Fine Structural Changes in the Sural Nerve of Patients with Acanthocytosis

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Summary. The fine structure of sural nerve biopsies is described in two brothers with normo-lipoproteinaemic acanthocytosis and an associated neurological syndrome. There was a severe reduction of myelinated fibres. The Schwann cells had an increased population of lysosomes and contained remnants of myelin. The myelin lamellae were often split at the intraperiod lines. Centrioles were found in Schwann cells, fibroblasts and endothelial cells. The significance of these findings is discussed.

Key words: Acanthocytosis — Sural Biopsy — Electron Microscopy — Demyelination.

Introduction

In 1967, Estes et al. reported a family with a new hereditary syndrome characterised by choreiform movements, wasting of the peripheral muscles of the limbs and a morphological abnormality of circulating erythrocytes. In affected members of the family the red cells had spicules which are characteristic of acanthocytes. There was no associated abnormality of serum lipid concentrations as occurs in the Bassen-Kornzweig syndrome (Bassen and Kornzweig, 1950). Similar features were present in the two other unrelated families which have since been separately reported (Critchley et al., 1968, 1970), but the aetiology of the syndrome remains obscure.

In the present communication we describe the ultrastructural abnormalities found in the sural nerves of two brothers with this rare syndrome. The clinical features have been reported elsewhere (Aminoff, 1972).

Case Reports

Case 1 (K 74817), aged 69 years, is the eldest of four sibs of a non-consanguineous marriage. In 1960 he developed weakness of the shoulders, his previous history having been uneventful. He had two grand mal convulsions in the following year and developed increasingly disabling involuntary movements of the face and limbs. In 1969 he complained of progressive weakness in the legs and then developed urinary retention with a flaccid bladder which necessitated sphincterotomy. He was reassessed in 1971 when examination revealed frequent choreiform movements of the face and limbs, marked wasting and weakness of the shoulder girdle and proximal limb muscles, absent tendon reflexes, flexor plantar responses and impaired vibration sense in both feet.

Case 2 (R 44591), aged 62, the brother of Case 1, has had involuntary movements of the face, limbs and trunk for six years. For the last three years he has required institutional care; over this time his gait has become unsteady, his speech slurred and swallowing difficult due to involuntary movements. He was admitted in 1971 when examination revealed facial
grimacing, choreiform movements of the limbs, wasted weak muscles of the shoulder girdle and the proximal muscles of the legs, absent tendon reflexes, flexor plantar responses and impaired vibration sense in both legs below the knees.

**Methods**

A sural nerve biopsy of each case was examined. They were cut into 1 mm³ pieces and immersed immediately in a mixture of 2% formaldehyde and 2.5% glutaraldehyde (one-half strength Karnovsky fixative) in 0.1 M cacodylate buffer at pH 7.4 for 4 h at 0–4°C. The tissue was washed overnight in 0.25 M sucrose in 0.1 M cacodylate buffer and then post-fixed in 1% (w/v) osmium tetroxide in phosphate buffer (pH 7.3) for 1 h. It was dehydrated in ethanol, treated with propylene oxide and embedded in Epon 812. Sections of 1 μm were stained with toluidine blue to select areas for electron microscopy. Thin sections were stained with uranyl acetate and lead citrate and examined with an AEI 801 electron microscope.

**Results**

Since the morphological alterations in both biopsies are very similar they will be described together.

Light microscopy reveals extensive demyelination of the nerves, an increase in the fibrous tissue and axonal damage.

A marked reduction in the number of myelinated fibres is readily apparent at electron microscopic examination; many fields do not have a single myelinated axon (Fig.1). Some of the myelinated fibres present are intact but others show advanced degeneration. Intact myelinated axons exhibit the normal distribution of organelles, display the structural integrity of the myelin lamellae and maintain their normal relation to the Schwann cells. The myelinated axons that undergo demyelination show varying degrees of alterations from small splits at the intraperiod lines to complete disruption and disintegration. These axons may contain swollen mitochondria, dense bodies, disintegrated filaments, damaged vesicles, vacuoles and debris (Fig. 2). Finely granular inclusion bodies surrounded by irregular mitochondria are occasionally seen in these axons; large, oval membrane-bound inclusions filled with glycogen-like particles may also occur. However, other axons with damaged myelin lamellae may have a normal distribution of intact organelles.

Numerous unmyelinated axons are present, encircled by one or more Schwann cell processes (Fig.1). Slender, plate-like processes of Schwann cells also form bands which do not contain axons (Fig. 1).

Schwann cells occasionally have large, indented and lobulated nuclei with prominent nucleoli (Fig. 3). The cytoplasm frequently contains numerous primary and secondary lysosomes (including large lipofuscin-like bodies), unidentifiable debris and inclusion bodies with a lamellar structure. Large inclusion suggestive of myelin remnants are present in Schwann cell processes (Fig. 4). Numerous small vesicles are found around the dilated Golgi cisternae (Fig. 3).

Fibroblasts are most numerous in areas adjacent to the perineurium and to the blood vessels. Some of them show signs of advanced degeneration with ballooned cisternae of the rough-surfaced endoplasmic reticulum, damaged mitochondria and heavy clumping of chromatin against the nuclear membrane. Mast cells occur frequently amongst the collagen fibres.