Beta-thalassaemia

Key facts

- The thalassaemias are a group of conditions, all of which are characterised by reduced synthesis of either the alpha (alpha-thalassaemia) or the beta (beta-thalassaemia) chain of the haemoglobin molecule.
- Beta-thalassemia major is the most common of the thalassaemias and is suspected in an infant or child in the first two years of life presenting with severe microcytic anaemia and hepatosplenomegaly.
- Treatment requires repeated blood transfusions; these help to maintain normal growth and development. Without treatment, affected children fail to thrive and have a shortened life expectancy.
- Beta-thalassaemia is an autosomal recessive condition.
- Beta-thalassaemia is caused by mutations in the beta-globin gene.
- The condition is extremely variable and symptoms in an affected individual often correlate to specific genetic alterations.
- Beta-thalassaemia is common in people from the Mediterranean, the Middle East, Southeast Asia and the Indian sub-continent.
- Antenatal screening for thalassaemia is available throughout the UK, apart from Northern Ireland. Screening is dependent on the prevalence of the condition in particular geographical areas. At a minimum, laboratory testing will be based on an assessment of risk which is determined by the ethnic origin of the baby's mother and father.

Clinical features

- Individuals with beta-thalassaemia are healthy at birth, but develop a severe anaemia between three months and one year of age.
- With correct treatment, children born in the UK with beta-thalassaemia should expect to live a near-normal life expectancy.
- Clinical manifestations are extremely variable.

Diagnosis

- The diagnosis depends on measuring red blood cell indices that reveal a microcytic hypochromic anaemia. Subsequent investigations should include: a peripheral blood film that shows an excess of primitive nucleated red blood cells; and haemoglobin electrophoresis that demonstrates decreased amounts of HbA and increased amounts of fetal hemoglobin (HbF) after 12 months of age.
- DNA testing (see below) may be useful for predicting the clinical phenotype in some cases.

Genetic basis

- Beta thalassaemia is an autosomal recessive condition, which means that the affected individual carries two altered copies of the beta-globin gene. The parents have one altered copy and one normal copy of the gene and are said to have beta thalassaemia trait. They usually have a mild anaemia. Each of their children has a 25% or 1-in-4 chance of inheriting both gene alterations, and is then at risk of developing complications of the condition.
- To date, more than 200 thalassaemia disease-causing alterations have been identified in the beta-globin gene. However, between four and 10 of these account for the majority of cases in the population groups where beta-thalassaemia is most common.

Clinical management

- The diagnosis may be anticipated by identifying parents as carriers during antenatal screening and confirmed by prenatal diagnosis when requested, or by neonatal testing. The family can then be seen before the development of symptoms, and arrangements for care discussed.
- All patients should receive an optimal level of care delivered close to home as well as access to clinical experts in specialist centres.
- Regular transfusions correct the anaemia, but transfusional iron overload needs to be prevented by adequate iron chelation. Transfusions are usually required every three to four weeks.
- A definitive cure is possible following bone marrow transplantation.

Genetic testing

Genetic testing can be used to:

- identify the gene alterations in the beta-globin genes in someone with beta-thalassaemia;
- provide information about the genetic status of relatives of someone with beta-thalassaemia through carrier testing; and
- offer prenatal and pre-implantation 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 pre-implantation genetic diagnosis must be referred to their local clinical genetics service.

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.