Becker's Muscular Dystrophy

The muscular dystrophies (MDs) are a group of inherited disorders characterised by progressive muscle wasting and weakness. Becker's muscular dystrophy (BMD) is similar to the more common muscular dystrophy - Duchenne muscular dystrophy (DMD) - but the clinical course is milder. As with DMD, there is muscle wasting and weakness which is mainly proximal. Generally, walking difficulties begin after the age of 16. [1]

Female carriers of BMD may be affected, either by some degree of muscle weakness and/or by cardiomyopathy.

Epidemiology

The incidence is about 1 in 17,000 live births (about one fifth of DMD incidence). [2] BMD is caused by abnormalities of the dystrophin gene, which is responsible for the muscle protein dystrophin. In BMD, abnormal but only partly functional dystrophin is produced (cf DMD, where dystrophin is lacking).

- It is inherited in an X-linked recessive pattern. There are various gene defects which give rise to BMD, affecting different parts of the dystrophin gene. The clinical severity of BMD varies and this is probably due to:
  - Variation in the individual genetic defects and hence in the dystrophins thus produced.
  - Factors other than the dystrophin gene, which determine the severity of BMD in an individual. In one reported family, two brothers with an identical gene defect had very different clinical manifestations of BMD. [1]

- BMD can occur as a new mutation. Therefore, not all mothers of BMD patients will be carriers of the gene. BMD can also occur through mosaicism (where only some cell lines are affected).

Presentation [2]

Symptoms
Symptoms usually begin in childhood. The average age at diagnosis is 11 years but there is a wide age range. The clinical severity varies.

Early symptoms
- Delayed walking (sometimes).
- Muscle cramps on exercise.
- Most BMD children are not ‘athletic’ and may struggle with school sports.

Later symptoms
- Muscle weakness:
  - Affects the proximal muscles of the limbs mainly.
  - May begin in teenage years or 20s, causing difficulty in climbing stairs, fast walking and lifting heavy objects.

- BMD patients can walk independently until the age of 16 or later (cf DMD, where patients cannot walk beyond the age of 12). Walking ability is lost (usually at the age of 40-60) but sometimes earlier, around the age of 20-30.
Signs

- Wasting of the proximal muscles; hypertrophy of others, particularly the calf muscles.

Other presentations

- Myoglobinuria.
- Anaesthetic complications - a dangerous, malignant hyperthermia-like reaction with some anaesthetic agents.
- Cardiomyopathy may be the first presentation, if muscle weakness is subclinical.
- There is a higher incidence of learning difficulties, behavioural problems and autistic spectrum disorders, compared with the general population.

Assessment

Investigations

Initial investigations

- Serum creatine kinase (CK) - shows moderate-severe increase in BMD (5-50 x normal levels). [2]
- Raised CK levels in this scenario merit specialist referral for further investigation.

Further investigations

- Genetic analysis
- Muscle biopsy - for dystrophin staining
- Genetic tests and counselling for the family
- Monitoring for cardiomyopathy (see 'Cardiac complications', below).

Differential diagnosis

- Other muscular dystrophies: differentiation is by the clinical features such as age of onset and pattern of muscle weakness, by muscle biopsy features and by DNA analysis.
- Other myopathies - eg. thyrotoxicosis, Cushing's syndrome.
- Neurological causes of muscle weakness: spinal cord lesions, spinal muscular atrophy, motor neurone disease, multiple sclerosis. These conditions may have additional features such as sensory loss, upper motor neurone signs or muscle fasciculation.

Management

Treatment is supportive and includes:

- Exercise programmes and physiotherapy. Recent evidence suggests that exercise training is beneficial. [3]
- Muscle cramps may be helped by night splints, massage or compression treatment using air-filled boots.
- Optimise nutrition:
  - Vitamin D and calcium for bone health.
  - Avoid obesity.
- After walking ability is lost - wheelchairs and other aids.
- Psychological support and employment advice.
- Monitoring/treatment of complications.
Complications and their management

Musculoskeletal complications
- Weakness can lead to joint contractures and scoliosis, which may require orthotic or orthopaedic treatment.
- Complications of immobility - eg, constipation and osteoporosis.

Cardiac complications [4]
The severity of cardiomyopathy and congestive heart failure may not parallel the severity of skeletal muscle disease. Atrial and ventricular arrhythmias may be life-threatening. The degree of hypoventilation and pulmonary dysfunction also affects cardiac function in muscular dystrophy. [5]

- Dilated cardiomyopathy:
  - Occurs in most BMD patients. [2, 6] It is the main factor influencing survival.
  - May be the presenting feature, if muscle weakness is mild. The severity of cardiac involvement does not correlate with the severity of skeletal muscle weakness. [7]
  - Asymptomatic (subclinical) cardiomyopathy is common. [8]
  - Symptoms may be nonspecific - eg, fatigue, poor sleep, weight loss, vomiting.

- Arrhythmias.

Monitoring and treatment
- Regular cardiac monitoring from diagnosis/from age 10 years, including:
  - Clinical evaluation.
  - Electrocardiogram (ECG) and echocardiogram - these may be difficult to interpret due to scoliosis.
  - Other possible tests - cardiac MRI, multigated acquisition study (MUGA) and tissue Doppler echocardiography may be more helpful than standard echocardiography. [9]

- Treatment is with standard regimens - eg, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers and diuretics for cardiac failure.
- Consider anticoagulation, as thromboembolism risk is increased.
- Nutrition and respiratory function should be optimised.
- Some patients require cardiac transplantation. [6]

Anaesthetic complications [4]
- Life-threatening rhabdomyolysis (malignant hyperthermia-type reaction) to some anaesthetic agents.
- Hyperkalaemia in response to succinylcholine.
- Higher risk of complications due to cardiac disease.
- Careful assessment and monitoring are required with any anaesthetic procedure or surgery.

Other complications
- Respiratory muscle weakness:
  - Depending on the clinical severity of muscle weakness, this is a possible complication. Management would be similar to that for DMD respiratory complications. See the separate Duchenne Muscular Dystrophy article.
- Pain in the lower back, spine and legs. [10]

Prognosis
- Life expectancy is often reduced but there is a wide variation in severity and the prognosis can be excellent.
- Cardiomyopathy is the cause of death in about half of BMD patients. [11]

Female carriers of Becker's muscular dystrophy

Cardiomyopathy risk
- Female carriers of the BMD gene may have an increased risk of cardiomyopathy.
- The extent of the risk is debatable; evidence is conflicting regarding rates of cardiomyopathy in carriers and regarding whether life expectancy is affected. [12]
- An international workshop in 2002 recommended regular cardiac screening for BMD carriers. [4] This recommendation has, however, been questioned. [12]

Manifesting carriers [2]
Most carriers are asymptomatic but a small percentage (2-5%) may have skeletal muscle symptoms; they are known as manifesting carriers of BMD:

- The reason why the gene manifests in some women but not in others may be through the mechanism of 'X-inactivation', where the normal X chromosome is inactive and the X chromosome carrying the BMD mutation is the active one.
As with BMD boys, there may be no family history of the disease. Some cases of BMD manifesting carriers were previously diagnosed as having another type of muscular dystrophy but, with new techniques such as dystrophin staining, have been identified as having BMD.

Clinical features

- There is wide individual variation in the severity of symptoms - from mild muscle weakness, aches or calf muscle enlargement, to a disease as severe as that in boys.
- Onset of symptoms can be in adulthood.
- There is usually some gradual progression of symptoms with time.
- Cardiac involvement can occur.

Diagnosis

- Muscle biopsy looking at dystrophin is usually helpful.
- Genetic tests, including X-inactivation patterns.

Management, follow-up and prognosis

This varies depending on individual severity of symptoms.

Further reading & references

1. Muscular Dystrophy, Becker Type, BMD; Online Mendelian Inheritance in Man (OMIM)

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