# SHORT REPORT

# Giant cell arteritis of the cervical radicular vessels presenting with diaphragmatic weakness

E A Burton, J B Winer, P C Barber

**Abstract**
**The clinical and histopathological details of a patient who succumbed to giant cell arteritis (GCA) of the cervical radicular vessels are described. The initial clinical presentation, with diaphragmatic weakness, has not previously been reported. Normal inflammatory indices and the unusual presentation prevented diagnosis during life, but GCA should be considered in the differential diagnosis of any unexplained neuropathic or radiculopathic syndrome, as corticosteroid therapy may lead to recovery. This is the first account of the pathological findings in cervical radiculopathy associated with GCA.**
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Keywords: giant cell arteritis; radiculopathy; diaphragm

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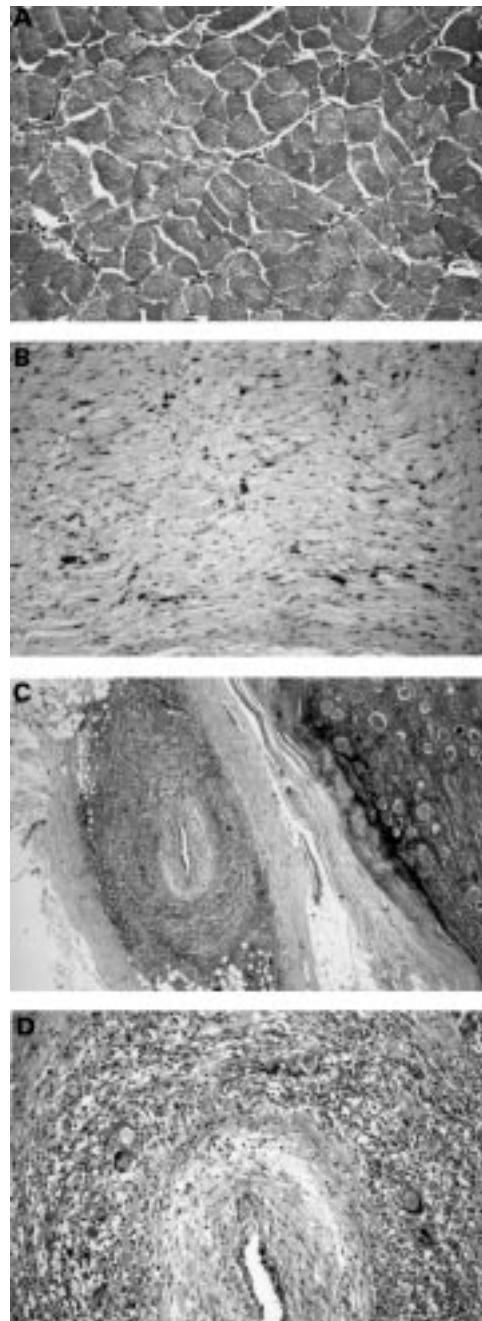E A Burton

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Giant cell arteritis (GCA) is a common, treatable condition. In this paper, we describe a previously unreported clinical presentation of GCA; the diagnosis was made postmortem. It is important to consider GCA in the differential diagnosis of any unexplained neuropathic or radiculopathic syndrome, as treatment may avert the inexorable decline that we found in this case. This is the first published account of the pathological features of GCA-associated cervical radiculopathy.

**Case history**
A 69 year old man presented with a 1 year history of increasing exertional dyspnoea and orthopnoea, and a 6 month history of upper limb weakness. The dyspnoea had followed an acute myocardial infarction, and was initially thought to represent pulmonary oedema. The symptoms failed to respond to treatment for heart failure, however, and echocardiography and coronary angiography showed relative preservation of left ventricular function. The upper limb weakness was initially a much less prominent symptom than dyspnoea, but was progressive and bilateral. At presentation he had been unable to perform fine manipulative tasks or lift his arms above his head for about 2 months. In addition, he had noted cramp-like sensations in the right arm, and had seen the muscles "flickering" on occasions, but there was no sensory loss or paraesthesiae. There

were no symptoms referable to the cranial nerves or legs, and no other historical features of note.

General physical examination disclosed diminished chest expansion and paradoxical movement of the abdominal wall on inspiration, but was otherwise normal. Vital capacity was 700 ml standing, but the patient was unable to lie down because he became dyspnoeic and distressed. He was alert and oriented, and the cranial nerves were unremarkable. There was mild weakness of neck flexion. There was severe asymmetric wasting of all muscle groups in both arms with fasciculation and weakness commensurate with the degree of wasting: all movements were possible against gravity but not resistance, with the exception of right shoulder abduction, which was not possible against gravity, and left elbow flexion, extension, and wrist flexion, which were possible against resistance, but weak. There was no wasting of the leg musculature, but occasional fasciculation was visible in both quadriceps. There was mild weakness of hip flexion but lower limb power was otherwise preserved. Sensory examination was normal to all modalities throughout. The deep reflexes were absent apart from the right knee jerk, which was diminished. Both plantar responses were flexor. Coordination was consistent with the degree of weakness in the upper limbs, and normal in the lower limbs. The gait was unremarkable.

Investigation showed hyponatraemia ($Na^+$123 mMol/l, serum osmolality 252 mOsm/l, urine osmolality 257 mOsm/l) and evidence of previous anterior myocardial infarction on electrocardiography. The remainder of the routine biochemical and haematological profiles, including thyroid function and serum electrophoresis, were unremarkable. Antibodies to acetylcholine receptors and gangliosides were not detected. Hexosaminidase A concentrations were normal. Genetic studies excluded expansion of the trinucleotide repeat associated with X linked spinal and bulbar muscular atrophy. Analysis excluded intoxication with lead, manganese, thallium, or arsenic. No porphyrin or porphobilinogen was detected in the urine, which was acellular and without casts.

Chest radiographs showed bilateral raised hemidiaphragms, but normal heart size, and no

focal collapse or consolidation. Abdominal ultrasound and CT examinations were unremarkable, as was MRI of brain, whole spine, and brachial plexus. His CSF was acellular and sterile, with a protein concentration of 0.12 g/l



*(A) Biceps brachii, paraffin wax section, showing small group fibre atrophy indicative of chronic denervation. Blood vessels in the muscles examined showed no evidence of inflammatory changes. (Haematoxylin and eosin originally×140.) (B) Part of a cervical nerve root, immunostained with an antibody to CD68 antigen, showing many macrophages within the tissue indicative of active fibre breakdown and phagocytosis. (Immunoperoxidase originally×140.) (C) Radicular artery branch adjacent to C6 dorsal root ganglion, showing active giant cell arteritis. Part of the ganglion is visible in the right of the field. (Haematoxylin and eosin originally×35.) (D) Detail from the same artery as above, showing dense mixed chronic inflammatory cell infiltrate, destruction of the internal elastic lamina with associated giant cells, and marked intimal thickening. (Haematoxylin and eosin originally×140.)*

and glucose of 4.6 mMol/l. Abnormal IgG bands were detected in serum and CSF—the pattern was identical in both, suggesting peripheral IgG synthesis. Biopsy of the right deltoid muscle showed histological features in keeping with chronic denervation (figure A); biochemical assays were normal.

Electrophysiological investigation showed normal sensory studies and motor conduction velocities. Reduced compound muscle action potential amplitudes were seen in the upper and lower limbs (for example, right median nerve at wrist to abductor pollicis brevis: 3 mV), and F wave latencies were prolonged with reduced frequencies. Electromyographic sampling showed evidence of denervation in muscles of all four limbs. Additional studies excluded the presence of proximal conduction block and showed normal central motor conduction.

On admission, the erythrocyte sedimentation rate (ESR) was 25 mm/h. He subsequently developed a persistent low grade fever and rising ESR (table). Assisted mechanical ventilation was instituted to alleviate respiratory embarrassment caused by weakness of the respiratory muscles. Unfortunately, he continued to deteriorate and died of respiratory failure.

POSTMORTEM EXAMINATION

General postmortem examination showed evidence of previous myocardial infarction and coronary artery atheroma, but no other abnormality.

Examination of the spinal cord showed diffuse pallor of myelin with minor loss of anterior horn cells. Scattered cells showed central chromatolysis indicative of acute axonal damage. The changes were most marked at the cervical level. Nerve roots showed patchy axonal loss and fibrosis consistent with ischaemic injury (figure B). Dorsal root ganglia showed neuronal loss with many ganglion cells undergoing degeneration with associated aggregates of lymphocytes and macrophages (figure C).

Scattered small blood vessels associated with spinal nerve roots had lymphocytic cuffs, and radicular arteries of the lower cervical roots and their branches displayed a florid giant cell arteritis with a dense infiltrate of lymphocytes and macrophages plus multinucleate giant cells throughout the media, destroying the muscle and internal elastic lamina and associated with intimal fibroblastic proliferation (figure C, D).

Peripheral nerves, including brachial plexus and femoral and median nerves were examined. A few fascicles showed evidence of axonal loss with corresponding fibrosis. Some of the associated blood vessels showed cuffs and occasional infiltrates of lymphocytes. A single

*Measurements of erythrocyte sedimentation rate (ESR) at various time points after admission to hospital*

| Days after admission | ESR (mm/h) |
| --- | --- |
| 0 | 25 |
| 13 | 69 |
| 42 | 100 |
| 60 | 114 |

meningeal vessel showed lymphocytic infiltration of the intima and adventitia, but thorough examination of blood vessels elsewhere showed no abnormality.

## Discussion

The histopathological abnormalities seen in blood vessels supplying the cervical cord and nerve roots suggest two possible diagnoses: extracranial giant cell arteritis (GCA) and granulomatous angiitis of the central nervous system (GANS). We favour the first diagnosis for two reasons: Firstly, GANS is almost always confined to the CNS,[1][2] but the most impressive histological changes in this case were in radicular arteries rather than the vessels within or supplying the cord, and there was evidence of involvement of tissues (peripheral nerves) remote from the CNS. Secondly, the lesions themselves showed intense inflammation and focal destruction of the media, which is typical of GCA[3]; lesions in GANS are commonly reported to spare the media.[1]

We suggest that this patient succumbed to a severe form of GCA, restricted mainly to vessels supplying the cervical nerve roots, resulting in motor axonal injury secondary to radicular ischaemia. This led to denervation and weakness of the upper limbs and diaphragm (as evidenced by the presence of paradoxical movement of the abdominal wall on respiration, extremely low vital capacity associated with orthopnoea, and bilateral raised hemidiaphragms on chest radiographs). Relatively mild histopathological abnormalities present in the lumbosacral expansion and lumbar nerve roots were associated with mild clinical and electrophysiological abnormalities in the legs. The coronary arteries were not examined histologically, so it is not possible to state whether myocardial infarction was a result of coronary angiitis.

The association of GCA with disease of the peripheral nervous system is well recognised, although the incidence has been variously reported as 1.1%-14%.[3-5] The commonest patterns of abnormalities seen are symmetric sensorimotor polyneuropathy (usually mild and chronic),[5-7] and single or multiple mononeuropathy.[5][8]

Neuropathy and radiculopathy with severe motor impairment associated with GCA is less well described. Details of six cases of cervical radiculopathy have been reported.[9-13] The C5 root was affected in all; the abnormalities were purely motor in four of the cases. There are two reported cases[7][14] of generalised proximal weakness and wasting associated with EMG evidence of denervation; these may also have been radiculopathic in origin. All eight of these patients had raised ESR at diagnosis, and improvement of neurological impairment with corticosteroid therapy was universal. There is a single case report of a patient with typical polymyalgia rheumatica and raised ESR, who went on to develop symmetric lower motor neuron weakness, including the facial nerve distribution, in association with brisk reflexes, an extensor plantar reflex, and mild sensory abnormalities.[15] It was suggested that the

patient had developed motor neuron disease, although the reported clinical features are atypical and postmortem examination was not carried out. The association of motor neuropathy and GCA is not definite in a further case in which the neuropathic features started to resolve before the introduction of steroid therapy.[16] Further cases of GCA associated with C5 radiculopathy are reported without details[5][3] as are two cases of unilateral arm weakness.[4]

The present case is unique for several reasons: Firstly, the initial symptom was dyspnoea, caused by diaphragmatic weakness. This has previously been described in only a single case of GCA, as a later component of a more extensive clinical picture involving the brainstem and oculomotor nerves.[13] Respiratory presentation is, however, well recognised in other diseases affecting the motor neurons of the cervical cord and their axons.[17-20] Secondly, there are no other reported patients with GCA associated radiculopathy or neuropathy of this severity in whom constitutional symptoms, abnormalities of the temporal pulses, and raised ESR were all absent at presentation, making diagnosis in the present case extremely difficult. This was further confounded by the resolute normality of the sural sensory nerve action potentials throughout the illness, precluding sural nerve biopsy. Finally, this is the first case of GCA associated radiculopathy in which histological examination of the spine and spinal nerve roots has been undertaken, facilitating understanding of the pathological process.

It is established that severe involvement of the vertebral arteries is a common pathological finding in GCA without peripheral nervous system disease.[21] The cervical cord and roots derive their blood supply from the vertebral vessels. It has been proposed that the mechanism of cervical root damage in GCA is ischaemia secondary to hypoperfusion through stenosed vertebral arteries,[10] and that the anatomy of the radicular vasculature may help explain the tendency for the midcervical roots to be preferentially affected.[13] Angiographic stenoses of the ipsilateral vertebral artery were showed in one case of GCA associated C5 radiculopathy,[12] but the authors of this report expressed doubt that the lesions could account for ischaemic nerve root injury on account of the rich collateral blood supply to cervical nerve roots. Our findings provide an alternative explanation. We have demonstrated florid arteritis of the radicular vessels themselves, rather than proximal feeding vessels, as the cause of ischaemic radiculopathy in this patient. Furthermore, we found no evidence of direct extension of the inflammatory process into the brachial plexus, as suggested in one report.[11] It is possible that previously reported cases of cervical radiculopathy had a similar pathological basis to the present case. An analogous mechanism seems to be true of peripheral nerve, where axon damage in GCA associated neuropathy has been reported to result from ischaemia arising from occlusion of the nutrient arteries to peripheral nerves, both

in mononeuropathy[22] and sensory polyneuropathy.[5]

In summary, we have described a case of giant cell arteritis causing ischaemic polyradiculopathy. The clinical presentation was unusual, and investigations were unhelpful in diagnosing the disease during life. The diagnosis should, however, be considered in any unexplained case of peripheral nerve or nerve root disease, even if initial investigations such as ESR are unremarkable, as previous reports suggest that corticosteroid therapy may lead to neurological recovery.

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**Notes**