Congenital fibre type disproportion

A case report

R. SANDYK

Summary

A case of congenital myopathy (fibre type disproportion) in a 14-year-old White girl is described. She was born a 'floppy baby' and her developmental milestones were delayed. A congenital muscle dystrophy was suspected clinically and a quadriceps biopsy examination revealed congenital fibre type disproportion.


'All that waddles is not dystrophy'.

The application of specialized techniques to muscle biopsy in recent years has led to the recognition of a number of new congenital myopathies. They can be broadly divided into two groups: (i) disorders with an unusual structural abnormality, such as central core disease, nemaline myopathy and congenital fibre type disproportion; and (ii) disorders with a specific enzyme defect, such as the glycogenoses affecting muscle.

Common to these diseases is the fact that they cannot be diagnosed on clinical grounds alone. Affected patients tend to present in a somewhat similar fashion — either as a 'floppy baby' with generalized hypotonia and associated weakness, or with a proximal muscle weakness resembling muscle dystrophy. The weakness tends to be non-progressive, but occasional cases seem to deteriorate more rapidly. Serum phosphokinase (CPK), which is grossly elevated in muscle dystrophy, is usually normal or only slightly elevated in these myopathies. Electromyography may show a nonspecific 'myopathic' pattern and is also of little diagnostic value in differentiating the disorders. The only means of diagnosis is muscle biopsy.

Congenital fibre type disproportion was initially described by Brooke in 1973 on the basis of a muscle biopsy picture. In the patients described by him, the type 1 fibres were smaller than the type 2 fibres by a margin of more than 12% of the diameter of the type 2 fibres, in contrast to normal muscle in children in whom the type 1 and type 2 fibres were of approximately equal size. All the patients were 'floppy infants', the condition being noted at or shortly after birth. Half of the patients also had unilateral or bilateral congenital dislocation of the hip. The weakness seemed to involve all the muscles of the trunk and the extremities. Some of the children showed initial progression of the weakness during the 1st year of life, but Brooke did not see any further progression of weakness once the children had reached 2 years of age.

Recurrent respiratory infections were frequently a problem during the 1st year of life. About half of the patients had a relative with a similar clinical condition. In some cases there were only affected siblings, suggesting an autosomal recessive pattern of inheritance, but 1 patient had both a father and brother who were affected, suggesting a dominant mechanism. The condition is generally considered to be benign, but Lenard and Goebel reported a patient with fairly severe weakness and associated respiratory deficit necessitating tracheostomy.

The pathogenesis of congenital fibre type disproportion is not entirely known. It is possible that the type 2 fibres, which may be small early on in the disease process, with time become hypertrophied, thus compensating for the weakness and accounting for the tendency to improvement. This could explain the very marked hypertrophy of type 2 fibres which one may see in some of the older children.

Associated abnormalities in stature are frequently present. Kyphoscoliosis and deformities of the feet (flat as well as arched feet) are also common. As a rule, kyphoscoliosis can affect all the muscles, but the legs seem to be involved most often. At times the weakness is mild, causing only a delay in the development of the motor milestones rather than any obvious paralysis. Occasionally, as the child grows older, the condition becomes stable or even improves.

Case report

For the last 5 years this 14-year-old White girl has been followed up at the clinic of the Johannesburg Hospital for slowly progressive muscle weakness. Her main complaints were gait difficulties and a progressive difficulty in walking up stairs.

From her history, it is known that her developmental milestones since birth were delayed. She was born extremely hypotonic and immobile, had difficulty in sucking and swallowing for the first couple of months and was fed via a tube. She developed very slowly. She could sit with slight support at the age of 15 months and walked with a waddling gait at 3 years of age. From the age of about 2 years her parents noted the development of scoliosis and a markedly expressionless face. From her history, it is known that her developmental milestones since birth were delayed. She was born extremely hypotonic and immobile, had difficulty in sucking and swallowing for the first couple of months and was fed via a tube. She developed very slowly. She could sit with slight support at the age of 15 months and walked with a waddling gait at 3 years of age. From the age of about 2 years her parents noted the development of scoliosis and a markedly expressionless face. During the last 5 years she became progressively weaker, with more weakness in the lower limbs than in the upper limbs, and more proximal than distal weakness. The distal muscles, however, were also affected.

On admission she had marked lordosis (Fig. 1). Her facial expression was frozen (Fig. 2). No weakness of ocular muscles was noted and she had no swallowing or sphincter problems. Tendon reflexes were absent. She had a grossly waddling gait with marked difficulty in lifting the right leg. Turning of the head against resistance was good, but a marked deltoid weakness was noted. No skeletal deformities were noted except for the lordosis. Her IQ seemed to be low. There was no family history suggestive of a neuromuscular disorder.

The ECG was normal. Serum CPK and aldolase values were in the normal range. On microscopic examination of routine haematoxylin and eosin-stained sections of left quadriceps muscle, no significant variation in fibre size and no other pathologica changes were seen. Enzyme histochemical study revealed smallish type 1 fibres and larger type 2 fibres. With ATPase staining, a marked predominance of type 1 fibres was noted. The type 2 fibres appeared mildly hypertrophic. No changes in muscular distribution, cellular reaction or architectural features were noted. The histological features were...
essentially those of a myopathy with marked type I fibre predominance (M.C.D. Gritzman, SAIMR, Johannesburg).

Discussion

Congenital fibre type disproportion is a rare familial type of congenital myopathy. The exact pattern of inheritance is not the same for all cases so far described. This condition is related to the distribution of muscle fibres according to size and type. The typical abnormality is present when the type 1 fibres are at least 12% smaller than the type 2 fibres. Smallness of type 2 fibres is common in a variety of medical conditions as well as in disuse or cachexia; smallness of type 1 fibres is relatively rare but is also seen in other congenital myopathies such as myotubular myopathy. Brooke and Kaiser suggested that the occurrence of type I or type 2 atrophy depends on which fibres are not contracting adequately, since any muscle will atrophy with disuse. They postulated that type 2 atrophy could involve voluntary muscle disuse, while atrophy affecting the type 1 fibres seems to involve reflex muscle relaxation produced by lack of muscle spindle activity. Fardeau et al. saw this condition as a variant of myotubular myopathy, reflecting lack of maturation of muscle fibres. In fact, both disorders were found in the same family.

It is important to diagnose this condition correctly for prognostic reasons. Some cases of this condition have been misdiagnosed as Werdnig-Hoffman disease and erroneously given a bad prognosis. Owing to the fact that the clinical condition frequently improves after the first 2 years of life, early differentiation from Werdnig-Hoffman disease and other congenital myopathies is important.

Congenital fibre type disproportion should be suspected in any baby presenting with the so-called 'floppy infant syndrome'. Because this condition is not easily detected with routine histological techniques, further histochemical and electron microscopic analysis should be performed for accurate diagnosis.

The field of congenital myopathies is still expanding and it is important that paediatricians and general practitioners appreciate the importance of detailed investigation of all infants with obscure congenital myopathies so that more of these groups of myopathies will be discovered. Further, newer techniques have shown that some of the conditions that belong to the group of congenital myopathies may be due to subtle defects in innervation rather than to a problem within the muscle tissue itself. Nonspecific diagnostic labels such as 'benign hypotonia' or 'amyotonia congenita' should not be used today to describe conditions of muscle weakness in children.

REFERENCES