Ultrastructure of Sural Nerve in a Case of Arsenical Neuropathy

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Summary. Examination of electron microscopical and teased preparations of a biopsied sural nerve from a patient with arsenical neuropathy is reported. Teased preparations and toluidine blue stained epon sections showed a decrease in the number of myelinated fibres and Wallerian degeneration. Electron microscopy revealed destruction of myelin sheaths, further disintegration associated with degeneration or disappearance of myelinated axons and numerous degenerative changes in the Schwann cell cytoplasm. There was no evidence of segmental demyelination. Occasional onion-bulb-like structures, however, associated with proliferation of Schwann cells, were observed. Obvious elongation of the basement membrane, except in an onion-bulb-like structure, or collagen fibril proliferation or evidence of phagocytosis was not found. These findings are considered to correspond mainly with Wallerian degeneration. Some consideration as given to the unusual onion-bulb-like structures.


Introduction

In addition to encephalopathy, peripheral nerve degeneration has been observed in patients who have accidentally taken arsenic. Some clinical reports have been published and treatment with BAL has been considered [3,7,8]. Pathological studies of peripheral nerves have demonstrated degenerative changes in both axons and myelin sheaths [3,7,8]. Dyck et al. [5] reported the presence of Wallerian degeneration in sural nerve biopsies. These results may imply that peripheral nerves degenerate in arsenical neuropathy in the same way as in the distal stumps of transected nerves.

Case Report

A 46-year-old man (No. 691304), suffering from chronic liver disease, had worked as a vermin exterminator from September 1968 to July 1969. His daily work was to spray arsenite to kill white ants. One months after commencing work, redness and swelling of the face
appeared and lasted about a week. Frequent nasal bleedings, congestion of the conjunctivae, epiphora, and occasional skin rashes occurred. In November 1968 mild puffiness developed in the tips of his fingers. In July 1969 he had an aching epigastralgia, anorexia, diarrhoea and jaundice, followed by recurrent skin rashes on the neck, left shoulder and abdomen. In August tingling and later burning sensations became apparent in his hands, feet and legs associated with epigastralgia, diarrhoea, and mild fever. Gait disturbance developed. Neurological examination in September 5, 1969 revealed diminished deep reflexes in the lower extremities, sensory impairment of hands and legs, as well as impairment of walking and standing. He was admitted to the Neurological Department of Kyushu University. Physical examination showed transverse white striae in the finger nails. Erythematous and pigmented rashes, irregularly demarcated, were found on the trunk. Neurological examination on admission showed almost absent deep reflexes, muscular weakness (proximal: mild, distal: moderate) and sensory impairment of all modalities in the extremities. Marked dysesthesia and hyperalgesia were also present. Deep sensation was completely absent. Gait was paretic and Gowers' sign was positive. No abnormalities in routine laboratory examinations were noted. The CSF protein was slightly elevated. Motor nerve conduction velocity in the extremities was definitely reduced (ulnar nerve: 42.5 m/sec and tibial nerve: 34.9 m/sec. Lower limits of normal range are 49 m/sec and 39 m/sec respectively). Arsenic in hair and nails was 90 ppm and 20 ppm (calculated in terms of arsenious acid). The normal ranges are 0.3—0.7 ppm and 1.5—4 ppm respectively.

Material and Methods

A fascicular sural nerve biopsy was performed. Immediately after excision, the specimen was fixed in 4% cacodylate buffered glutaraldehyde for 2 hours and then divided into two parts. One part was dissected into 10 blocks in the cacodylate buffer and postfixed in 2% OsO₄ for 2 hours, followed by acetone dehydration and embedding in Epon 812. Another part was fixed in 1% OsO₄ for 12 hours, washed thoroughly and placed into glycerin for teasing. Thick sections of each Epon block were stained by toluidine blue. Thin sections were stained by uranyl acetate and lead hydroxide. Electron micrographs were made with a JEM 7A electron microscope.

Results

Light Microscopy. Teased fibre preparations showed Wallerian degeneration as the main pathological change (Figs. 1 and 2). Vacuoles and osmiophilic droplets of degenerating myelin were detected in many nerve fibres. These myelin droplets were sometimes globular and distributed over the entire internodal segment. There was, however, some predominance near the nodes of Ranvier. Almost intact fibres were also present. Segmental demyelination was not present.

Transverse sections of Epon-embedded blocks showed a moderate reduction in the number of myelinated fibres (Fig.3). Many Schwann cells contained centrally located degenerated myelin ovoids of various sizes. Large ovoids could occupy almost the whole cytoplasm of a Schwann cell: small ovoids, which were sometimes eccentrically located, were found between the other organelles of the Schwann cells cytoplasm. Some Schwann cells, not associated with myelin sheaths, contained material lightly stained with toluidine blue. Onion-bulb-like structures, in which a single layer of the cytoplasm of a Schwann cell surrounded a core of a degenerating myelinated fibre, were very occasionally found.

These changes were present focally. In some places apparently intact myelinated and unmyelinated fibres and their Schwann cells were found. There was no evidence suggesting typical onion bulb formation.

In longitudinal sections changes similar to those seen in the teased preparations were seen. Many myelin ovoids, or myelin or myelin debris, as well as small vacuoles, were observed in the degenerating fibres (Fig.4).

Increase of collagen fibre bundles was not apparent. Fibroblasts, located near the epineurium, around the vessels and in the endoneurium, were not increased. Phagocytes were not obviously increased. Regions containing metachromatic material were not identified. There were no abnormalities in the capillary walls and perineurium.