J. Neurol. Neurosurg. Psychiat., 1971, **34**, 93-97

Familial muscular dystrophy of late onset

PAUL A. BACON AND BARBARA SMITH

From St. Bartholomew's Hospital and Medical College, London

SUMMARY Two related cases of a proximal muscular dystrophy are described with the full post-mortem findings in one of them. The strong family history is recorded. The condition was clinically predominant in the proximal limb muscles and showed an autosomal dominant type of inheritance with complete penetrance.

A classification of muscular dystrophies into three main groups, plus some rarer distal and ocular types, on a clinico-genetic basis has recently been proposed by Walton and Gardner-Medwin (1969). However, these authors agree that not all cases can be fitted into such a classification and suggest that further case and familial studies are needed in these instances. We describe here two cases of muscular dystrophy with a strong family history which appears clinically closer to the 'limited quadriceps myopathy' first reported by Bramwell (1923) than any of the above categories.

CASE 1

H.G., a 48 year old man, was admitted to hospital in deep coma in January 1970, with a history of severe headache followed by sudden collapse. The cerebrospinal fluid was heavily blood-stained and he died 12 hours later. He was noted to have marked symmetrical wasting of upper arms and quadriceps muscles with apparently normal musculature elsewhere. There was no spontaneous movement and he was areflexic so that no estimation of muscular power was possible. The following history was obtained from his wife.

He had had a normal active childhood until, at the age of 18, some weakness of the upper arms was noted at an army medical examination. This caused him no disability then, but by the time of his marriage when aged 25, he had obvious weakness of his upper arms on exertion, although he was able to perform everyday tasks normally. At the age of 28, he first noted weakness of the right leg and soon after of the left. The weakness increased very slowly for the next 15 years, but remained confined to the upper arms and thighs. It had been apparently static for the past five years. He was able to walk with the aid of knee calipers and a pair of sticks, travelling to work regularly on public transport. His grips and hand movements remained very strong, in contrast to his upper arms, so that he could perform his work as a clerk with no difficulty. He had never experienced muscle pain or tremor.

CASE 2

D.H., a 66 year old woman, a first cousin of case 1, was visited in her own home. She had a normal active childhood and at the age of 15 started work which included heavy lifting. She first noted weakness in her thighs at the age of 21, when her knees 'gave out' after walking two miles. The weakness progressed insidiously until she injured her right knee in a fall when 43 years old. Recovery from this traumatic arthritis was slow because of her thin weak quadriceps and she was left with a flexion contracture at the knee. After this she was unable to walk upstairs but could still get around the house holding on to furniture. Definite weakness of the upper arms was first noted at this time. In 1951 she was given a course of cortisone with no effect on the weakness. Eight months later after a further fall she had acute low back pain and since then she has not walked. The weakness of the arms progressed insidiously, gradually involving the shoulders as well, but the forearms and hands remained strong so that she could perform much of her housework from her wheelchair, including ironing clothes and preparing food. She had recurrent back pain, but was able to sit upright unsupported, and had no respiratory difficulties. She had had no muscle pain or skin rash, and no paraesthesiae or numbness.

On examination, she had normal facial musculature, sternomastoid muscles, and trapezii. There was chest deformity due to marked lordosis with some scoliosis. Both scapulae were winged, with wasting and weakness of deltoids, pectoral muscles, and serrati. The upper arms were very thin with no triceps contraction visible. The biceps muscles were wasted and weak, but visible contraction was present and she was able to flex the elbow against gravity. Both triceps and biceps reflexes were absent. The forearms appeared normal with strong grips and finger movements, although pronation and supination were somewhat weak. The supinator jerks were present but sluggish. Trunk muscles appeared strong but hip movements were all weak, although assessment was hampered by severe lumbar spine and sciatic pain. The quadriceps muscles showed only a flicker of contraction but no knee extension and knee jerks were absent. The hamstrings were also weak, but knee flexion against

gravity was present. The calf muscles were well developed in contrast to the wasted thighs, with normal plantar flexion, inversion and eversion of the feet, but weak dorsiflexion. Toe movements were normal. The ankle jerks were present but diminished, the plantar reflexes were flexor and there was no sensory loss.

She had attended another hospital many years previously and was unwilling to be investigated further.

FAMILY HISTORY This is shown in Fig. 1. The common grandmother of the two cases had died of a stroke aged 69, with no history of muscle disease. Little information could be obtained about the grandfather who had not been seen since the birth of his last child, but there was no definite history of muscular weakness. This couple had nine children, of whom at least four had been affected by a similar muscle disorder. The oldest two brothers had both been severely affected. In D.G. the arms were chiefly involved with only minor leg weakness, but in P.G. the arms and legs were markedly involved, so that he was unable to walk after middle age. The third brother emigrated in his late teens. He was unaffected then, but has not been heard of since. The fourth brother, O.H.G., the father of case 1, was again affected more in the arms than the legs. All the brothers retained strong grips and hand movements in spite of upper arm involvement and all lived until the age of 60 or more. The sisters were apparently affected to a lesser degree. The oldest sister S.G. had weakness of the arms but not as severe as her brothers. She died at the age of 88 and was able to walk unaided until then. The next two sisters died aged over 80 and both they and the two younger sisters, who are alive, were not affected by the muscular weakness.

The third generation consists of three separate families. The unaffected sister M.G. had six children all of whom are alive and apparently unaffected. The oldest sister and the youngest brother both married unrelated spouses and each produced one child, D.H. and H.G., who are described above. The only known members of the fourth generation are the two teenage children of H.G. who have been personally examined by one of us (P.A.B.). Both are healthy children of above average athletic ability. Neither showed any evidence of muscular weakness or neurological disturbance. Their haemoglobin, ESR, and serum muscle-enzymes (SGOT and CPK) are within normal limits.

PATHOLOGY The patient (case 1) had died from a large pontine haemorrhage and the heart showed left ventricular hypertrophy.

There was marked wasting of the upper arms and of the quadriceps muscles. The muscles of the forearms and lower legs were rather more prominent than normal. When the muscles were dissected out, the triceps brachii and the quadriceps femoris muscles were extremely pale, and although the shape of the muscle was retained, it was smaller than normal and was obviously largely replaced by adipose tissue. Beneath the pale quadriceps, which appeared to represent rectus femoris, vastus lateralis and vastus medialis, there was a macroscopically normal vastus intermedius muscle (Fig. 2).

Histology of the muscles was variable, but could be divided into three groups. Group A consisted of the left biceps humeri, the left and right flexor digitorum longus, the psoas, the vastus intermedius, and the biceps femoris muscles. In these muscles the changes were oedema, central nuclei and some swollen fibres (Fig. 3). Group B consisted of the left and right deltoids, the right pectoralis major and the sartorius muscles. In this group the changes were more marked. There was variation in fibre size with some fibre loss and replacement by adipose tissue, and a great deal of oedema and nuclear migration (Fig. 4). Group C consisted of the left and right triceps, the right biceps, the rectus femoris, and the adductor magnus muscles. In these muscles there were very few fibres left, and they were almost completely replaced by adipose tissue (Fig. 5). Sections from all groups showed an occasional necrotic fibre and a few small collections of inflammatory cells. Silver preparations of the pectoralis major muscle showed a normal terminal innervation.

DISCUSSION

This appears to be a genetically determined form of muscular dystrophy coming on in adult life, with a clinically localized distribution.

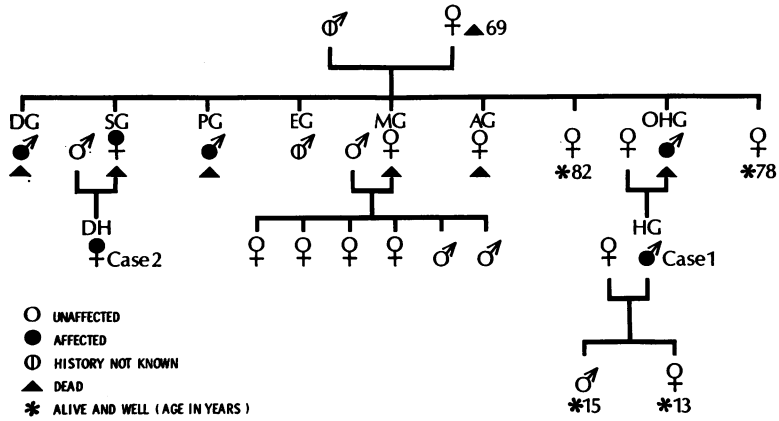

FIG. 1. *The family tree of cases 1 and 2 showing the other affected members in the second generation. All members of the third generation except the two cases described are alive and well.*

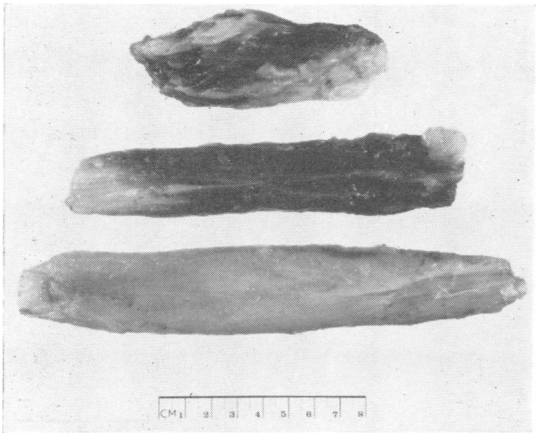

FIG. 2. *Three muscles removed from the right thigh. From above down they are the vastus intermedius, the sartorius and the rectus femoris. The first two are normal in colour, but the rectus is pale and almost completely replaced by adipose tissue.*

It is probably a similar type of condition to that which has been described under the title of quadriceps myopathy (Bramwell, 1922; Denny-Brown, 1939; Walton, 1956; Turner and Heathfield, 1961). In none of the other recorded cases has there been a positive family history. All the cases except one have had clinical weakness confined to the lower limbs, but one case described by Turner and Heathfield (1961) had weakness of the triceps muscle. Histologically one of Walton's (1956) cases showed muscular dystrophy, but the findings in those of Turner and Heathfield (1961) were interpreted as polymyositis.

The differential involvement of the quadriceps with relative sparing of the vastus intermedius muscle is interesting. This same sparing has been seen in another personal case in which both the vastus medialis and intermedius muscles were biopsied. Walton (1956) reported atrophy of the vastus medialis and hypertrophy of the vastus lateralis muscle in two patients.

One of the problems of interpreting muscle pathology is the extreme infrequency in the literature of

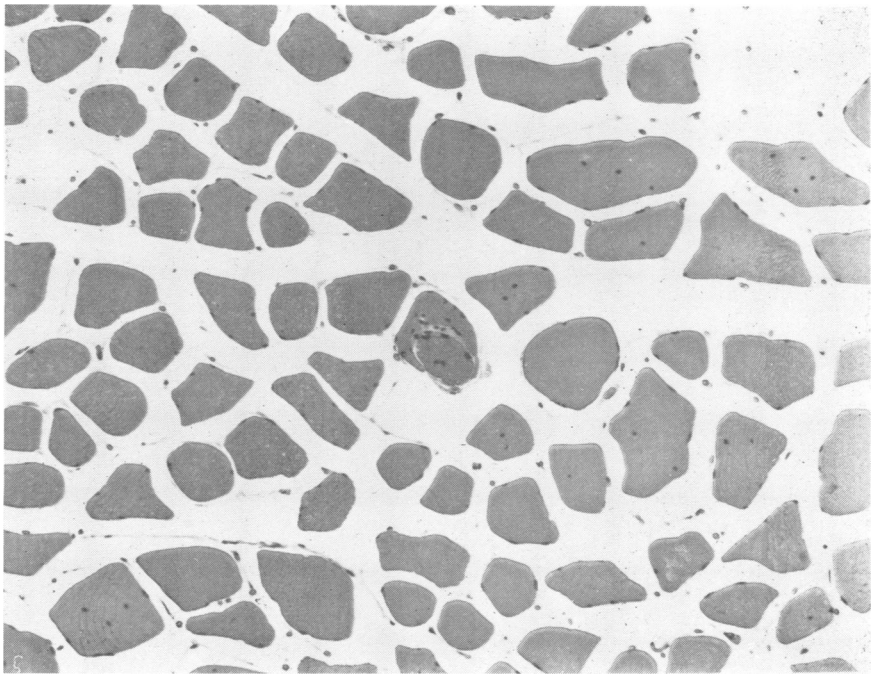

FIG. 3. *A section from the right psoas muscle. There is some oedema, an abnormal variation in fibre size and a number of central nuclei. The fibre in the centre is necrotic.* $\times 150$.

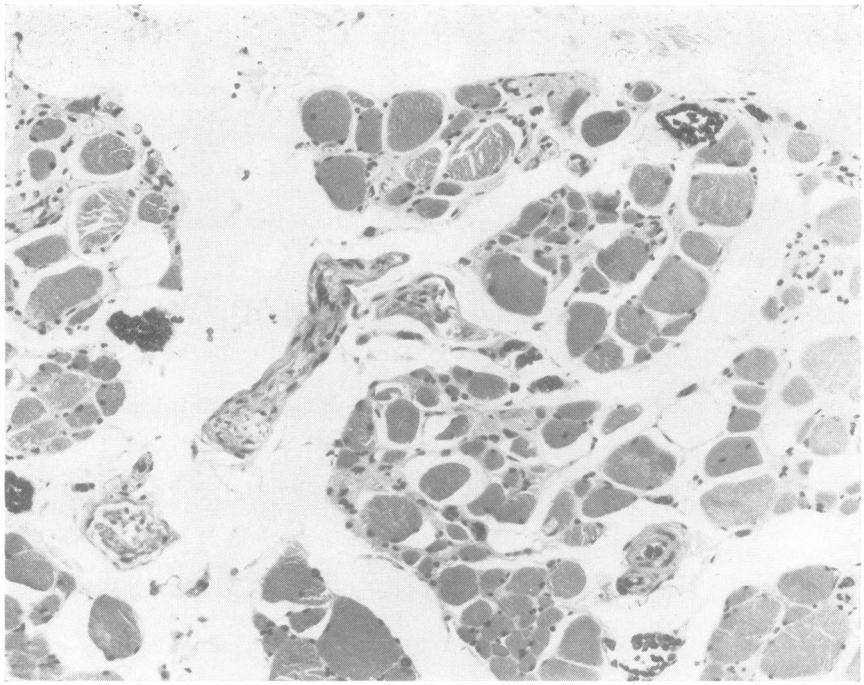

FIG. 4. *A section from the left deltoid. There is variation in fibre size and some fibres are lost with fat and fibrous tissue replacement.* ×150.

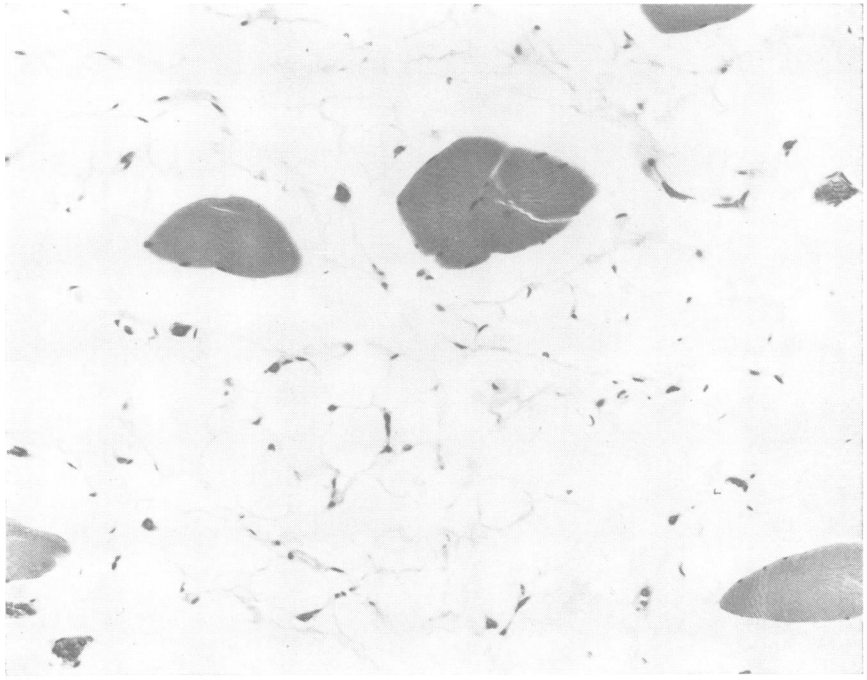

FIG. 5. *A section from the left adductor magnus. This muscle is largely replaced by adipose tissue, only a few single fibres remaining.* ×150.

cases in which a post-mortem investigation of a large number of muscles, including those clinically unaffected has been done. This may lead to cases which are confined to one group of muscles at the time of examination and show dystrophy on muscle biopsy being interpreted as local disease. In the case described here, the clinically unaffected muscles were all histologically abnormal, although much less so than the weak and wasted ones. It is thus in fact a generalized disease. This is borne out by the late spread of clinical weakness to the shoulder and pelvic girdles in case 2. Case 1 of Turner and Heathfield (1961), when examined by Denny-Brown in 1939, had only quadriceps weakness but 22 years later showed involvement of triceps and to a minor extent of shoulder girdle and trunk muscles. The cases of Bramwell (1922) and Walton (1956) were younger and their later history is not described.

The family history and histology of these cases suggest that it is a form of muscular dystrophy with an autosomal dominant type of inheritance with complete penetrance. The finding of at least four affected siblings out of nine is in keeping with this as is the fact that both the affected siblings who had children passed on the disorder to their solitary child while the unaffected sister M.G. produced a family of six unaffected children. This suggests that the children of H.G. (case 1) are highly liable to develop the disorder in time. It also suggests that the grandfather of our two cases must have been affected but unfortunately nothing further could be discovered about him.

The autosomal dominant inheritance with complete penetrance is seen in facio-scapulo-humeral dystrophy. Neither of our cases or their relations had involvement of the facial muscles and the predominant clinical involvement of the proximal limb muscles suggests that this is a different, though related, disorder.

We are very grateful to Dr. G. W. Hayward for permission to report the case under his care and to Mr. P. Crocker, Mr. P. Cull, and Mr. D. Tredinnick for the preparation of the illustrations.

REFERENCES

Bramwell, E. (1923). Observations on myopathy. *Proc. roy. Soc. Med.*, **16,** 1-12.

Denny-Brown, D. (1939). Myopathic weakness of quadriceps. *Proc. roy. Soc. Med.*, **32,** 867-869.

Turner, J. W. A., and Heathfield, K. W. G. (1961). Quadriceps myopathy occurring in middle-age. *J. Neurol. Neurosurg. Psychiat.*, **24,** 18-21.

Walton, J. N. (1956). Two cases of myopathy limited to the quadriceps. *J. Neurol. Neurosurg. Psychiat.*, **19,** 106-108.

Walton, J. N., and Gardner-Medwin, D. (1969). Progressive muscular dystrophy. In *Disorders of Voluntary Muscle*, edited by J. N. Walton. (2nd edition.) Churchill: London.