Hypertrophic Changes in Diabetic Neuropathy
R. H. M. Ball and P. K. Thomas
Institute of Neurology, London, England
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Summary. Observations have been made on 10 consecutive nerve biopsies from patients with diabetic neuropathy. 1 patient showed the typical appearances of hypertrophic neuropathy on light and electron microscopy. 5 displayed typical hypertrophic changes visible only on electron microscopy and minor abnormalities of a similar nature were seen in 2 others. It was considered that they were likely to have resulted from recurrent segmental demyelination.

Zusammenfassung. Beobachtungen an Nervenbiopsien bei 10 aufeinanderfolgenden Patienten mit diabetischer Neuropathie wurden unternommen. 1 Patient wies die für eine hypertrophische Neuropathie typischen licht- und elektronenmikroskopischen Veränderungen auf. 5 zeigten typische hypertrophische Veränderungen, die aber nur bei elektronenmikroskopischer Untersuchung sichtbar waren; bei 2 weiteren wurden ähnliche geringe Veränderungen entdeckt. Es wird angenommen, daß diese Veränderungen durch segmentale Demyelinisation verursacht wurden.


Following the original descriptions of hypertrophic neuropathy by Gombault and Mallet (1889) and Dejerine and Sottas (1893), considerable debate ensued as to whether the characteristic whorled “onion-bulb” cell formations were the result of the proliferation of Schwann cells or of fibroblasts. This has been resolved recently by a number of electron microscope studies in which it was demonstrated that the whorled formations are composed of concentric laminae of Schwann cells with intervening layers of collagen fibrils (Dyck, 1966; Garcia et al., 1966; Thomas and Lascelles, 1967; Webster et al., 1967; Weller, 1967). Although it has been realized that hypertrophic changes may occur in neurofibromatosis (Bielschowsky, 1922; Bailey and Herrman, 1938), in amputation neuromas (Krücke, 1949) and sometimes in isolated peripheral nerve lesions (Imaginário et al., 1964; Simpson and Fowler 1966), it has often been assumed that hypertrophic neuropathy is a distinct entity seen only in the hereditary hypertrophic neuropathy of Dejerine and Sottas and in Refsum's syndrome (e.g. Andermann et al., 1962; Greenfield, 1963). Austin (1956), Thomas and Lascelles (1967) and Webster et al. (1967) on the other hand, have suggested that hypertrophic neuropathy is a non-specific process, in view of the considerable variations in the clinical presentation of such cases. This is supported by the finding of hypertrophic changes in a patient with diabetic neuropathy (Thomas and Lascelles, 1966). Hypertrophic changes visible by light microscopy were only present in this one instance out of a series of eight nerve biopsies from patients with diabetic neuropathy that were reported and such changes have not been encountered in
biopsies from two further cases examined subsequently. It was therefore decided to examine these biopsy specimens by electron microscopy in order to establish whether hypertrophic appearances of lesser severity, not detectable by light microscopy, could be recognized.

The findings are presented in this report.

**Material and Methods**

Sural or radial nerve biopsies from ten patients with diabetic neuropathy were examined. Clinical details of Cases 1—8 have already been published (Thomas and Lascelles, 1966) and those for the additional two cases are given below. The portions of the biopsy specimens processed for electron microscopy were fixed by immersion for three hours at 4°C in a one per cent solution of osmium tetroxide in mammalian Ringer solution, buffered to pH 7.4 with veronal-acetate. After dehydration in graded concentrations of ethanol, part of the material was stained for 3 hours in a one per cent solution of phosphotungstic acid in absolute ethanol. The specimens were then embedded in Araldite and sections cut with a Porter-Blum MT2 ultramicrotome, mounted on carbon-coated copper mesh grids and examined with a Siemens Elmiskop I. Sections from the material not treated with phosphotungstic acid were stained on the grids for 10 minutes with a saturated aqueous solution of uranyl acetate followed by lead citrate for 10—15 minutes according to the method of Venable and Coggeshall (1965).

**Case Reports**

**Case 9 (Whittington Hospital No. C89153)**

W. M., a man aged 29, was admitted to the Whittington Hospital in June, 1966, for stabilization of his diabetes, which had been discovered in 1952 and treated since then with insulin. There was no family history of diabetes. He had no symptoms of peripheral neuropathy, but examination revealed absent ankle jerks and loss of vibration sense distally in the legs. Examination also showed a mild diabetic retinopathy and slight cataracts in both eyes. Bilateral ankle oedema was present, attributable to an early nephrotic syndrome. His blood pressure was 160/100 and his dorsalis pedis and posterior tibial pulses were readily palpable.

Nerve conduction was examined in the right lateral popliteal nerve. Conduction velocity in the fastest motor nerve fibres to the extensor digitorum brevis was within normal limits (40 m/sec). However, on stimulating the anterior tibial nerve at the ankle and recording from needle electrodes buried alongside the lateral popliteal nerve at the knee by the technique described by Gilliatt et al. (1961), no nerve action potential could be detected.

A sural nerve biopsy (Mr. L. Gracey) was performed on 30. 6. 1966.

**Case 10 (Whittington Hospital No. B83689)**

J. S., a man aged 55, was originally admitted to the Whittington Hospital in 1960 because of headache, blurring of vision and vertigo of sudden onset. Ataxia of the left arm and leg was observed on examination and he was found to be diabetic. His neurological symptoms subsided after 2—3 weeks and the diabetes was controlled by diet alone. He subsequently attended another hospital for treatment and was started on chlorpropamide in January, 1966. He was readmitted to the Whittington Hospital in October, 1966, because of progressive weakness of his legs which had begun about 3—4 months before and which was accompanied by aching pain in the thighs, most troublesome at night, together with a sensation of numbness in both feet and lower legs over the same period. He had also had intermittent numbness of the left hand. There was no family history of diabetes.

Examination in October, 1966, revealed reduced visual acuity in the right eye with some pallor of the right optic disc, but no other cranial nerve abnormality. There were no abnormalities of motor function in the arms, but he showed bilateral wasting of the thighs of moderate severity with proximal weakness in both legs, more marked on the right. The tendon reflexes in the arms were all obtainable but were sluggish, as were the knee jerks, and the ankle jerks were absent. The right plantar response was extensor, the left flexor. On sensory testing he