

Case report

Polyarteritis nodosa associated with acute cytomegalovirus infection

M. DOHERTY AND J. W. B. BRADFELD

From the University Departments of Medicine and Pathology, Bristol Royal Infirmary, Bristol BS2 8HW

SUMMARY A case of polyarteritis nodosa is described in which the onset of the disease was associated with acute infection by cytomegalovirus. Peripheral neuropathy was the predominant clinical feature, and death occurred 4 years after the onset. This is the first recorded case of polyarteritis in which cytomegalovirus is of possible aetiological significance.

Several aetiological factors, including hypersensitivity reactions to serum and drugs, have been proposed in the pathogenesis of polyarteritis.¹⁻³ A more important association is that with circulating hepatitis B antigenaemia, which occurs in up to 25-40% of patients with polyarteritis nodosa.^{4,5} Other viruses have not been definitely implicated. We report a case in which the onset of polyarteritis was associated with acute infection by cytomegalovirus. This is believed to be the first recorded association.

Case report

A previously fit 66-year-old woman presented with a 2-week history of progressive weakness of her arms and legs associated with sweats, severe generalised myalgia, abdominal pain, and constipation. On examination she was febrile (38.5°C) and had bilateral ankle oedema and generalised abdominal tenderness. She showed asymmetrically decreased distal power and tone in all limbs, absent tendon reflexes, and sensory loss in a glove-and-sock distribution; cranial nerves were intact.

Investigations showed: haemoglobin 14 g/dl; white blood cell count $24.7 \times 10^9/l$ ($24\,700/mm^3$) with 80% neutrophils and no atypical lymphocytes; plasma viscosity 1.80 centipoise; urea 10 mmol/l (60 mg/100 ml); albumin 21 g/l. Her urine showed a trace of protein, several red cells, but no casts. Cytomegalovirus complement fixation test (plate microtitre using killed cytomegalovirus in human fibroblasts from Public Health Laboratory,

Colindale) showed a diagnostic rise in titre from $<1/8$ to $1/1500$ over 20 days. Electromyographic studies confirmed the presence of peripheral neuropathy. Her chest x-ray film showed basal emphysema. Other tests, including cerebrospinal fluid analysis, were normal.

Because of the rapidly progressive nature of her neuropathy she was given prednisolone (initially 60 mg daily). This appeared to halt further progression, and her white blood cell count fell to $12.5 \times 10^9/l$ ($12\,500/mm^3$) (70% neutrophils). On steroids, however, she rapidly developed hypertension (blood pressure 190/115 mmHg), which was controlled with bendrofluazide 5 mg and atenolol 100 mg daily. Steroids were stopped after 2 months, leaving her with wasting, weakness, and numbness of her hands and feet. Her hypertension continued to require treatment with bendrofluazide 5 mg and atenolol 100 mg daily, and it was noted that her neutrophil leucocytosis persisted, with a total white cell count in the range $13.0-18.5 \times 10^9/l$ ($13\,000-18\,500/mm^3$).

She was lost to follow-up, but 4 years after her initial illness she was readmitted with increasing weakness of all limbs, weight loss, and depression. Her neuropathy had progressed to involve her forearms and calves: she was unable to walk unassisted. She had bilateral ankle oedema and reduced breath sounds at both bases; blood pressure was 130/80 mmHg.

Investigations showed: haemoglobin 13.1 g/dl; white blood cell count $22.1 \times 10^9/l$ ($22\,100/mm^3$) with 82% neutrophils; plasma viscosity 1.79 centipoise; urea 12.7 mmol/l (76 mg/100 ml); albumin 18 g/l; calcium 1.88 mmol/l (7.52 mg/

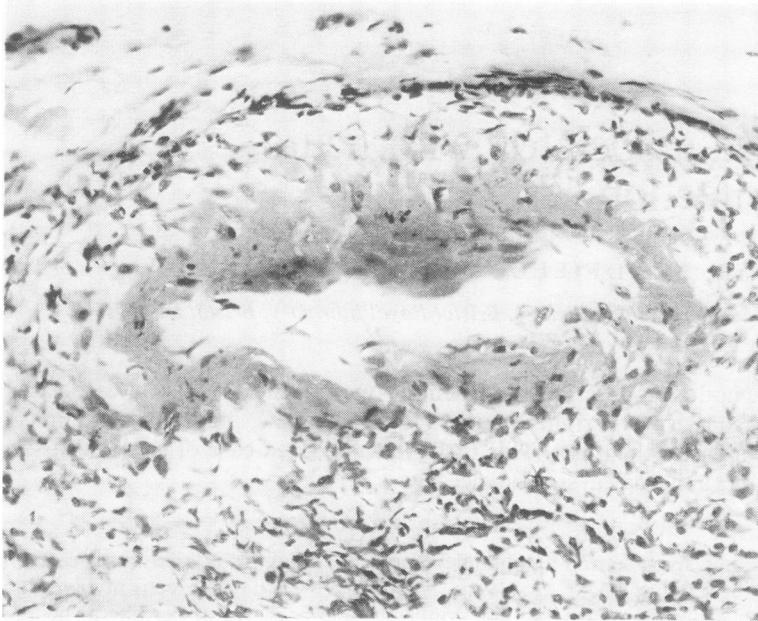


Fig. 1 Rectal biopsy specimen. Submucosal blood vessel showing fibrinoid necrosis of the subendothelial region, accumulation of inflammatory cells including neutrophils, and prominence of endothelium. (Haematoxylin and eosin, $\times 275$).

100 ml); autoimmune profile and Australia antigen negative; cytomegalovirus titre $<1/10$. Serum $\alpha 1$ antitrypsin 0.7 g/l (normal 2–4 g/l). Her chest x-ray film showed bilateral basal bullous emphysema. Rectal biopsy (Fig. 1) showed vasculitis with fibrinoid necrosis and a mixed inflammatory cell infiltrate which included neutrophil polymorphs. Other tests including liver function, immunoglobulins, 24-hour urinary protein, and barium studies were normal.

The diagnosis was made of polyarteritis nodosa together with $\alpha 1$ antitrypsin deficiency emphysema. She was given prednisolone 60 mg daily with little improvement. Her condition deteriorated, and she died after developing a hemiplegia. Permission for necropsy was refused.

Discussion

Cytomegalovirus infection in adults may present in several ways, the most common being an infectious mononucleosis-type illness.⁶ Vasculitis has been reported in a diabetic patient with acute cytomegalovirus infection.⁷ However, vasculitis in that instance was remarkably sensitive to steroids and occurred in association with a low white cell count, atypical lymphocytes, and abnormal liver function. Such was not the case here.

Cytomegalovirus may cause peripheral neuropathy and polyneuritis,⁸ but this usually recovers completely, commonly involves cranial nerves, causes

proximal rather than distal weakness, and is associated with a raised cerebrospinal fluid protein. It therefore seems unlikely that this patient's illness can be explained by acute cytomegalovirus infection alone.

The combination of a predominantly motor peripheral neuropathy, fever, abdominal pain, malabsorption, hypertension, and marked peripheral neutrophil leucocytosis fits well with a diagnosis of polyarteritis.⁹ This is further supported by the histology obtained on her second admission.

A 4-fold rise in antibody titre is considered diagnostic of active infection,¹⁰ and it therefore appears that acute cytomegalovirus infection occurred at the onset of this patient's polyarteritis. No other known aetiological factors were present. Cytomegalovirus may thus be another antigen that may initiate polyarteritis, the arteritis then persisting independently after elimination of the original triggering antigen (there was no evidence of acute infection at the time of the biopsy). Interestingly, this patient's illness shows some similar features to those cases of polyarteritis nodosa with hepatitis B antigenaemia⁵ (initial myalgia and rash progressing to severe, often fatal, polyarteritis with fever, abdominal pain, neuropathy, and hypertension; pulmonary involvement is not prominent), but differs in not being a 'one shot' disease.

Little is understood of the mode of transmission of cytomegalovirus. Perhaps $\alpha 1$ antitrypsin deficiency emphysema provided a portal of entry in this case.

Cytomegalovirus should be considered as another virus which may be of aetiological significance in some cases of polyarteritis. A search for virus infection at the very onset of polyarteritis may help to elucidate problems of aetiology.

We thank Dr David Boyd for his permission to report this case and Dr Paul Dieppe for his useful advice and discussion.

References

- ¹ Rich A R. The role of hypersensitivity in periarteritis nodosa as indicated by 7 cases developing during serum sickness and sulphonamide therapy. *Johns Hopkins Med J* 1943; **72**: 65–82.
- ² Citron B P, Halpern M, McCarron M, *et al.* Necrotising angiitis associated with drug abuse. *N Engl J Med* 1970; **283**: 1003–10.
- ³ Halpern M, Citron B P. Necrotising angiitis associated with drug abuse. *A J R* 1971; **111**: 663–71.
- ⁴ Gocke D J, Hsu K, Morgan G, Bombardieri S, Lockshin M, Christian C L. Association between polyarteritis and Australia antigen. *Lancet* 1970; **ii**: 1149–53.
- ⁵ Lockshin M D, Sargent J S. Necrotising vasculitis and HB antigen. In: Hughes G R V, ed. *Modern Topics in Rheumatology*. London: Heinemann, 1976: 121–5.
- ⁶ Klemola E, Kääriäinen L. *Br Med J* 1965; **ii**: 1099–102.
- ⁷ Bamji A, Salisbury R. (1978). Cytomegalovirus and vasculitis. *Br Med J* 1978; **i**: 623–4.
- ⁸ Leonard J C, Tobin J O'H. Polyneuritis associated with cytomegalovirus infections. *Q J Med* 1970; **40**: 435–42.
- ⁹ Travers R L, Allison D, Hughes G R V. (1979). *Semin Arthritis Rheum* 1979; **8**: 184–98.
- ¹⁰ Foster K M, Jack I. *N Engl J Med* 1979; **280**: 1311–6.