Duchenne muscular dystrophy

Key facts

- Duchenne muscular dystrophy (DMD) is a disorder characterised by progressive muscle weakness commencing in the legs and pelvis, then extending to other muscles of the body.
- DMD should be considered in all boys who have delayed motor milestones and speech delay.
- Most individuals with DMD can today expect to survive until at least their early 20s, some even longer, and many maintain a good quality of life.
- Improvements in life expectancy result from early and aggressive treatment of respiratory and cardiac complications.
- Complications of DMD include respiratory failure, cardiomyopathy, scoliosis, osteoporosis and learning disability.
- DMD is an X-linked recessive disorder caused by genetic alterations (mutations) in the dystrophin gene. This means it usually affects boys, though in rare cases girls can be affected.
- There is a high spontaneous new mutation rate in DMD, which is why a boy with the condition may be born in a family where there is no family history.
- DMD is the most common form of muscular dystrophy in children.
- Symptoms are not usually evident until 18 months of age, and many boys are not diagnosed until five years of age. Increasing awareness of the condition should improve early diagnosis.

Clinical features

- Speech delay, weakness, falls and difficulty with motor skills.
- Progressive muscle weakness of the legs and pelvis, which is associated with a loss of muscle mass. Muscle weakness also occurs in the arms, neck and other areas, but not as severely or as early as in the lower half of the body.
- Examination reveals muscle wasting, calf muscle hypertrophy, lordosis and contractures.
- A positive Gower's sign, though this is not pathognomonic of DMD as it can be seen in other forms of muscular dystrophy.
- Often wheelchair dependent by early teens.
- Complications include permanent, progressive disability, decreased mobility, contractures, scoliosis and skeletal deformities, osteoporosis, obesity, respiratory failure and pneumonia or other respiratory infections, cardiomyopathy, congestive cardiac failure and arrhythmias. Learning disability is seen in about one-third of affected boys.

Diagnosis

- A diagnosis of DMD should be considered in all boys who have delayed motor milestones.
- Serum concentration of creatine phosphokinase (CK) level is nearly always at least five times as high as the maximum for unaffected people. It is sometimes 50 to 100 times higher. A very high CK makes a diagnosis of DMD probable; a normal (or slightly raised) CK excludes a boy having DMD.
- The diagnosis can usually be confirmed by DNA studies; this has replaced the need for a muscle biopsy and electromyogram in most cases.

Genetic basis

- DMD is an X-linked recessive disorder. The probability of siblings of an affected individual also being affected depends on the carrier status of the mother. For females who are known to be carriers, each son has a 1-in-2 (50%) chance of inheriting the condition, and each daughter 1-in-2 (50%) chance of being a carrier.
- Different types of alterations in the dystrophin gene cause Duchenne muscular dystrophy and Becker muscular dystrophy. Becker muscular dystrophy (BMD) is characterised by muscle weakness of later onset, and most individuals remain ambulatory into their 20s. Genetic testing can establish the diagnosis of DMD and BMD in the majority of, but not all, individuals with these conditions.

Clinical management

- Receiving optimum care from a multidisciplinary team, with the input of specialists in many different areas, dramatically improves the quality of life and life expectancy of individuals with DMD, and international guidelines have been agreed to this effect.
- DMD is a condition where needs change with time. The different areas of care required at each stage of DMD after diagnosis include neuromuscular, orthopaedic, rehabilitation, pulmonary, cardiac, gastro-intestinal and psychosocial management.

There are a number of therapeutic clinical trials under way in DMD that are aimed at overcoming the effects of certain types of mutations, highlighting the importance of genetic testing (see below).

Genetic testing

Genetic testing can be used to:

- confirm the diagnosis in someone with possible DMD or BMD (diagnostic testing);
- provide information about the genetic status of female relatives of someone with DMD through carrier testing; and
- offer prenatal and preimplantation genetic diagnosis. Prenatal diagnosis is usually possible by chorionic villus sampling (CVS) or amniocentesis. If a couple are considering prenatal diagnosis, referral should be made to the local clinical genetics service prior to a pregnancy. This ensures that appropriate advice and investigations are undertaken and confirms whether or not prenatal diagnosis is possible. All couples considering preimplantation genetic diagnosis must be referred to their local clinical genetics service. Fetal sex determination by non-invasive prenatal diagnosis is now available, potentially reducing the need for invasive procedures by 50%. It should be discussed with families, but needs to be facilitated by clinical genetics departments or fetal medicine units.

Genetic testing is available in the UK and usually provided through specialist clinics or regional genetic centres.

This information is intended for educational use and was current in March 2015. For clinical management, it is recommended that local guidelines and protocols are used.