Sensory perineuritis

W B MATTHEWS, M V SQUIER

From the University Department of Clinical Neurology and Department of Neuropathology, Radcliffe Infirmary, Oxford, UK

SUMMARY A case of sensory perineuritis is described, affecting individual cutaneous nerves in the extremities and with a chronic inflammatory exudate confined to the perineurium in a sural nerve biopsy. No cause was found. The condition slowly resolved on steroid treatment.

In 1972 Asbury, Picard and Baringer¹ described two patients with sensory peripheral neuropathy, in whom chronic inflammatory and fibrotic changes limited to the perineurium were found on cutaneous nerve biopsy. The only related published case appears to be that of Bourque *et al*² where similar changes were found in a patient with sensory-motor neuropathy. We here report a case closely resembling the description of Asbury *et al*.¹

Case report

A married woman, born in 1932, rapidly developed pain and numbness in the hands and feet in November 1983. The distribution of these symptoms was patchy and, as far as she could determine, the affected areas were involved simultaneously. The areas of numbness did not extend but the pain became more intense, especially during cold weather. Pain was not induced or aggravated by stretch but was continuous, interfering with sleep.

When seen in August 1984 the following areas were found to be involved: the lateral aspect of the left fifth finger and the medial side of the left thumb, the first interdigital cleft and proximal phalanges of the dorsal surface of the right thumb and index, the entire lateral aspect, plantar and dorsal, of the left foot and the plantar surface of both heels. Within these areas all forms of cutaneous sensation were much reduced, but rubbing the skin was painful. There was no nerve hypertrophy and Tinel's sign could not be elicited from any nerve trunk. At no time was there any impairment of postural or vibration sense. There was no muscular wasting or weakness, tendon reflexes were normal and plantar reflexes flexor. There was no past history of significant ill health and no other signs of disease. She was not diabetic. Investigations showed a normal full blood count, with 1% eosinophils, and an ESR of 4 mm/h. Antinuclear antibody and rheumatoid factor were not present. Serum electrophoresis was normal as were thyroid function, serum B12 and folate and routine blood chemistry. Serological tests for

syphilis were negative. Chest radiograph was normal. The CSF was not examined.

Electromyography (Dr G Rushworth) showed no evidence of denervation in the intrinsic muscles of the hand or foot. Motor nerve conduction velocity in the main nerve trunks of the upper and lower limbs was normal and the latency of the H reflex recorded from the triceps surae was not prolonged. The amplitude of the sensory action potential in the right radial nerve was 13 μ V and velocity 44 m/s. Values of amplitude and velocity for the right and left sural nerves was abnormal, being 5 μ V and 35 m/s and 5 μ V and 30 m/s respectively.

A biopsy was obtained from the left sural nerve. Three of seven fascicles had thickened, fibrous perineurial sheaths with increased numbers of small blood vessels in the outer layers and in the epineurium. The perineurium of one fascicle was focally inflamed (fig 1) with an infiltrate consisting mainly of lymphocytes and foamy histiocytes (fig 2). An occasional multinucleated cell was seen but there were no granulomas. The infiltrate did not extend into the endoneurium. Occasional epineurial vessels were cuffed with lymphocytes. No acid fast bacilli were identified. No interstitial immunoglobulin, complement, albumen or amyloid deposition was demonstrated. Silver stains demonstrated axonal loss in all fascicles but particularly severe in the inflamed fascicle. In semi-thin, resin-embedded sections there was an

Fig 1 Oblique section of inflamed fascicle. There is a chronic inflammatory infiltrate in the perineurium, macrophages are numerous in the inner part of this layer. HVG $\times 10$.

Address for reprint requests: Dr M V Squier, Department of Clinical Neurology, Radcliffe Infirmary, Oxford OX2 6HE, UK.

Received 21 July 1987 and in revised form 3 November 1987.
Accepted 9 November 1987

Fig 2 Inflammatory infiltrate, mainly macrophages, between the nerve fibres (N) and the inner perineurium (P). One macrophage appears to be multinucleated (arrow) H & E $\times 400$. Original magnification $\times 400$.

obvious loss of large and small myelinated fibres. Clusters of small myelinated axons suggestive of sprouting were identified. Endoneurial and perineurial collagen was increased. In teased preparations abnormally myelinated axons were identified with many myelin ovoids. Only very rare demyelinated segments were identified. Electron microscopy showed degenerating axons. The basement membrane of perineurial cells was markedly thickened measuring up to 600 nm (normal is less than 100 nm).

Treatment with oral prednisolone 60 mg a day was begun on 2 January 1985, and within 2 weeks there had been considerable relief of pain, but no change in the areas of sensory loss. Steroid treatment was maintained in a gradually reducing dose, with almost complete absence of pain except during very cold weather. However, in November 1985, while on 7.5 mg of prednisolone a day, a new painless area of sensory loss developed, involving the dorsal surface of the right first and second toes. By March 1987 steroid treatment had been discontinued for a month. Some pain was still present in cold weather but areas of sensory loss had diminished

although still present over the left heel and in the distribution of the termination of the right radial nerve.

Discussion

The clinical features of the cases of sensory perineuritis described by Asbury *et al*¹ differed in some respects from those of our patient. In their Case 1 the onset was with relapsing and remitting painful areas of numbness in the distribution of individual cutaneous nerves in the extremities, but later in the course of the disease symmetrical distal sensory loss developed, more suggestive of a diffuse neuropathy. The trigeminal and occipital nerves were also involved and weakness occurred when one axillary nerve was transiently affected. The response to steroids was initially good but was not maintained, perhaps because treatment was not energetically pursued. In the second case individual cutaneous nerves were also involved with no motor or reflex changes although the patient became impotent. No clear remission was described and only a brief course of steroids was given without benefit. In neither case was any significant underlying disease detected.

The early symptoms of the patient described by Bourque *et al*² were of paraesthesiae and pain, particularly in the soles of the feet, followed after 4 months by progressive weakness of the limbs. The physical signs were those of diffuse sensory-motor neuropathy with distal sensory loss rather than involvement of individual cutaneous nerves. Tendon reflexes were reduced or absent. Motor nerve conduction velocities were slowed and sensory potentials unobtainable. Response to steroids was not immediate but was subsequently excellent. Perineuritis was found on cutaneous nerve biopsy, virtually the only point in common with our own case.

In all biopsy specimens the selective nature of the inflammatory process had been clearly seen, some fascicles being unaffected, while others were surrounded by chronic inflammatory cells and fibrosis. Nerve fibre changes are limited to fascicles affected in this way and may be presumed to be due to perineurial compression. Asbury *et al*¹ were concerned by the resemblance of the histological appearances to those of leprosy but no evidence of this disease had been found and no skin lesions have developed.

The only other instance of perineuritis in our experience was found in the sural nerve biopsy of a man who initially presented with extensive areas of sensory loss, paraesthesiae and pain on pressure over the trunk and limbs. There was no response to steroids and disseminated carcinoma soon became apparent. Unfortunately the peripheral nervous system was not examined at necropsy in another hospital. No evidence of carcinoma has been found in

prolonged follow-up in our patient or those of Asbury *et al*¹ although their Case 1 had stage 1 carcinoma of the cervix treated by hysterectomy some 3 years before the onset of the neuropathy.

Asbury *et al*¹ believed that their cases were unique and could only suggest some unknown infective cause or a hypersensitivity reaction. Bourque *et al*,² on the basis of focal deposits of IgG and IgM in the perineurium, suggested an auto-immune mechanism. Proliferation of fibroblasts and lymphocytic infiltration in the perineurium was a prominent feature of the toxic rapeseed oil syndrome³ and a histological picture resembling that of the present case has been reported in mononeuritis multiplex associated with cryoglobulinaemia.⁴ In both these conditions there was severe involvement of motor nerves.

Our case throws no further light on the possible aetiology of sensory perineuritis. The aggravation of symptoms by cold weather was not accompanied by any overt vascular change.

Sensory perineuritis is evidently very rare although in the absence of motor and reflex changes it might be confused with other causes of "burning feet" if detailed sensory examination is omitted. It is clinically distinct from the much more common migrant sensory neuritis of Wartenberg⁵ where individual

cutaneous nerves are apparently damaged by stretch, producing sudden brief pain followed by localised numbness. This condition is no more than a mild nuisance and steroid treatment should not be contemplated. In the only reported biopsy no inflammatory changes were present. Whether the two conditions could always be distinguished by biopsy is uncertain, in view of the focal distribution of the lesions of sensory perineuritis.

References

- 1 Asbury AK, Picard EH, Baringer JR. Sensory perineuritis. *Arch Neurol* 1972;**26**:302-12.
- 2 Bourque CN, Anderson BA, del Campo DM, Sima AAF. Sensorimotor perineuritis—an autoimmune disease? *Can J Neurol Sci* 1985;**12**:129-33.
- 3 Ricoy JR, Cabella A, Rodriguez J, Tellez I. Neuropathological studies on the toxic syndrome related to adulterated rapeseed oil in Spain. *Brain* 1983;**106**:817-36.
- 4 Konishi T, Saida K, Ohnishi A, Nishitani H. Perineuritis in mononeuritis multiplex with cryoglobulinemia. *Muscle Nerve* 1982;**5**:173-7.
- 5 Matthews WB, Esiri MM. The migrant sensory neuritis of Wartenberg. *J Neurol Neurosurg Psychiatry* 1983;**46**:1-4.