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Progressive Peripheral Neuropathy in Patient with Primary Hyperoxaluria

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Summary

In a patient suffering from primary hyperoxaluria with oxalosis a progressive peripheral neuropathy was associated with intra-axonal deposition of microcrystals of calcium oxalate. Probably his neuropathy was the result of mechanical obstruction of axoplasmic flow.

Introduction

Primary hyperoxaluria is an autosomal recessive disorder in which the rate of formation of oxalate is up to three times greater than normal[1] and calcium oxalate crystals become widely deposited throughout the body.[2 3] Variation in the density of deposition of oxalate depends partly on the availability of calcium ions in local tissue.[4] Deposition of calcium oxalate crystals in nervous tissue has not been described in oxalosis. We describe here a case of primary hyperoxaluria in which peripheral neuropathy was a definite clinical and pathological feature.

Case Report

A 23-year-old man presented in April 1971 in advanced uraemia (glomerular filtration rate 5 ml/min). He had passed hundreds of small renal stones, often with renal colic, for about 10 years, and an older sister had a similar history. A high-dose intravenous pyelogram showed much calcification at the corticomedullary junctions. His parathyroid glands had been explored three years earlier and were normal. He was normotensive, and his reflexes were normal.

His uraemia could not be controlled by conservative measures, and he was admitted to the chronic haemodialysis programme. Over the next six months of apparently adequate dialysis (predialysis serum creatinine <884 μmol/l (10 mg/100 ml)) his arm and leg tendon reflexes diminished and disappeared permanently. Nerve conduction studies showed gross slowing of conduction. Painful paraesthesiae and weakness of his legs prevented walking. Repeated episodes of ventricular arrhythmias occurred, and in January 1974 he suffered a cardiac arrest and died. He had taken 2 mg pyridoxine daily throughout the entire period of intermittent dialysis.

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NECROPSY

The heart weighed 525 g; the ventricles were considerably thickened, and their cut surfaces were gritty. The kidneys were moderately atrophied, with numerous small (1-3 mm) stones in the calices and throughout the parenchyma. The retia testes had gritty cut surfaces.

Paraffin sections were stained with haematoxylin and eosin. Sections of psoas and gastrocnemius muscle were stained for lactate dehydrogenase, reduced diphosphopyridine nucleotide diaphorase,[5] and myosin adenosine triphosphatase.[6] Teased nerve preparations were made from sciatic and peroneal nerve, and were stained with 1% osmium tetroxide.[7] Oxalate crystals were shown in sections using polarized light. They had the appearance of broken plates or of sheaves and rosettes of needles.

Heavy deposits of calcium oxalate crystals were seen throughout the renal parenchyma, the retia testes, the myocardium, and the media of the aorta and arterioles in all organs except the brain and meninges. Moderate deposits were present in the seminiferous tubules, thyroid, and voluntary muscle. Sparse deposits were present in the bronchial cartilage, bone marrow and trabeculae, parathyroids, pancreas, prostate, gastric submucosa, and choroid plexus. Sections of psoas and gastrocnemius muscle showed deposits within the endomysium which were surrounded by prominent foreign-body granulomata. The arterioles of these muscles contained deposits within the media and the intima; marked intimal proliferation had often occluded the lumen. Groups of muscle fibres showed typical neurogenic atrophy (fig. 1). Parts of the muscle showed ischaemic changes.

Teased nerve preparations of both sciatic and peroneal nerve showed deposits of calcium oxalate within the endoneurium. Single leaflets of crystals tended to lie in the longitudinal axis of nerve fibres (fig. 2) and many axons contained multiple crystals along their length.

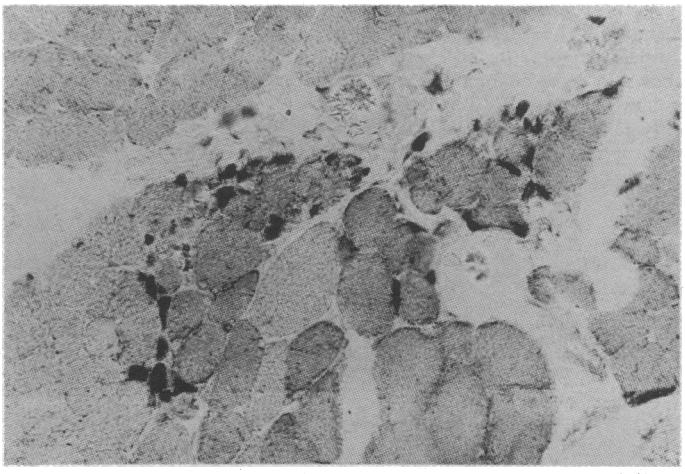

FIG. 1—Groups of atrophied fibres in psoas major muscle showing strong activity for lactic dehydrogenase. (×10.)

Irregular swellings of the axons were seen (fig. 3), and there was severe demyelination.

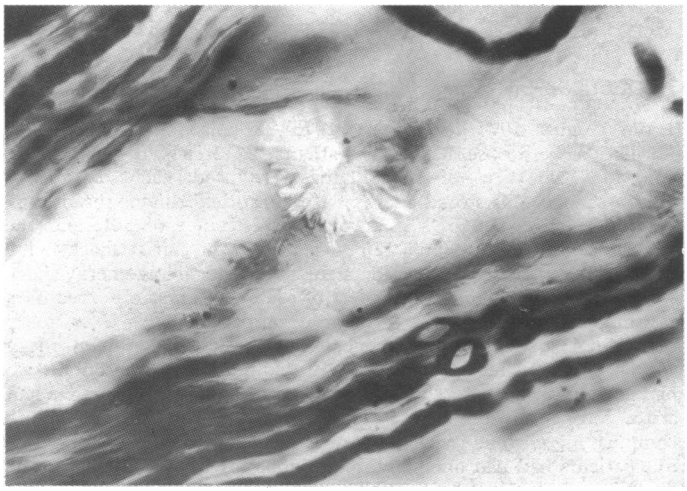

FIG. 2—Teased nerve preparations showing rosettes of oxalate crystals within perineurium and single leaflets of oxalate crystals within axon. (Osmium tetroxide. ×285.)

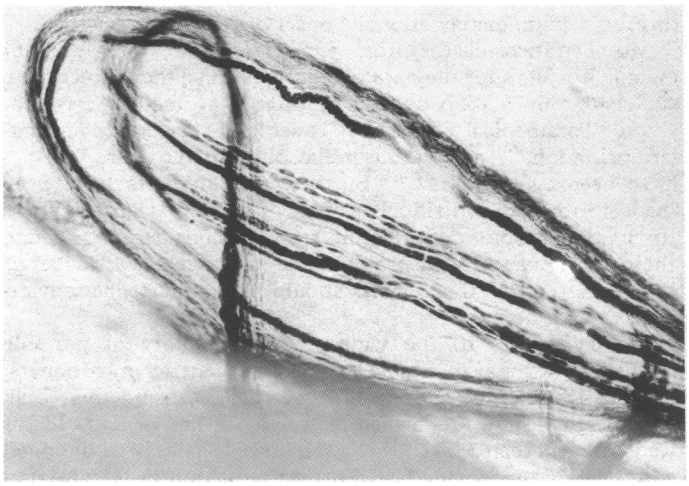

FIG. 3—Teased nerve preparation showing severe demyelination and irregular swelling of axons. (Osmium tetroxide. ×57.)

Discussion

Our general necropsy findings did not materially differ from those in the literature except in the nervous system. The failure of clinical response to adequate dialysis has already been noted.[8] In our patient peripheral neuropathy began at about the time intermittent haemodialysis was first started and progressed throughout life.

The most striking feature was the presence of microcrystals of calcium oxalate actually within axons (fig. 2). There is little doubt that such crystals, which are about the same diameter as the axon, would interfere with normal axoplasmic flow. The axonal migration of protein takes place in various peripheral nerves and in the central nervous system[9] and is essential to the viability of distal parts of the axon. It is possible that a microcrystal of calcium oxalate proximally placed would suffice to impair the function of an axon considerably more distally if axonal circulation were only incompletely obstructed. Demyelination of the peripheral nerve in our case was probably a secondary event.

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PRELIMINARY COMMUNICATIONS

Electrical Requirements for Ventricular Defibrillation

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Summary

Most deaths from ischaemic heart disease are sudden, occur outside hospital, and result from ventricular fibrillation. But defibrillators have only limited availability because of their size and weight. A miniature defibrillator has been developed. A single low-energy shock succeeded in removing ventricular fibrillation in 73 out of 82 episodes, and a further shock was successful in seven more episodes. Primary ventricular fibrillation probably always responds to low-energy electrical shocks, which challenges the conventional view that correction of ventricular fibrillation requires high-energy direct-current shock. Thus even smaller and lighter defibrillators are possible. Furthermore low-energy shocks cause less myocardial damage.

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Introduction

Ischaemic heart disease is the major cause of premature death in the Western world. Over 60% of the deaths from acute coronary attacks among middle-aged and younger people occur within one hour of the onset of symptoms,[1] and more than 90% of these sudden deaths result from ventricular fibrillation.[2 3] The limitations[4-6] of prophylactic antiarrhythmic therapy in the prevention of sudden deaths are probably related to the