Hypertrophic mononeuropathy

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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 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...
erythrocyte sedimentation rate, white cell count, blood glucose and electrolytes, blood Wassermann reaction, and serum phytic 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 capri 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, × 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 endoneurial 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-
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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-

![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, ×16,000.](http://jnnp.bmj.com/)

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, ×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 fibrillar material was present in the endoneurial space and between the lamellated Schwann-cell cytoplasm. The endoneurial space also contained an amorphous or finely fibrillar 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, × 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**

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

‘Onion-bulb’ formation is a characteristic feature of classical hypertrophic polynuertis, 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 correlated with the appearances previously described in the nerves in progressive interstitial hypertrophic polynuertis 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


