis, hypervitaminosis A, and with various types of drug therapy.<sup>13,14</sup> These cells have stimulated considerable interest since Hruban *et al.*<sup>13</sup> suggested that they may have a role as fibroblast precursors, possibly related to the fibrosis and cirrhosis which may develop in hypervitaminosis A.

The histogenesis of the hepatic changes which occur in giant cell arteritis/polymyalgia rheumatica syndrome remains obscure. It is clear that abnormal liver function tests can occur as part of the diffuse character of this disorder and both histological, and biochemical aberrations appear to return to normal with adequate treatment.

#### References

- 1 Barber A S. Myalgia with constitutional effects: Polymyalgia Rheumatica. *Ann Rheum Dis* 1957; 16: 230-4.
- 2 Hamilton C R Jr, Shelley W M, Tumulty P A. Giant cell arteritis: Including temporal arteritis and polymyalgia rheumatica. *Medicine* 1971; 50: 1-27.
- 3 Malmvall B E, Bengtsson B A. Giant cell arteritis. Clinical features and involvement of different organs. *Scand J Rheumatol* 1978; 7: 154-8.
- 4 Rynes R I, Mika P, Bartholomew M. Development of giant cell (temporal) arteritis in a patient 'adequately' treated for polymyalgia rheumatica. *Ann Rheum Dis* 1977; 36: 88-90.
- 5 Healey L A, Wilske K R. Manifestations of giant cell arteritis. *Med Clin North Am* 1977; 61: 261-70.
- 6 von Knorring J, Wasastjerna C. Liver involvement in polymyalgia rheumatica. *Scand J Rheumatol* 1976; 5: 179-204.

- <sup>7</sup> McCormack L R, Astarita R W, Foroozan P. Liver involvement in giant cell arteritis. *Digestive Dis* 1978; **23**: 72s-4s.
- <sup>8</sup> Dickson E R, Maldonado J E, Sheps S G, Cain J A. Systemic temporal arteritis and polymyalgia rheumatica. Reversible abnormalities of liver function. *JAMA* 1973; **224**: 1496-8.
- <sup>9</sup> Long R, James O. Polymyalgia rheumatica and liver disease. *Lancet* 1974; **i**: 77-9.
- <sup>10</sup> Russell R W R. Giant cell arteritis: A review of 36 cases. *Q J Med* 1959; **28**: 471-7.
- <sup>11</sup> Liang G C, Simkin P A, Mannik M. Immunoglobulins in temporal arteries: An immunofluorescence study. *Ann Intern Med* 1974; **81**: 19-24.
- <sup>12</sup> Bacon P A, Doherty S M, Zuckerman A J. Hepatitis B antibody in polymyalgia rheumatica. *Lancet* 1975; **ii**: 476-8.
- <sup>13</sup> Hruban Z, Russell R M, Boyer J L, Glagov S, Bagheri S A. Ultrastructural changes in livers of two patients with hypervitaminosis A. *Am J Pathol* 1974; **76**: 451-68.
- <sup>14</sup> Hopwood D, Nyfors A. Effect of matrotrexate therapy in psoriasis on the Ito cells in liver biopsies, assessed by point counting. *J Clin Pathol* 1976; **29**: 698-703.