Intraneural neurofibromas involving the posterior interosseous nerve

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SUMMARY Two patients presented with a posterior interosseous nerve palsy with supinator weakness. In each case an intraneural neurofibroma was found proximal to the supinator tunnel with no other stigmata of von Recklinghausen's disease. Both tumours showed a whorl-like histological pattern that has been previously confused with onion-bulb structures in hypertrophic polyneuropathy. Electron-microscopy was useful for the pathological diagnosis. The prognosis and treatment of the lesions are discussed.

Isolated posterior interosseous neuropathy is uncommon. It frequently follows trauma (Mulholland, 1966) either with acute damage to the nerve or with compression due to insidious fibrosis (Sherrard, 1966). Freeing of the nerve from constricting bands of fibrous tissue may lead to complete recovery (Sherrard, 1966). Compression of the nerve by extrinsic tumours such as lipomas (Capener, 1966) or by a ganglion (Bowen and Stone, 1966) has also been described. The tendinous proximal portion of the supinator muscle may compress the posterior interosseous nerve in some cases (Capener, 1966) and recovery of nerve function may follow decompression of the nerve.

Intrinsic lesions of the posterior interosseous nerve have rarely been described. Their true incidence is not known as many of the reported cases of posterior interosseous nerve lesions have not been explored surgically (Hunstead *et al.*, 1958). Nevertheless, Osterasek (1947) described an atypical fibroma associated with a posterior interosseous nerve palsy. Subsequently two other cases of fibrous lesions have been recorded within this nerve (Whiteley and Alpers, 1959; Mulholland, 1966).

In this paper we present two cases of posterior interosseous neuropathy caused by intrinsic

nerve tumours. Both tumours have a whorl-like cellular pattern which has been compared with hypertrophic interstitial neuropathy (Imáginario, *et al.*, 1964; Simpson and Fowler, 1966). Histological and ultrastructural studies of our cases, however, allow a firm distinction to be made between the two conditions.

CASE 1

Miss M.P. was a 20 year old Portuguese student who presented in January 1972 with inability to extend the right middle and ring fingers and thumb. She first noticed the weakness five years earlier whilst playing the piano. There was no sensory disturbance or pain. Examination revealed wasting of the dorsal aspect of the right forearm with total paralysis of the digital extensors and the ulnar extensor of the wrist. Supination of the extended forearm was weak, but the radial extensor muscle of the wrist was normal. No other abnormality was found in either the central or peripheral nervous system. During surgical exploration the radial nerve was seen to be normal but there was a thickened segment of the posterior interosseous nerve, 20 mm long, proximal to where the nerve entered the supinator muscle. The capsule of the swelling was incised longitudinally and a small nerve fascicle, again with a bulbous swelling along its length, was taken for histology. Recovery from the operation was uneventful but no change in the clinical condition has occurred.

CASE 2

Mrs. P.F. was a 40 year old right-handed housewife

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FIG. 1. Case 1. Transverse sections of the swollen nerve fascicle showing cellular whorls up to 50 μ m diameter. Paraffin section stained with H and E, $\times 430$.

who presented in January 1972 with a 10 year history of gradually increasing weakness of the left hand with wrist drop. There was no pain or sensory disturbance. Examination revealed wasting of the extensor muscle mass in the forearm with selective weakness of the ulnar extensors of the wrist, supinator, digital extensors, and abductor pollicis longus. Radiographs of the chest, cervical spine and forearm were normal as was the blood picture. The erythrocyte sedimentation rate was 7 mm in the first hour and the blood Wassermann reaction was negative. Electromyography showed evidence of denervation of the

FIG. 2. Case 2. Transverse section of nerve showing whorl-like structures, some with hyaline centres (h), others with densely staining bands (*) and dense endoneurial collagen. Close to the whorls are clusters of regenerating fibres (cl) and further away are normal myelinated fibres. Araldite section stained with toluidine blue, $\times 430$.

muscles of the ulnar side of the forearm with a normal sensory action potential in a branch of the radial nerve.

A clinical diagnosis of right posterior interosseous nerve palsy was made and the nerve was explored. At operation a fusiform white swelling 12 $\times$ 7 mm was found situated 50 mm proximal to the supinator tunnel and a wedge biopsy was taken. The nerve distal to the swelling appeared slightly shrunken and

grey. No indication of compression from fibres of the supinator muscle or fibrosis was observed. The patient recovered well from the operation but no change in the clinical state has been seen and reconstructive surgery is contemplated.

CASES 1 AND 2 *Histological preparations* The specimen from case 1 was fixed in formalin, dehydrated, and embedded in paraffin wax. Transverse and longitudinal sections were stained with HE, PAS, Congo red, Van Gieson, Glees and Marsland silver stain for axons, and Loyez myelin stain. A wedge of tissue from case 2 was fixed in 3% glutaraldehyde in sodium cacodylate buffer, post-fixed in osmium tetroxide, dehydrated, and embedded in Araldite. One-micron longitudinal and transverse sections were stained for light microscopy with 1% toluidine blue. Thin sections were stained with uranyl acetate and lead citrate and examined in an RCA EMU4 electron microscope.

CASE 1 *Pathology* The specimen was a white cord-like structure 14 mm long with a fusiform enlargement 6 mm by 2 mm centred on its mid point. Microscopically, a transverse section through the widest part revealed an almost total loss of myelinated fibres from the fasciculus and a moderate increase in cellularity. The cells were elongated and formed whorls some 50 μ m in diameter (Fig. 1). No axons could be identified within the whorls. There was frequently a central core of argyrophilic, PAS-positive mucopolysaccharide in the whorls; this core had no discernible connection with any axon.

There was thickening and fibrosis of the endoneurial septa and the perineurium; the endoneurial collagen was also increased. No inflammatory cells were seen and the vessels appeared normal.

In longitudinal sections the lesion was seen to merge gradually with the nerve fascicle. At one end of the swelling the myelinated nerve fibres were well

FIG. 3. Case 2. An electron micrograph of a cellular whorl. The centre contains collagen and probably mucopolysaccharide. At least three cells (nuclei N) make up the whorl. Their processes interdigitate. Non-myelinated axons (a). Stained with uranyl acetate and lead citrate, $\times 4,000$.

preserved, while at the other end no myelinated fibres were seen.

CASE 2 *Light microscopy* A wedge biopsy 4 mm long, 1 mm deep, and 1 mm wide was taken from the swelling on the posterior interosseous nerve and embedded in Araldite. When examined microscopically, much of the specimen was composed of thickened epineurium containing blood vessels and normal, small nerve fasciculi. The sample of the main nerve showed extensive loss of large myelinated fibres; many of the small fibres were in clusters (Fig. 2), which suggests that they may be regenerating nerve sprouts (Ochoa and Mair, 1969b). Distributed among the myelinated fibres were structures that appeared as whorls when cut in transverse section. Some whorls had a lake of amorphous, pale staining material in the centre; others had deeply staining

bands within them (Fig. 2). No myelinated nerve fibres were definitely identified in the centre of any whorl or in any of its layers. There was an increase in the endoneurial collagen especially between the cellular whorls.

Electron microscopy The cells forming the whorls differed in several ways from normal human Schwann cells (Weller, 1967; Ochoa and Mair, 1969a). Ring shaped structures that were seen in transverse sections of the nerve were often formed by several cells (Fig. 3). Their processes interdigitated and frequently formed junctional complexes (Fig. 4). The centre of the cellular ring was occupied by collagen and fragments of amorphous material. Some of the collagen bundles were orientated circumferentially. The cytoplasm of the cells in the whorls stained more densely than the normal Schwann cells

FIG. 4. A cell from the whorl in Fig. 3. Many fibrils are present in the dense cytoplasm and there are junctional complexes (j) between interlocking cell processes. The basement membrane (b) is incomplete and there are fine extracellular fibres (f) associated with the cell surface. Schwann cell (SC). Uranyl acetate and lead citrate stained, $\times 7,700$.

and contained more fibrils (Fig. 4). Dark patches were seen on the inside of the plasma membrane (Fig. 4); these are similar to those seen in perineurial cells and in pericytes. Furthermore, the basement membrane was very incomplete around these cells in contrast with the complete basement membrane of the Schwann cell. Groups of fine fibrils, similar in size to those in the cytoplasm, were often associated with the plasma membrane of the abnormal cells.

In addition to the whorls, the abnormal cells were seen in compact groups sometimes around blood vessels. Those Schwann cells associated with normal axons, or with the occasional axon balloon, appeared normal. Scattered fibroblasts were seen and could be distinguished from the abnormal cells.

DISCUSSION

The histological appearance of the nerve swellings in the two patients presented here resembles that of the cases described by Imaginário *et al.* (1964) and Simpson and Fowler (1966). Both these groups of authors emphasize the similarity of the lesions to the hypertrophic neuropathy of Dejerine and Sottas. However, the swellings from the posterior interosseous nerve in our cases present a combination of features which excludes hypertrophic neuropathy. There is a marked loss of axons from the affected section of nerve; this is reflected in the histology by the sparsity of large myelinated fibres and by clusters of small regenerating fibres. Furthermore, electromyography of one case suggests denervation with no reduction of nerve conduction velocity in branches of the radial nerve. The cells forming the whorls differ in several respects from normal Schwann cells and most of the whorls have disorientated collagen or lakes of mucopolysaccharide at the centre.

These features differ fundamentally from hypertrophic polyneuropathy where the major pathology is widespread segmental demyelination (Thomas and Lascelles, 1967; Weller, 1967), which is reflected in the very slow nerve conduction times. The cells that form the whorls in hypertrophic neuropathy are very similar to normal Schwann cells and many contain non-myelinated axons (Weller, 1967). A demyelinated or partially remyelinated axon occupies the centre of many of the whorls. There is often an increase in endoneurial collagen. Lakes of mucopolysaccharide may be seen but these are

between the cellular whorls and not usually at their centre (Thomas and Lascelles, 1967).

It seems much more likely that these isolated nerve swellings are benign tumours and not a localized form of hypertrophic polyneuropathy. Whorl-like patterns have been described in peripheral nerve tumours (Bailey and Hermann, 1939; Harkin and Reed, 1969) and previous electron microscope reports have shown a close resemblance of the tumour cells to normal Schwann cells (Poirier *et al.*, 1968; Ohnishi and Nada, 1972). In the case that we have examined with the electron microscope, however, the tumour cells differ from normal Schwann cells in their cytological characteristics and in their relationships with other cells. They do not resemble fibroblasts but are more like perineurial cells.

Schwannomas and neurofibromas are usually distinguishable from one another, even though Schwann cells and perineurial cells appear to be major cell components of both tumours. Schwannomas tend to be encapsulated and separate from the nerve trunk (Harkin and Reed, 1969). Neurofibromas, on the other hand, are often plexiform and are intimately mixed with other nerve components (Poirier *et al.*, 1968). As in our two cases, this tumour may cause progressive axonal degeneration as it enlarges within the nerve. On the basis of these nosological criteria our cases are neurofibromata; but no other stigmata of von Recklinghausen's disease were detected.

Two previous histological studies of intrinsic posterior interosseous nerve lesions resemble our two cases; those described as an atypical fibroma by Otenasek (1947) and as interstitial fibrosis by Mulholland (1966). In the latter case, myxoid change was described in some areas. The intraneural swelling in Whiteley's and Alpers's (1959) case was thought to be a traumatic neuroma.

It is not clear why neurofibromata should arise at this particular site on the posterior interosseous nerve. There are several features in both cases that are against trauma being directly responsible. Firstly, the onset of the paresis was slow. Secondly, the nerve lesions in both cases were proximal to the usual site of compression by the supinator muscle (Capener, 1966). There was also some weakness of the supinator muscle, as

in Otenasek's case; much of the nerve supply to this muscle arises from the posterior interosseous nerve before it enters the supinator tunnel (Hollinshead and Markee, 1946). Thirdly, the histology does not resemble that of a traumatic neuroma (Harkin and Reed, 1969).

The prognosis of posterior interosseous nerve neuropathy varies very much with the pathology of the lesion. Recovery of nerve function is often complete when the nerve compression can be adequately relieved, as by the removal of a lipoma or other intrinsic factors (Sharrard, 1966). A small fascicular biopsy of an intraneural lesion may be very helpful in establishing a diagnosis and prognosis. The biopsies in our cases caused very little, if any, increase in muscular weakness. Once it can be established that the nerve palsy will not improve, plans can be made for possible excision of the lesion and reconstruction of the nerve.

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