Neuromuscular Involvement in Pituitary Gigantism

P. D. LEWIS

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Summary

Investigation of two pituitary giants complaining of severe muscular weakness showed a peripheral neuropathy in both cases. Histological appearances suggestive of myopathy were also present in one case.

Introduction

Initially, the muscles of pituitary giants are often disproportionately well developed (Ford, 1966). They may be extremely powerful, and careful examination shows no suggestion of myopathy (Sacrez, Levy, and Bernardy, 1958). Later, fatiguability and weakness become severe, and muscular wasting may be prominent. Pituitary-adrenal insufficiency is usually proposed as the cause of the motor symptoms in these patients (Montgomery and Wellbourn, 1963; Grollman, 1964), but this can hardly explain the muscular atrophy which is seen, particularly when in some instances shoulder girdle and distal limb muscles are electively involved (Prezio, Griffin, and O'Brien, 1961).

Detailed clinical and neuropathological information about such cases is lacking, and the purpose of the present report is to describe the cases of two pituitary giants who came under neurological observation.

Case 1

A 26-year-old man was admitted to hospital complaining of being unable to walk for four months. Excessive growth seems to have begun between the age of 5 and 7 years. Shortly after his seventh birthday he developed an acute illness with headache, photophobia, drowsiness, and a left external rectus palsy. At this time his height was 52 in (132 cm) and his weight 74 lb (33·5 kg). Coarse features and large digits were noted. No cause for his illness was found, and he recovered fully within a few weeks. In view of the clinical suggestion of gigantism and acromegaly his pituitary fossa was radiographed and lumbar air encephalography performed, but no abnormality was detected.

His growth over the next 12 years was excessive; by the age of 14 he was taller than his schoolteachers, and by 20 his height had reached 7 ft 4 in (2·24 m). He remained in reasonable health until five months before his admission to the Hammersmith Hospital, when he developed an indolent chest infection which made him weak and lethargic and necessitated inpatient treatment at another hospital for a month. He found walking difficult because of weakness of the legs, and over the next three months he became unable to stand and bedridden. On readmission to hospital he was noted to have acromegalic features. There was some evidence of hypopituitarism, urinary ketosteroid and ketogenic steroid excretion being low, though his serum cortisol level was normal. He was treated with cortisone 37·5 mg daily and transferred to the Hammersmith Hospital for a fuller assessment.

On admission he was seen to be a pituitary giant with acromegalic facial features and extremities. Optic fundi were normal and visual fields were full. His dorsal spine was kyphoscoliotic, and there was obvious arthritic change in the left elbow, fingers, left hip, and both knees. Bilateral footdrop with contracture of the Achilles tendon was present. All limbs showed muscle wasting, affecting girdle and distal musculature electively, but involving also the intermediate parts. The wasted muscles were all weak. Tendon reflexes were barely elicitable in the upper limbs, while knee and ankle jerks were absent. Plantar responses were flexor. Vibration was not sensed at the ankles, and joint position sense was reduced in the toes. The ulnar and anterior tibial nerves were thickened to palpation. Abnormalities on investigation were a mild normochromic anaemia (haemoglobin 11·2 g/100 ml; very high serum growth hormone level (330 μ1U/ml); normal creatine phosphokinase (4 1U/l.); and gross, symmetrical enlargement of the sella turcica on skull x-ray film. Electromyographic sampling of several proximal and distal muscles in upper and lower limbs showed a reduced interference pattern in all the muscles examined, while brief-duration polyphasic potentials were recorded from the biceps and fibrillation from the quadriceps. Motor conduction velocity in the right ulnar nerve was reduced to 35 m s^{-1} (normal 54·5 $\pm$ 5·5 m s^{-1}), while the ulnar nerve action potential recorded at the wrist after stimulation of the little finger measured 4 μV (normal 7-20 μV) and had a latency of 5 msec (normal 2·2-3·4 msec).

Histological examination of tissue taken from the left gastrocnemius showed great variation in muscle fibre size with rounding off of fibres and pronounced increase of connective tissue, the overall appearance being myopathic. Random enlargement of fibres up to 130 μm in diameter and many atrophic fibres were seen, sometimes in groups reminiscent of denervation atrophy. Occasional necrotic fibres were present. Sarcolemmal nuclei were increased, central nuclei and short nuclear chains were common, and some weakly basophilic fibres showed vesicular nuclei with prominent nucleoli, suggesting regeneration. Ringbinden were present. Glycogen was not increased. Intramuscular nerve bundles contained reduced numbers of axons and myelin sheaths and greatly increased endoneurial collagen. Fibroblast nuclei were increased in number. No "onion-bulb" formations were present.

Histochemical examination of cryostat sections of the same tissue revealed very marked, patchy atrophy of type II fibres, which was interpreted as a possible consequence of denervation. Type I fibres showed a wide variation of fibre diameter and contained increased quantities of acid phosphatase. Target fibres were absent.

Stained sections of a fascicle of sural nerve taken at the same time as the muscle biopsy showed a moderate loss of large myelinated fibres and increased endoneurial collagen. There was no Schwannian overgrowth and no "onion-bulb" formations. Segmental demyelination was not visible in longitudinal sections, though paranodal widening was seen.

It was concluded that the patient's weakness could be attributed to a combination of myopathy and peripheral neuropathy. He improved with intensive physiotherapy to the extent of being able to walk short distances with support, but his weakness remained severe over the next three months.

Case 2

A 23-year-old man from overseas presented with increasing difficulty in walking of five years' duration. He was first noted to be growing excessively in early childhood, and by the time he was 23 he was 8 ft $0\frac{3}{4}$ in (2·46 m) tall. At the age of 18 pituitary ablation by a radioactive implant was carried out, and soon afterwards he developed an insidiously progressive weakness of the legs, associated with pain in the calves and feet, which ultimately restricted his walking to no more than 100 metres.

Examination showed a giant with coarse features but no clear signs of acromegaly. Visual fields and optic fundi were normal. He showed wasting of the small muscles of the hands, more pronounced on the right than the left affecting both median and ulnar innervated groups. The wasted muscles were moderately weakened. Wasting of the forearms and mild weakness of finger flexion and extension were present. Shoulder girdle and proximal upper limb muscles were not wasted, but their power was less than normal.

Departments of Medicine (Neurology) and Pathology, Hammersmith Hospital, London W.12

P. D. LEWIS, M.D., M.R.C.P., Consultant Pathologist

The lower limbs showed gross loss of muscle bulk below the knees on both sides, the right side again being worse affected than the left. The affected muscle groups, especially the distal ones, were weak. The proximal muscles were less obviously affected, but there seemed to be some wasting of the quadriceps and weakness of knee extension and flexion.

Tendon reflexes in all limbs were reduced to flickers. Plantar responses were absent. Sensory testing showed bilateral impairment of pinprick and touch sensation distal to the ankle, depressed vibration sense from mid-tibia downwards, and minimal reduction of joint position sense in the toes. Peripheral nerves were thicker than normal. Electromyographic examination (Dr. P. M. Le Quesne) showed evidence of severe denervation of tibialis anterior and gastrocnemius, in which there was profuse fibrillation and very few motor units under voluntary control. The latency of one unit after stimulation of the lateral popliteal nerve at the head of the fibula was 6 msec (normal), indicating that there was no slowing of conduction in surviving nerve fibres. No motor units were present either under voluntary control or following nerve stimulation in muscles of the dorsum and sole of the foot. Median nerve conduction velocity in the forearm was 59 m s^{-1} (normal).

The patient was considered to have a chronic polyneuritis. He returned to his homeland and no further information is available.

Discussion

The findings in these two patients suggest that neuropathy and myopathy may be responsible for the disabling weakness which develops in the later stages of pituitary gigantism. The occurrence of neuropathy in this disorder seems to have been described only in Humberd's (1937) report of the Alton giant. In this patient, all sensory modalities were absent in the feet, while pain and temperature sensation were lost below mid-calf level. Trophic ulceration of the feet was linked to this abnormality. The precise nature of the neuropathy in the Alton giant and the present cases is uncertain, and it may be that the group is a heterogeneous one. Thus Case 1 had marked slowing of nerve conduction, suggesting segmental demyelination, while Case 2 had a normal nerve condition velocity. In Case 1 segmental demyelination was not confirmed at biopsy, and the findings—loss of large myelinated fibres and increased endoneurial collagen—must be regarded as non-specific. Similar but less severe changes have been described in the sural nerve of an acromegalic (Stewart, 1966); it is tempting to suggest an effect of growth hormone on endoneurial fibroblasts as a primary event, though how connective tissue overgrowth so induced could cause loss of axis cylinders and myelin sheaths is unexplained.

Peripheral neuropathy seems to have been the major disturbance producing weakness in Case 2, but accounts for only a part of the neuromuscular disturbance in Case 1. Although the muscle in this case showed areas of grouped fibre atrophy, indicating denervation, the main pathological alterations were those of a myopathy. Primary muscle disease in pituitary giants, although suggested by an illustration in Kinnier Wilson (1955) and the report of Prezio *et al.* (1961), has not been well documented. In contrast, acromegalic myopathy has become widely recognized (McCullagh and Hewlett, 1947; Mastaglia, Barwick, and Hall, 1970).

The present cases show that more than one mechanism may possibly be implicated in the weakness of pituitary gigantism. Peripheral nervous involvement seems to be the predominant abnormality, however, and in view of recent observations apparently linking myopathic changes to primary denervating processes (cf. Bradley, 1971), it may indeed be the only lesion. Nevertheless, the pathogenesis of the neuropathy and myopathy in this condition, and their possible interrelation, awaits further study.

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PRELIMINARY COMMUNICATIONS

Ultrasonically-guided Liver Biopsy

S. NØRBY RASMUSSEN, H. H. HOLM, J. KVIST KRISTENSEN, H. BARLEBO

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Summary

A method is described of fine-needle aspiration biopsy of liver metastases under direct guidance by ultrasonic scanning. Comparing the results with this technique and those with liver biopsy by Menghini's method in 18 cases, we found that it was more accurate than the usual blind method.

Ultrasonic Laboratory, Department of Surgery and Department of Pathology, Gentofte Hospital, DK-2900 Hellerup, Denmark
S. NØRBY RASMUSSEN, M.D., Research Fellow in Ultrasound
H. H. HOLM, M.D., Chief Surgeon
J. KVIST KRISTENSEN, M.D., Research Fellow in Ultrasound
H. BARLEBO, M.D., Research Fellow in Pathology

Introduction

Advances in ultrasonic techniques (Holmes and Howry, 1963; McCarthy *et al.*, 1970; Holm, 1971) have made it possible to locate focal liver lesions as small as 2 cm in diameter. We have recently devised a method of using ultrasound as an aid to greater accuracy in obtaining specimens for biopsy (Holm *et al.*, 1972). This paper describes a preliminary trial of its use in 18 patients diagnosed by ultrasonic scanning as suffering from malignant metastases in the liver.

Equipment and Technique

The ultrasonic scanning equipment used was a modified Hewlett-Packard Diagnostic Sounder 7214-A, a modified Tektronix 564 Storage oscilloscope, and an Escoline-B-scanner. The transducer used for the puncture (2 megacycles per second, 20 mm in diameter, focused at a distance of 10 cm) has been described in detail (Holm *et al.*, 1972). It is perforated by a central canal with an internal diameter of 2·5 mm. When taking a liver biopsy specimen a reduction tube with an inner diameter of 1·6 mm is fitted into the canal.