Hypertrophic mononeuropathy

C. H. HAWKES¹, J. M. JEFFERSON, E. L. JONES,
AND W. THOMAS SMITH

*From the Queen Elizabeth Hospital and Department of Pathology,
University of Birmingham, Birmingham*

SUMMARY A case of hypertrophic mononeuropathy is described in a 19-year-old female. The entity is very rare as only three previous cases have been reported. The light and electron-microscope appearances resemble those of progressive hypertrophic polyneuritis.

A case of localized hypertrophy, apparently involving only the posterior interosseous nerve is described. Hypertrophic mononeuropathy is a rare and benign disorder that is characterized histologically by periaxonal 'onion-bulb' formations similar to those that occur in progressive hypertrophic polyneuritis.

CASE REPORT

A 19-year-old cook had been well until two years before admission, when she noticed difficulty in extending the left thumb and forefinger. The weakness slowly advanced and eventually also involved the extensors of the middle finger. There was no history of trauma to the arm though the patient frequently performed rapid wringing movements in the course of her work. There were no sensory symptoms.

Examination revealed abnormalities confined to the left upper limb. There was weakness especially of abduction and extension of the left thumb, the extensors of the index finger, and to a lesser extent of the ulnar three digits. Dorsiflexion of the wrist was only slightly weak, and produced radial deviation, suggesting weakness of the extensor carpi ulnaris. Supinator, brachioradialis, and triceps were all strong; sensory loss could not be elicited and the tendon reflexes were unimpaired.

On this basis it was felt that the posterior interosseous nerve was involved at some point distal to its supinator branch.

Electromyography of the extensor muscles of the left forearm revealed an interference pattern of normal amplitude associated with a moderate degree of 'gapping' and an increase of short duration

polyphasic potentials, suggestive of chronic denervation. No abnormalities were detected elsewhere.

Radiographs of the left elbow and forearm were normal but the cervical spine films showed minor disc narrowing at C4-5 and C5-6. The haemoglobin

FIG. 1. *Posterior interosseous nerve biopsy. Transverse section showing concentric proliferation of Schwann cells ('onion-bulbs') around individual axons and endoneurial fibrosis. H and E, $\times 480$.*

¹ Present address: Wessex Neurological Centre, Southampton General Hospital, Southampton, SO9 4XY.

erythrocyte sedimentation rate, white cell count, blood glucose and electrolytes, blood Wassermann reaction, and serum phytanic acid assay were all normal.

OPERATION AND PROGRESS Under general anaesthesia an incision was made from the left external epicondyle running vertically down the forearm medial to the extensor carpi radialis muscle. The posterior interosseous nerve was exposed as it penetrated the supinator muscle and was found to be

normal. However, as the nerve left this muscle, it became greatly expanded and thickened, having a grey-white appearance, suggestive of neoplastic infiltration. A small piece of affected nerve was excised. Although the histological appearances were considered to be benign, it was thought advisable to remove the tumour *in toto*, to reduce the possibility of further extension. Accordingly, some two weeks later the peripheral portion of the nerve distal to its branches to extensor carpi ulnaris was excised.

Recovery from both surgical procedures was un-

FIG. 2. Electron micrograph. Multiple non-myelinated axons (A) encircled by Schwann cells (SC) surrounded by excessive endoneurial collagen fibres (CF). Note concentric Schwann cells (bottom right). Uranyl acetate/lead citrate, $\times 6,000$.

eventful except for some increase in weakness of extension of the wrist and fingers, later corrected by a tendon transplant operation. The patient has remained well since then.

HISTOLOGICAL EXAMINATION *Light microscopy* Sections showed marked concentric fibrosis involving mainly the endoneurium, although the perineurium was also thickened. There was increase in endo-

neural collagen associated with mild proliferation of fibroblasts. The most prominent feature was a striking circumferential proliferation of Schwann cells (Fig. 1) around individual axons. In transverse sections these formations resembled 'onion bulbs'. The intercellular material stained positively as collagen with Van Gieson's mixture. The intercellular substance also stained weakly with Congo red but there was no evidence of amyloid deposi-

FIG. 3. Electron micrograph of 'onion-bulb' formation. Endoneurial collagen bundles (EC), ensheathed by concentric lamellae of Schwann cell cytoplasm (SCC) interspersed with collagen fibres (CF). Note endoneurial fibroblast (F) with dense nucleus (N) and numerous intracytoplasmic vacuoles (V). Uranyl acetate/lead citrate, $\times 12,000$.

tion. Glees-Marsland's silver-impregnation technique showed degeneration and loss of axons. Diffuse demyelination was present.

ELECTRON MICROSCOPY Tissue was fixed in 2.5% buffered glutaraldehyde, post-fixed in osmium tetroxide, embedded in Araldite, and ultra-thin sections stained by uranyl acetate and lead citrate

were examined in an AEI EM801 electron microscope.

Marked concentric endoneurial fibrosis was confirmed; numerous small non-myelinated axons were ensheathed by mature, banded, collagen fibres (Fig. 2). These axons were further surrounded by concentric or imbricated lamellae consisting of cell processes of proliferated Schwann cells (Fig. 3), corre-

FIG. 4. *Electron micrograph depicting detail of Schwann cells (SC). A thick moderate electron dense basement membrane (BM) surrounds the cell plasmalemma. Many small micropinocytotic vesicles (arrow) are present along the cell membranes. Uranyl acetate/lead citrate, $\times 16,000$.*

sponding to the 'onion-bulb' formations noted on light microscopy. Occasional endoneurial fibroblasts were identified in these formations, although the majority of the cells were clearly Schwann cells, often with a prominent, thick, hyperplastic basement-membrane applied to the plasmalemma (Fig. 4). Numerous fascicles of collagen fibres were interdigitated between the hyperplastic Schwann cell processes.

Excessive amount of fibrillary material was present in the endoneurial space and between the lamellated Schwann-cell cytoplasm. The endoneurial space also contained an amorphous or finely fibrillary ground substance. The fibrils were regularly arrayed, always in juxtaposition to mature collagen fibres (Fig. 5) and measured approximately 100 Å (10 nm) in diameter, resembling newly-formed collagen. In size and appearance the fibrils resembled those described

FIG. 5. Electron micrograph illustrating microfibrils (MF) in endoneurial space and between interdigitations of the Schwann cell cytoplasm (SCC). The fibrils measure 100 Å (10 nm) in diameter. Note the transversely beaded mature collagen (C). Uranyl acetate/lead citrate, $\times 30,000$.

in hypertrophic neuropathy and interpreted as elastic fibrils by Thomas and Lascelles (1967).

DISCUSSION

Hypertrophic mononeuropathy is undoubtedly rare and only three similar cases have been reported (Da Gama Imaginário *et al.*, 1964; Simpson and Fowler, 1966). These cases and the present case are summarized in the Table. It seems that the condition occurs in children and young adults, and shows a particular tendency to affect the radial nerve.

TABLE

CLINICAL FEATURES OF PREVIOUSLY RECORDED CASES OF HYPERTROPHIC MONONEUROPATHY

Case	Age (yr)	Sex	Occupation	Site of lesion
Da Gama Imaginário <i>et al.</i> (1964)	27	M	Sailor	Right radial nerve in spiral groove
Simpson and Fowler (1966) Case 1	12	M	Schoolboy	Right common peroneal nerve below neck of fibula
Case 2	11	M	Schoolboy	Left radial nerve in spiral groove
Hawkes <i>et al.</i> (1974)	19	F	Cook	Left posterior interosseous nerve below supinator

‘Onion-bulb’ formation is a characteristic feature of classical hypertrophic polyneuritis, but by no means pathognomonic. Such changes have been described in a variety of disorders including Refsum’s syndrome, neurofibromatosis, amputation neuromas and diabetic neuropathy (Jefferson, 1968). It, therefore, appears to be a non-specific phenomenon which bears much the same relationship to the overall picture of classical diffuse hypertrophic polyneuropathy as the histological sarcoid lesion does to the clinical syndrome of systemic sarcoidosis.

Electron microscopy in our case confirmed that the ‘onion-bulb’ formation consisted of concentric fibrosis and lamellae of hypertrophic Schwann cells and collagen; these findings corre-

lated with the appearances previously described in the nerves in progressive interstitial hypertrophic polyneuritis of Dejerine and Sottas type (Thomas and Lascelles, 1967), although there were no other clinical manifestations of the generalized disease.

The mechanism of ‘onion-bulb’ formation is uncertain, but the process seems basically to be related to remyelination of axons, both in human disease and experimental situations (Weller and Das Gupta, 1968); the formations may be a non-specific reaction to recurrent segmental demyelination. It has been suggested (Pleasure and Towfighi, 1972) that in onion-bulb neuropathies the abnormal nerves have a marked reduction in myelin content but a rapid rate of synthesis, that in the onion-bulb formations the excess peripheral Schwann cells do not appear to participate in attempts at myelin repair, and that the central cells are abnormally active in myelin regeneration.

A history of trauma was absent in our case, but the involvement of exposed nerves in the three previously documented examples suggests that trauma may have played some part. Alternatively, the lesion may have a genetic basis in view of its relationship to hypertrophic polyneuropathy.

The prognosis is probably good, as, according to D. A. Simpson (personal communication) who followed up his cases for eight years, there was no evidence of recurrence either locally or in other peripheral nerves.

REFERENCES

Da Gama Imaginário, J., Coelho, B., Tomé, F., and Sales Luis, M. L. (1964). Névrite interstitielle hypertrophique monosymptomatique. *Journal of Neurological Sciences*, **1**, 340–347.

Jefferson, J. M. (1968). The syndrome of progressive hypertrophic polyneuropathy. In *British Encyclopaedia of Medical Practice. Medical Progress*, 271–275.

Pleasure, D. E., and Towfighi, J. (1972). Onion bulb neuropathies. *Archives of Neurology*, **26**, 289–301.

Simpson, D. A., and Fowler, M. (1966). Two cases of localized hypertrophic neurofibrosis. *Journal of Neurology, Neurosurgery, and Psychiatry*, **29**, 80–84.

Thomas, P. K., and Lascelles, R. G. (1967). Hypertrophic neuropathy. *Quarterly Journal of Medicine*, **36**, 223–238.

Weller, R. O., and Das Gupta, T. K. (1968). Experimental hypertrophic neuropathy: an electron microscope study. *Journal of Neurology, Neurosurgery, and Psychiatry*, **31**, 34–42.