

Neurogenic scapulo-peroneal syndrome in childhood

RUDOLF MERCELIS, JOHAN DEMEESTER, AND JEAN-JACQUES MARTIN

From the Born-Bunge Foundation, the Universitaire Instelling Antwerpen, Antwerp, and the Dominique Savio Instituut, Gits

SUMMARY Two brothers presented with a slowly progressive scapulo-peroneal syndrome starting in early childhood. Initially there were myopathic EMG changes, but these changed to those of denervation. Neuromuscular biopsies at an interval of five years confirmed the neurogenic character of the muscle atrophy.

Muscle weakness and atrophy in scapulo-peroneal distribution is a heterogeneous group of neurogenic and myogenic disorders with different modes of inheritance.¹ We report a scapulo-peroneal syndrome affecting two brothers in whom diagnosis was made difficult by contradictory initial electromyographic and biopsy findings. A second evaluation, five years later, allowed the cases to be classified as neurogenic.

Case reports

The two patients were the second and the fourth sons in a sibship of five brothers. Information concerning the family was limited. The parents were not related. The father died at the age of 35 years from a brain tumour. Six brothers of the mother died of unknown causes shortly after birth or during the first year of life. In the sibship, three brothers, respectively aged 18, 14 and 9 years in 1979, were healthy. Clinical and electromyographic investigations (EMG) on the 14 year old brother were normal. The two affected brothers were examined in 1972, 1977 and 1979.

Case 1 *FV*, was born in June 1963. He came to our attention aged 9 years for evaluation of a stepping gait and shoulder girdle weakness. Walking was delayed until aged 3 years and never had been normal. Examination confirmed a scapulo-peroneal distribution of weakness. Laboratory studies included normal creatine kinase serum levels and electrocardio-

gram, a myogenic EMG with a 25% shortening of the mean potential duration in the tibialis anterior and deltoid muscles, and a nerve and muscle biopsy was taken. When aged 12 years motor conduction velocities (MCV) in the lateral popliteal nerves were 45 m/s (normal values: 40–60 m/s). Several EMGs performed elsewhere confirmed the myogenic involvement of the deltoid, tibialis anterior and gastrocnemius, but fibrillation was found at rest in tibialis anterior. EMG studies of hand, gluteal and quadriceps muscles were normal.

Clinical examination when aged 14 years showed that the patient had to wear leg braces to counteract excessive steppage, and winged scapulae were present. Strength was graded 4 (MRC scale) in the deltoid, serratus anterior, latissimus dorsi and rhomboid muscles. Distal atrophy and a limitation of the foot-leg angle to 90° were present in the lower extremities. The strength of the tibialis anterior and peroneal muscles was graded 3. Deep tendon reflexes could be elicited. Sensation was normal. No hypertrophic nerves were felt. Creatine kinase values were normal and there was only a 10–15% decrease of the mean potential duration in deltoid and tibialis anterior muscles. MCV was slower than before in the left lateral popliteal nerve (37 m/s). A second muscle biopsy was performed.

Review when aged 16 years showed a slight progression of weakness in the serratus anterior muscles, the extensors of the toes and the gastrocnemius, atrophy of the hypothenar muscles and a slight decrease of strength in the gluteal and adductor muscles. A few coarse fasciculations were elicited by percussion of the deltoids. Sensory examination was normal. There

Address for reprint requests: Prof JJ Martin, Department of Medicine, Gebouw T, Room 5.18, Universitaire Instelling Antwerpen, Universiteitsplein 1, B-2610 Wilrijk, Belgium.

Accepted 6 March 1980

was no limitation of the neck movements and no elbow contractures. Cardiac examination was normal except for a sinus tachycardia. There was a decrease (20%) of the pulmonary vital capacity. The intelligence quotient (IQ) was 99 (WISC).

Case 2 GV, the brother of case 1 was born in September 1966. He came to our attention at the age of 6 years because of a stepping gait which appeared one year previously. Clinical examination revealed weakness of the shoulder girdle and a bilateral foot drop. Investigations showed normal creatine kinase levels, myogenic EMG alterations (a 35% reduction of the mean potential duration and a marked increase of polyphasic potentials in the deltoid and tibialis anterior muscles). A nerve and muscle biopsy was performed. EMGs in 1975 and 1977 were normal in masseters, distal muscles of upper extremities and quadriceps, while combined myogenic and neurogenic features were discovered in deltoid and tibialis anterior muscles with fibrillations and positive sharp waves at rest. MCV of lateral popliteal and ulnar nerves were between 44 and 50m/s.

Clinical examination when aged 11 years showed winged scapulae and bilateral foot drop. Sensation was intact. Creatine kinase level was normal. EMG showed loss of motor units, increase of polyphasic potentials with normal mean potential duration in tibialis anterior, extensor of the toes, deltoid and quadriceps muscles. Motor and sensory conduction velocities in upper and lower extremities were between 48 and 60 m/s. A second muscle biopsy was performed.

Review when aged 13 years confirmed the scapuloperoneal distribution of muscle atrophy and weakness. The weakest muscles (grade 3 on the MRC scale) were the serratus anterior, tibialis anterior and peroneal muscles. Less severely affected (grade 4) were the deltoid, pectoralis major, latissimus dorsi, supra- and infraspinatus in the upper extremities, the toe extensors in the lower extremities. Deep tendon reflexes were present. Sensation was normal. No hypertrophy of the nerve trunks could be palpated. Neck and elbow movements were free. Cardiac examination was normal with a pulse rate of 96/min. Lung function tests were normal. The IQ (WISC) was 85 (verbal 76, performance 91).

Materials and methods

All biopsies were processed for histochemistry,

electron microscopy, teased nerve studies, quantitative evaluation of the distribution of myelinated nerve fibres and muscle fibres according to standard techniques used in our laboratory.²⁻⁴ Histograms showing the distribution of the myelinated nerve fibres were derived from photographs of semi-thin sections enlarged 1000 times and also, for case 1, from electron micrographs magnified 3700 times.

Results

Nerve biopsies (1972) Light and electron microscopy of the superficial peroneal nerve in both cases did not show any loss of myelin (fig 1A), and there was no evidence of recent or chronic demyelination or of brown metachromatic deposits. Non-myelinated axons were normal. Schwann cells were unremarkable and there were no abnormal inclusions. The density of the myelinated axons was 12 000–15 000 fibres/mm² (normal values: 11 000–16 000 fibres/mm²). Both histograms had a normal bimodal distribution, the second peak corresponding to slightly smaller fibres than in control cases (fig 1B). Teased nerve studies were performed, about 200 internodes being measured in each case (fig 2). Slight variations were found in the internodal lengths of the largest myelinated axons in case 1. The slope of the regression curve was less steep than in case 2 and in controls.

Muscle biopsies (1972, 1977)

Case 1 The first biopsy (fibularis brevis muscle, 1972) (fig 3A and B) showed limited numbers of small groups of angular fibres; a few very large fibres contained centralised nuclei. Histochemistry revealed only one type of fibre, intermediate between type 1 and type 2, simultaneously positive for NADH-TR, menadione-alpha linked GDH, ATPase at pH 9.4, ATPase-EDTA and phosphorylase. Electron microscopy was unremarkable. The second biopsy (tibialis anterior muscle, 1977) (fig 3 C-D) was characterised by a marked fibre type disproportion; the type 1 fibres were smaller than the largest type 2A fibres by at least 55% (fig 4). Considerable variation was found from field to field: in some, large numbers of type 1 fibres formed islands of 10–12 elements between enlarged type 2A and a few type 2B muscle fibres; in others, there was a more even distribution between type 1 and type 2 fibres, type 1 elements being always much smaller; other fields were exclusively made of type 1 fibres. Type 1 fibres represented 84.5% of the whole population. Electron microscopy showed

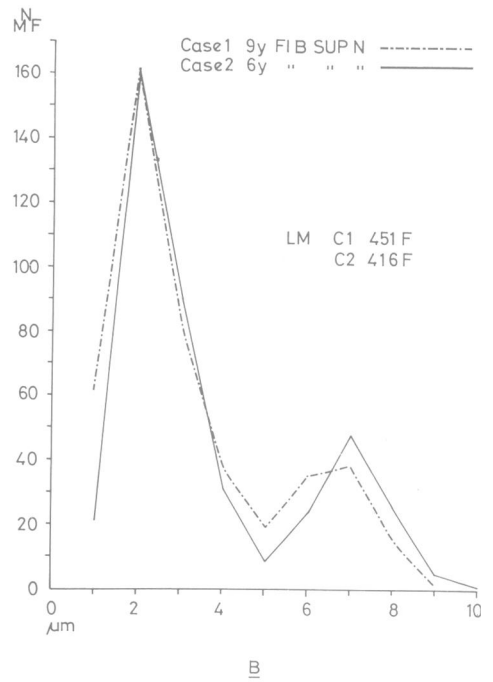
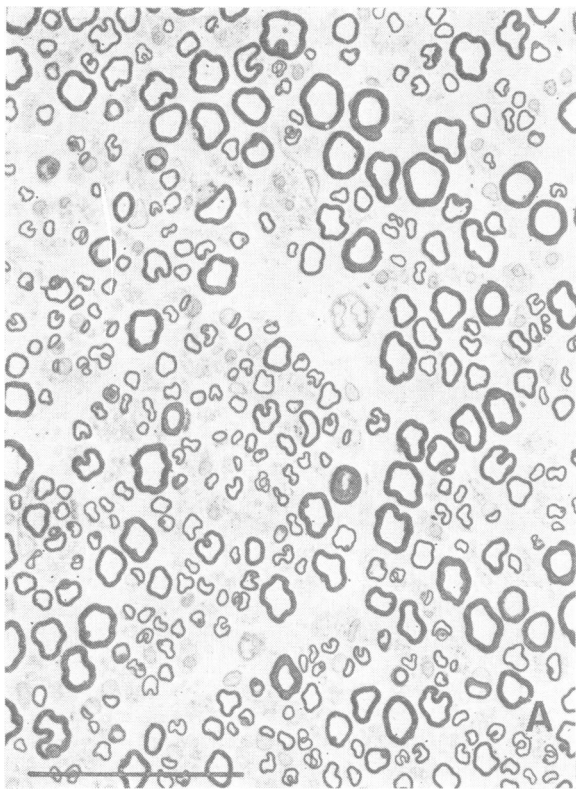


Fig 1 Superficial peroneal nerve (case 2 at age 6). A, Normal appearance of myelin sheaths on a semi-thin section. (Glutaraldehyde-osmium tetroxide fixation, epoxy resin embedding, toluidine blue 0.5% staining, bar=50 μm). B, Histograms showing the bimodal distribution of the myelinated nerve fibres in both cases (in ordinate, the number of myelinated fibres; in abscissa, the diameters).

reduced amounts of myofibrils in the atrophic fibres and occasionally a cytoplasmic body or a lipofuscin granule.

Case 2 In the first biopsy (fig 5A), small angular fibres were found between normal sized elements. The numerical preponderance of type 2 fibres was overwhelming, nearly all the examined fields being made of such fibres. In one field only, type 1 fibres were clearly prevalent as demonstrated on the ATPase-EDTA preparations. Electron microscopy confirmed the presence of angular fibres with severe loss of myofibrils and numerous sarcoplasmic triads.

In the second biopsy (fig 5B, C and D), large field neurogenic atrophy was extremely conspicuous. Fatty degeneration and increase of connective tissue were found in the most affected areas. Quantitative analysis of a less severely damaged portion showed 65% of type 1 fibres and a selec-

tive atrophy of these fibres compared to the larger sizes of type 2A and 2B elements (fig 4). Targetoid type 1 fibres were present. Endomysial nerve bundles and neuromuscular spindles were normal. Electron microscopy demonstrated loss or disarray of myofibrils, widening of Z-bands and numerous sarcoplasmic triads in the atrophic muscle fibres.

Discussion

Kaeser¹ identified four main types of scapuloperoneal syndrome: (1) a scapuloperoneal muscular dystrophy; (2) a scapuloperoneal syndrome with distal sensory disturbances; (3) a spinal scapuloperoneal atrophy with dominant inheritance; (4) a recessive type of scapuloperoneal atrophy. The identification of a fifth type with X-linked recessive inheritance has been proposed by Rowland *et al*⁵; it is characterised by early

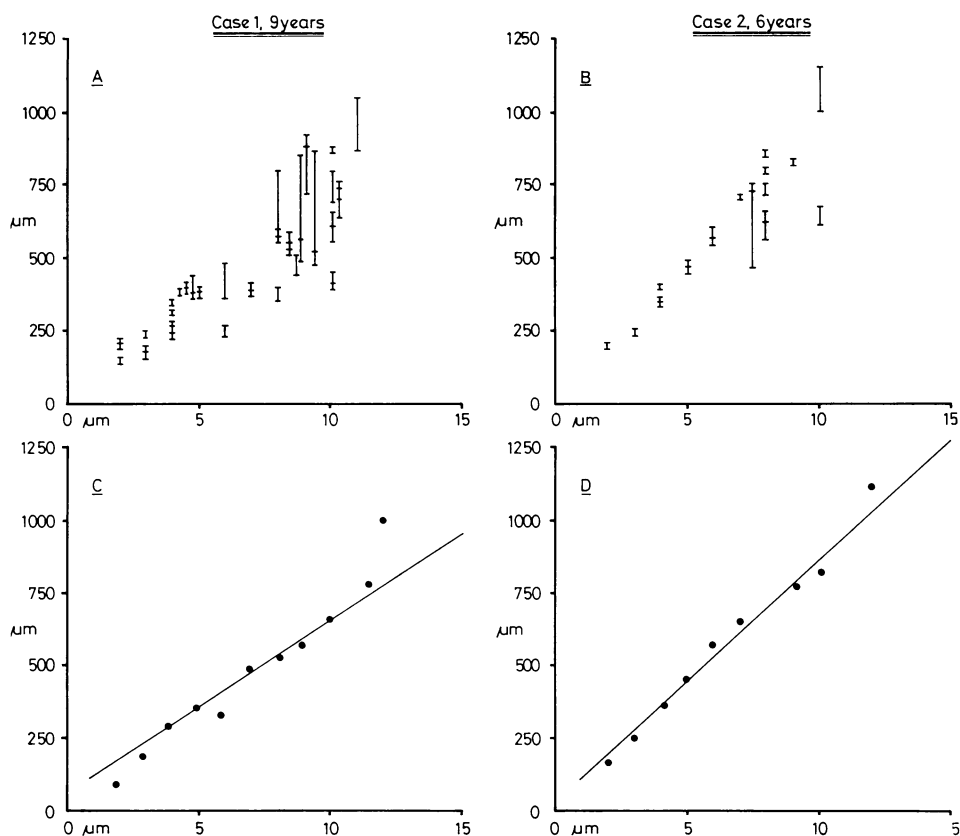


Fig 2 Superficial peroneal nerves; teased nerve studies on myelinated fibres. A-C: case 1 at age 9 yr, B-D: case 2 at age 6yr. Internodal lengths are plotted in ordinate against fibre diameter in abscissa. In A and B, measurements on the same fibre are connected by a vertical line. Wider variations of the internodal lengths are noted in case 1 than in case 2 for the largest fibres. In C and D, regression lines according to the method of the least squares are shown. The slope is less steep in case 1 (66) than in case 2 (84). Slopes of regression lines from age-matched controls (age 5 to 16) vary from 73 to 98 with an age-related steady increase of the slope.

onset of contractures of neck, elbows and calves, heart block often responsible for sudden death in adult life, and late onset of muscle weakness of humeroperoneal distribution. The eponym of Emery-Dreifuss has been attached to this syndrome although the topography of the weakness in the cases reported by Emery and Dreifuss⁶ was scapulopelvic. In all types of scapuloperoneal syndrome, laboratory investigations frequently indicate a mixture of myopathic and denervation features. A present classification is summarised in the table.

Our own cases illustrate the nosological problems raised by the discordance between EMG and biopsy data. In 1972 myogenic EMG changes

were stressed and a diagnosis of scapuloperoneal muscular dystrophy was proposed. However a

Table Scapuloperoneal syndrome. Types and references

1. Scapuloperoneal muscular dystrophy (Ref 7-11; Ref 12, cases 1-3; Ref 13-15) autosomal dominant or sporadic, late onset
2. Scapuloperoneal muscular atrophy
 - A. Without sensory involvement
 - (1) autosomal dominant or sporadic, late onset (Ref 16-19; Ref 20, case 2; Ref 21-23)
 - (2) autosomal recessive or sporadic, early onset (Ref 12, cases 4-10; Ref 20, case 1; Ref 24-30)
 - B. With distal sensory disturbances
 - (1) autosomal dominant or sporadic, late onset (Ref 31-33)
 - (2) autosomal recessive, early onset (Ref 34)
3. X-linked scapuloperoneal syndrome (Ref 5; Ref 20, cases 3, 4; Ref 35-39)

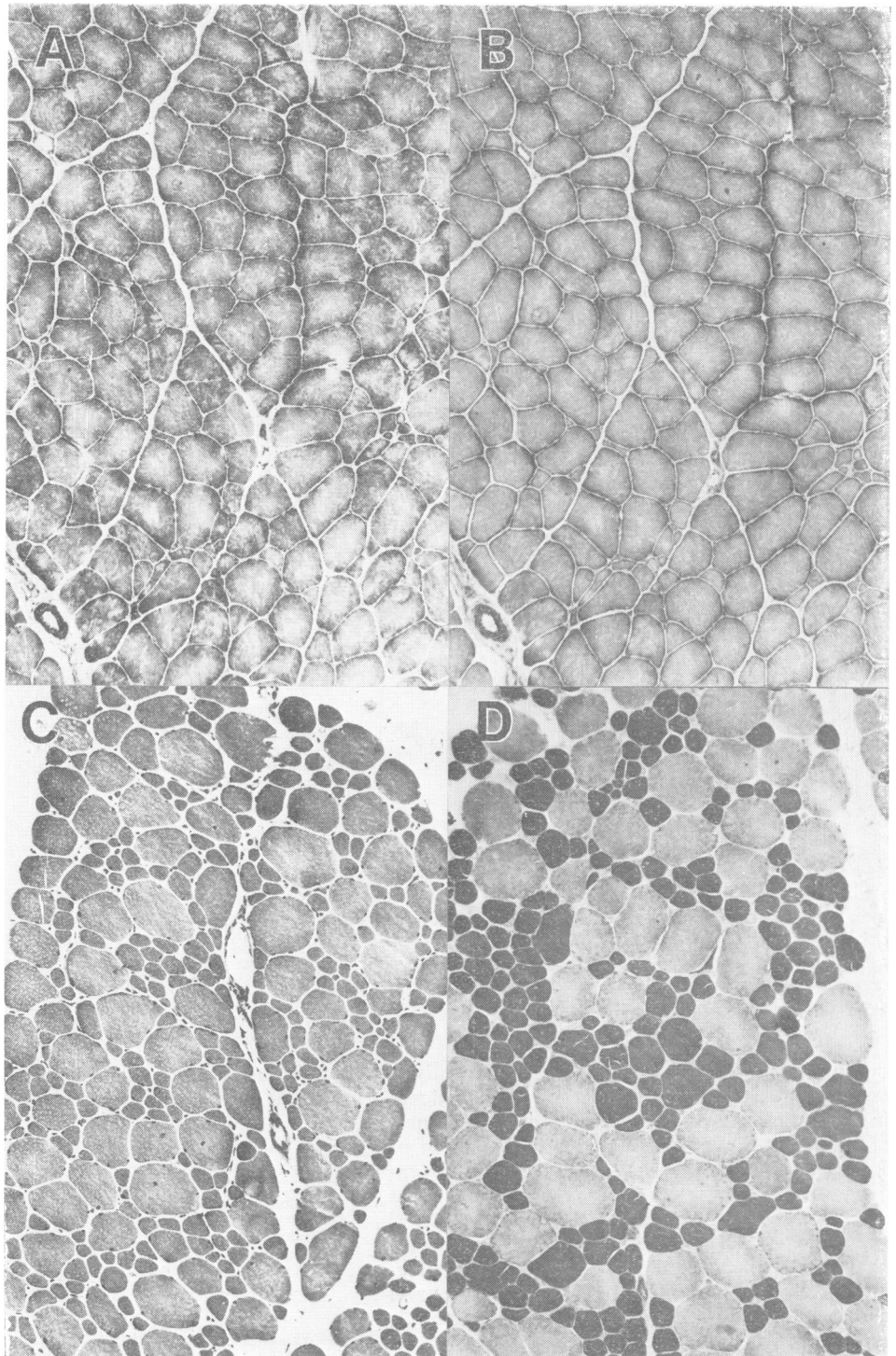


Fig 3 Muscle biopsies of case 1 (cryostat sections). In the fibularis brevis muscle (1972, A-B), scattered groups of atrophic fibres are shown. There is only one fibre type intermediate between type 1 and 2 (A=NADH-TR, $\times 75$; B=menadione linked α -GDH, $\times 75$). In the tibialis anterior muscle (1977, C-D), large type 2 fibres are interspersed between numerous small type 1 fibres (C=H&E, $\times 120$; D=ATPase pH 4.2, $\times 120$).

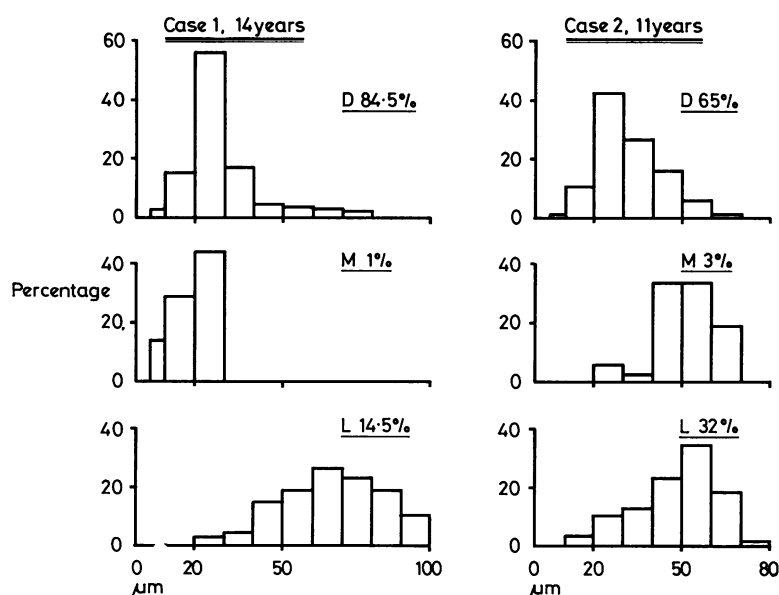


Fig 4 Histograms showing the distribution of the fibres according to their size (tibialis anterior muscles, 1977). Fibre type differentiation is based on cryostat sections stained for myofibrillar ATPase after preincubation at pH 4.6. Therefore the dark (D) fibres belong to type 1, the medium (M) to type 2B and the light (L) ones to type 2A. In both cases, there is a predominance of type 1 fibres while type 2 fibres belong nearly exclusively to type 2A. In case 1, type 1 fibres are markedly atrophied and type 2A fibres are hypertrophied. Similar changes were found in case 2 but are less marked because of the arbitrary selection of a moderately involved field in order to make reliable measurements.

re-evaluation of the histologic features showed a few scattered angular fibres in both cases, the presence of only one fibre type with characteristics intermediate between those of type 1 and type 2 in case 1, and clearcut fibre type grouping in case 2, evidence all pointing towards a denervating disorder. Teased nerve studies and histograms of the distribution of the myelinated fibres in the superficial peroneal nerve gave results within normal limits in case 2 and discrete alterations in case 1, although no clinical sensory symptoms could be detected; qualitative evaluation of more than 200 fibres on electron micrographs failed to show evidence of acute or chronic demyelination-remyelination. Five years later EMG alterations were interpreted as neurogenic in case 2 and less myopathic or slightly neurogenic in case 1. Motor and sensory conduction velocities were normal except for a slight slowing of the motor conduction velocity in the lateral popliteal nerve, again in case 1. Muscle biopsy showed in case 1 atrophic type 1 fibres which were smaller than the largest type 2 fibres by at least 55%, mimicking a congenital fibre type disproportion (CFTD).⁴⁰ The histological features illustrated in fig 3 reinforce the idea that CFTD is mainly a histological diagnosis.⁴¹ In a previous study,⁴ one of us has shown that a similar disproportion can be observed in neurogenic disorders such as for example, globoid

cell leukodystrophy. On the other hand, we do not wish to draw any conclusion from the observed type 1 fibre preponderance since it represents a normal feature of the tibialis anterior muscle.⁴²

In case 2, one field only showed a CFTD-like picture while the rest demonstrated unequivocal large field atrophy and fibre type grouping. Comparison of the morphological data led to the conclusion that the changes were purely neurogenic.

The mother's brothers died shortly after birth which makes it unlikely that they were suffering from the same disorder. Although only two brothers appear to be affected in this family, none of the clinical features of the X-linked scapuloperoneal syndrome, are present. We think our cases are examples of the recessive neurogenic type of scapuloperoneal syndrome. The provisional character of such a classification must be emphasised since the exact pathogenic mechanisms and molecular defects responsible for these genetic disorders remain unknown.

Professor JG Leroy, Dr H Jorens and Mr MR Van Cappel provided helpful advice and data. The skilful help of Mrs C Joris and of Mr R van Hove is gratefully acknowledged. This work has been supported by the FGWO (3.0033.77) and by the Baron Charles Bracht Foundation.

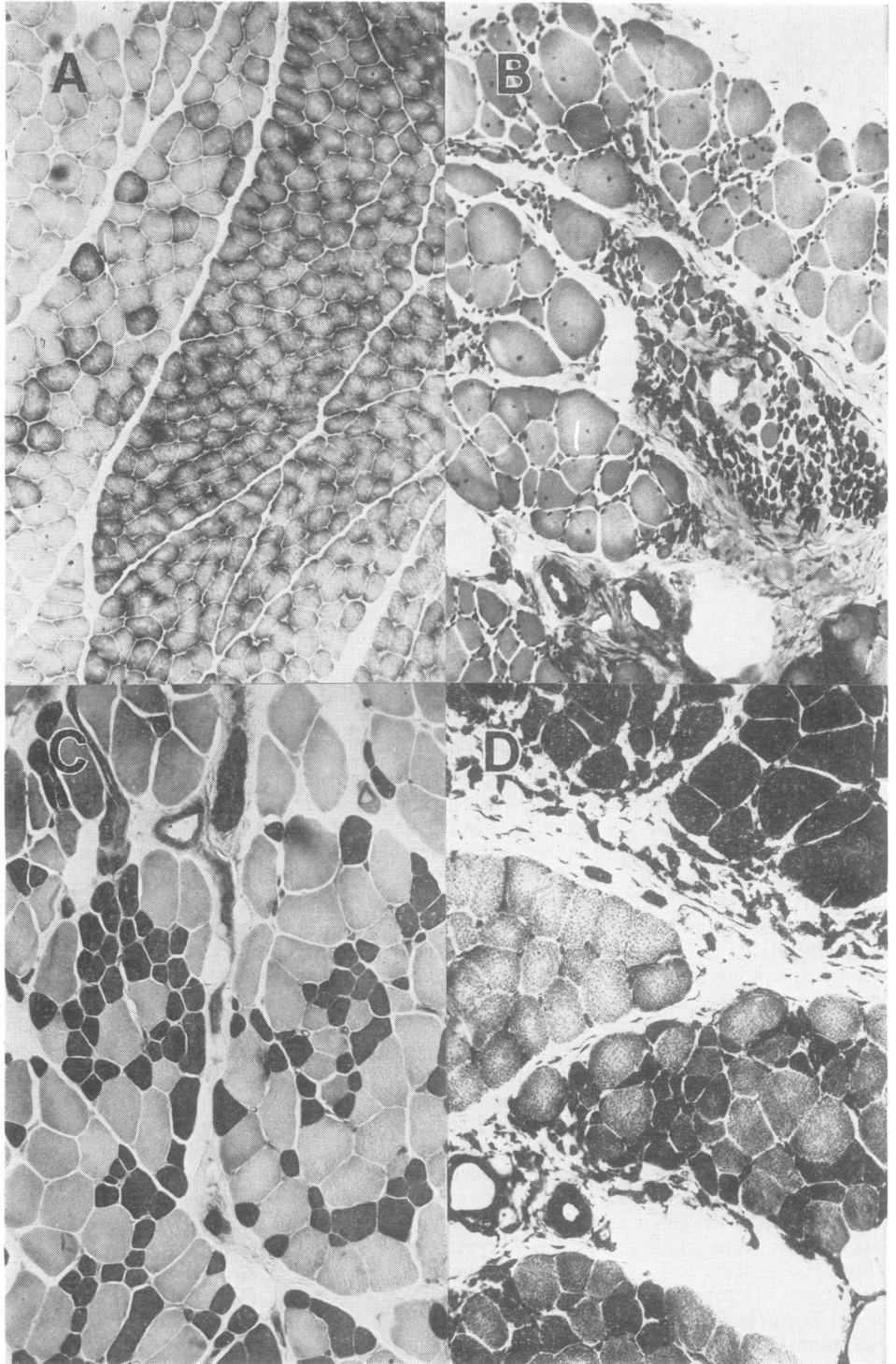


Fig 5 Muscle biopsies of case 2 (cryostat sections). Fibre type grouping in the fibularis brevis muscle (1972, A: menadione linked α -GDH, $\times 75$). Tibialis anterior muscle (1977, B-C-D): large field neurogenic atrophy in B, selective atrophy of type 1 fibres in C, fibre type grouping in D (B=H&E, $\times 120$; C=ATPase pH 4.2, $\times 120$; D=NADH.TR, $\times 120$).

References

- 1 Kaeser HE. Scapulo-peroneal syndrome. In: Vinken PJ, Bruyn GW, eds: *Handbook of Clinical Neurology, Vol. 22: System Disorders and Atrophies part 2*. Amsterdam: North-Holland/Elsevier, 1975; 57-65.
- 2 Reniers J, Martin L, Joris C. Histochemical and quantitative analysis of muscle biopsies. *J Neurol Sci* 1970; **10**:349-67.
- 3 Martin JJ, Joris C. The sciatic nerve in juvenile metachromatic leucodystrophy: a quantitative evaluation. *Acta Neurol Belg* 1973; **73**:175-91.
- 4 Martin JJ, Clara R, Ceuterick Ch, Joris C. Is congenital fibre type disproportion a true myopathy? *Acta Neurol Belg* 1976; **76**:335-44.
- 5 Rowland LP, Fetell M, Olarte M, Hays A, Singh N, Wanat FE. Emery-Dreifuss muscular dystrophy. *Ann Neurol* 1979; **5**:111-7.
- 6 Emery AE, Dreifuss FE. Unusual type of benign X-linked muscular dystrophy. *J Neurol Neurosurg Psychiatry* 1966; **29**:338-42.
- 7 Seitz D. Zur nosologischen Stellung des sogenannten scapulo-peronealen Syndroms. *Dtsch Z Nervenheilk* 1957; **175**:547-52.
- 8 Hausmanowa-Petrusewicz I, Zielinska S. Zur nosologischen Stellung des scapulo-peronealen Syndroms. *Dtsch Z Nervenheilk* 1962; **183**:377-82.
- 9 Ricker K, Mertens HG. The differential diagnosis of the myogenic (facio)-scapulo-peroneal syndrome. *Europ Neurol* 1968; **1**:275-307.
- 10 Lovelace RE, Menken M. The scapulo-peroneal syndrome: dystrophic type. *Excerpta Medica Int Congress Ser* 1969; **193**:247-8.
- 11 Serratrice G, Roux H, Aquaron R, Gambarelli D, Baret J. Myopathies scapulo-péronières. A propos de 14 observations dont 8 avec atteinte faciale. *Sem Hôp Paris* 1969; **45**:2678-83.
- 12 Feigenbaum JA, Munsat TL. A neuromuscular syndrome of scapulo-peroneal distribution. *Bull Los Angeles Neurol Soc* 1970; **35**:47-57.
- 13 Kazakov VM, Bogorodinsky DK, Skorometz AA. Myogenic scapulo-peroneal syndrome—muscular dystrophy in the K. kindred. Re-examination of the K. family described for the first time by Oransky in 1927. *Europ Neurol* 1975; **13**:350-9.
- 14 Thomas PK, Schott GD, Morgan-Hughes JA. Adult onset scapulo-peroneal myopathy. *J Neurol Neurosurg Psychiatry* 1975; **38**:1008-15.
- 15 Delwaide PJ, Schoenen J. Atrophie scapulo-péronière sporadique d'origine myogène. *Res Neurol (Paris)* 1976; **132**:424-9.
- 16 Stark P. Etude clinique et génétique d'une famille atteinte d'atrophie musculaire progressive neurale (amyotrophie de Charcot-Marie). *J Génét Hum* 1958; **7**:1-32.
- 17 Kaeser HE. Scapulo-peroneal muscular atrophy. *Brain* 1965; **88**:407-18.
- 18 Fotopulos D, Schulz H. Beitrag zur Pathogenese des scapulo-peronealen Syndroms. *Psychiat Neurol Med Psychol (Leipz)* 1966; **18**:129-36.
- 19 Ricker K, Mertens HG, Schimrigh K. The neurogenic scapulo-peroneal syndrome. *Europ Neurol* 1968; **1**:257-74.
- 20 Takahashi K, Nakamura H, Nakashima R. Scapulo-peroneal dystrophy associated with neurogenic changes. *J Neurol Sci* 1974; **23**:575-83.
- 21 Serratrice G, Gastaut JL, Pellissier JF, Pouget J. Amyotrophies scapulo-péronières chroniques de type Stark-Kaeser (à propos de 10 observations). *Rev Neurol (Paris)* 1976; **132**:823-32.
- 22 Probst A, Ulrich J, Kaeser HE, Heitz Ph. Scapulo-peroneal muscular atrophy. Full autopsy report. Unusual findings in the anterior horn of the spinal cord. Lipid storage in muscle. *Europ Neurol* 1977; **16**:181-96.
- 23 Scarlato G, Valli G, Bracchi M. Quantitative histological and neuro-physiological studies in scapulo-peroneal syndrome. *Acta Neurol (Napoli)* 1978; **33**:327-41.
- 24 Emery ES, Fenichel GM, Eng G. A spinal muscular atrophy with scapulo-peroneal distribution. *Arch Neurol (Chic)* 1968; **18**:129-33.
- 25 Munsat TL. Infantile scapulo-peroneal muscular atrophy. *Neurology (Minneapolis)* 1968; **18**:285.
- 26 Zellweger H, McCormick WF. Scapulo-peroneal dystrophy and scapulo-peroneal atrophy. *Helv Paediatr Acta* 1968; **23**:643-9.
- 27 Meadows JC, Marsden CD. Scapulo-peroneal amyotrophy. *Arch Neurol (Chic)* 1969; **20**:9-12.
- 28 Schuchmann L. Spinal muscular atrophy of the scapulo-peroneal type. *Z Kinderheilk* 1970; **109**:118-23.
- 29 André JM, André M, Floquet J, Tridon P, Arnould G. Les amyotrophies scapulo-péronéales (à propos de deux cas de syndrome de Stark-Kaeser) *Ann Méd Nancy* 1972; **11**:925-38.
- 30 Negri S, Caraceni T, Cornelio F. A case of scapulo-tibio-peroneal syndrome. Electromyographic and histoenzymologic considerations. *Europ Neurol* 1973; **10**:31-40.
- 31 Davidenkow S. Scapulo-peroneal amyotrophy. *Arch Neurol Psychiatry* 1939; **41**:694-701.
- 32 Schwartz MS, Swash M. Scapulo-peroneal atrophy with sensory involvement: Davidenkow's syndrome. *J Neurol Neurosurg Psychiatry* 1975; **38**:1063-7.
- 33 Spalke G, Hökendorf H, von Roques P. Zur Differentialdiagnose der scapulo-peroneal-Amyotrophie. *J Neurol* 1976; **212**:253-69.
- 34 Tohgi H, Tsukagoshi H, Toyokura Y. Neurogenic scapulo-peroneal syndrome with autosomal recessive inheritance. *Clin Neurol (Tokyo)* 1971; **11**:215-20.
- 35 Rothauwe HW, Mortier W, Beyer H. Neuer Typ einer recessiv X-chromosomal vererbten Muskeldystrophie: Scapulo-humerodistale Muskeldystrophie mit frühzeitigen Kontrakturen und Herzrhythmusstörungen. *Humangenetik* 1972; **16**:181-200.

- 36 Thomas PK, Calne DB, Elliott CF. X-linked scapuloperoneal syndrome. *J Neurol Neurosurg Psychiatry* 1972; **35**:208-15.
- 37 Mawatari S, Katayama K. Scapuloperoneal muscular atrophy with cardiopathy. An X-linked recessive trait. *Arch Neurol (Chic)* 1973; **28**:55-9.
- 38 Camman R, Vehreschild T, Ernst K. Eine neue Sippe von X-chromosomaler benigner Muskeldystrophie mit Frühkontrakturen (Emery-Dreifuss). *Psychiat Neurol Med Psychol (Leipz)* 1974; **26**:431-8.
- 39 Waters DD, Nutter DO, Hopkins LC, Dorney ER. Cardiac features of an unusual X-linked humeroperoneal neuromuscular disease. *New Engl J Med* 1975; **293**:1017-22.
- 40 Dubowitz V, Brooke MH. Muscle biopsy: a modern approach. In: Walton JN, ed. *Series Major Problems in Neurology*, Vol 2. London: WB Saunders Co Ltd, 1973: 280-8.
- 41 Cavanagh NPC, Lake BD, McMeniman P. Congenital fibre type disproportion myopathy. A histological diagnosis with an uncertain clinical outlook. *Arch Dis Child* 1979; **54**:735-43.
- 42 Johnson MA, Polgar J, Weightman D, Appleton D. Data on the distribution of fibre types in 36 human muscles. An autopsy study. *J Neurol Sci* 1973; **18**:111-29.