Lesson of the week: Late diagnosis of Duchenne's muscular dystrophy presenting as global developmental delay

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Lesson of the week

Late diagnosis of Duchenne's muscular dystrophy presenting as global developmental delay

Charles Essex, Helen Roper

Duchenne's muscular dystrophy is an X linked recessive disorder that occurs in around 1 in 3500 baby boys.[1] There may be no family history of the disorder, as the large gene responsible for it is prone to mutation, but even so subsequent sons are at risk. Most health professionals who work with children think that a boy with Duchenne's muscular dystrophy will present only with difficulties in walking. They have a mental picture of a child who is late to walk and who performs the Gowers's manoeuvre when getting up from the floor—that is, he gets up from the floor by first getting on to his hands and knees and then, from a kneeling position, pushing with his hands against his knees and thighs until upright.

Although this is the classic picture of Duchenne's muscular dystrophy, relying on delay in development of gross motor skills as the only indicator will delay diagnosis in a high proportion of cases—by which time the parents might have had other sons with the disorder. In our experience, late diagnosis of Duchenne's muscular dystrophy is especially likely in boys with considerable associated learning difficulties and who present with global developmental delay. We report three such cases (see table for details of these and three other cases).

Many boys with Duchenne's muscular dystrophy present with global developmental delay before specific motor disabilities are noticed

Case reports

Case 1—This boy's mother began to be worried about him when he was 16 months old and had made no progress with language. She attributed this to his measles, mumps, and rubella vaccination. He walked at

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continued over

Boys with late diagnosis of Duchenne's muscular dystrophy

Case No	Age (months) when boy first walked	Age (months) when concerns were first raised	Types of developmental delay or difficulty	Age (months) when concerns at motor skills were first raised	Age (months) when creatine kinase concentration was measured
1*	13	16	Speech, language	64	64
2*	23	24	Global delay	90	90
3*	17	25	Behaviour	61	61
4	13	48	Learning	48	90
5	30	<12	Global delay	24	76
6	15	24	Speech, language	70	81

*Described in text.

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13 months, usually on his toes. He was referred for speech and language therapy, and at the age of 2 years he underwent a multidisciplinary assessment at his local child development centre. Before he started school a statement of his special educational needs was made, based on his language and learning difficulties. He attended a mainstream primary school but received additional support. At the age of 5 years 4 months he was referred for paediatric assessment, as his teacher was concerned about his motor skills. In the examination he was noted to have a waddling gait, tight Achilles tendons, and pseudohypertrophy of the calf. He used the Gowers's manoeuvre to get up from the floor. His creatine kinase concentration was >10 000 U/l (normal range <200), and he had a deletion in the dystrophin gene that included exons 3-8. At age 8 years 7 months he could walk only a few metres indoors.

Case 2—This boy presented with severe global developmental delay. He walked just before his second birthday. He never developed any verbal or signed communication. Metabolic and chromosomal tests were normal. His special educational needs were assessed, and he was placed in a school for children with severe learning difficulties. His younger brother presented with similar, though somewhat milder, difficulties—he developed some communication with signing—and was placed in the same school. The younger boy was referred for further paediatric assessment at 6 years old as the school had concerns about bruising, which was attributed to frequent falls. Examination showed that he had hypertrophy of the calf and a waddling gait and that he used the Gowers's manoeuvre. His creatine kinase concentration was >9000 U/l. No deletion in the dystrophin gene was detected, but muscle biopsy showed dystrophic histochemistry and absence of dystrophin. The older brother was then tested, and the diagnosis of Duchenne's muscular dystrophy was confirmed at the age of 7 years 6 months.

Case 3—This boy was referred by a health visitor for assessment at the age of 2 years 1 month because she was concerned about global developmental delay. He had walked at 17 months, and his mother had concerns about his behaviour. He underwent a multidisciplinary assessment at the child development centre, where his gross motor skills were thought to be appropriate for his age but his cognitive, language, and self help skills raised concerns. He received ongoing support from the child development centre. Appointments for further medical assessment at the age of 4, as part of the assessment of his educational needs, were not kept, and he was placed in a school that had a specialist language unit. At 5 years 1 month he had a medical examination at the school, at which the doctor noted his abnormal gait and use of the Gowers's manoeuvre. His creatine kinase concentration was >4800 U/l, and he had a deletion of the dystrophin gene that included exons 47-51. At 7 years, he was unable to get up from the floor unaided.

Discussion

In the West Midlands region, Duchenne's muscular dystrophy was diagnosed in 23 boys in the three years 1997 to 1999 at the Birmingham paediatric neuromuscular clinic. In five cases a family history was known. Of the other 18 boys, 13 were older than 4 years and seven were older than 7 years at the time of diagnosis. Of the 13 boys diagnosed after 4 years of age, all but one had been referred to health professionals and assessed some time before the further referral that led to the diagnosis of Duchenne's muscular dystrophy. Eight of these initial contacts occurred because of concerns about language or cognitive development and four because of abnormalities in gait. In all these cases opportunities were missed to make the diagnosis earlier. Bushby et al drew attention to the fact that, in the NHS Northern region, the age at which Duchenne's muscular dystrophy is diagnosed has not decreased over the past 20 years.[2]

Duchenne's muscular dystrophy can have a number of features related to muscle pathology: delay in development of gross motor skills; muscle weakness; falls; waddling gait; Gowers's manoeuvre; pseudohypertrophy of the calves; and failure to thrive (thought to be because of the energy needs of intense muscle necrosis and regeneration).[3] However, 30% of boys with Duchenne's muscular dystrophy have major learning difficulties.[4] Dystrophin is needed for continuing normal muscle function, but its isoforms are thought to have a function in the central nervous system, which could explain the learning difficulties in some children with Duchenne's muscular dystrophy.[5 6]

When seeing boys with developmental delay, paediatricians often consider the fragile X syndrome or chromosomal abnormalities and perform cytogenetic or DNA tests. Duchenne's muscular dystrophy is more common than the fragile X syndrome, which has an incidence of roughly one case in 6000 boys a year, and measurement of creatine kinase concentration is a simple, rapid, and cheap test. We alert colleagues to consider Duchenne's muscular dystrophy among diagnoses in boys who have developmental problems but whose gross motor skills are not disproportionately delayed. Paediatricians should measure the creatine kinase concentration of boys with global developmental delay to avoid a late diagnosis of Duchenne's muscular dystrophy.

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Endpiece

A book

A book should serve as an axe for the frozen sea within us.

Franz Kafka