Sickle cell disease in pregnancy

Eugene Oteng-Ntim
Shazia Nazir
Tasneem Singhal
Jo Howard

Abstract

Sickle cell disease (SCD) is an autosomal recessive condition, which leads to life-long haemolytic anaemia. Clinical features are intermittent episodes of severe pain and chronic complications including a high risk of stroke, renal dysfunction, retinopathy and cardiopulmonary disease. Advances in treatment have enabled affected women to live to child-bearing age. Pregnancy and childbirth with SCD are considered high-risk, and are associated with increased maternal and fetal morbidity and mortality. A universal newborn screening programme provides for early identification of all affected newborns. The antenatal screening programme identifies women with haemoglobinopathies and offers them the option of fetal screening. Management of women with SCD begins with preconceptual care, which involves counselling, screening for end organ damage and a review of their medications. Multidisciplinary antenatal care is desirable. Contraception should be discussed post pregnancy. The only proven cure for this condition is correction of the genetic defect by haematopoietic stem cell transplantation.

Keywords fetal complications; haemoglobinopathy; maternal complications; preconceptual care; pregnancy; sickle cell disease

Introduction

Sickle cell disease (SCD) is the most common inherited condition in the UK and worldwide. About 300,000 children with SCD are born each year, two-thirds of these in Africa. In the UK, it is estimated that there are 12–15,000 affected individuals and over 300 infants are born yearly with SCD in the UK who are now diagnosed as part of the neonatal screening programme.

Eugene Oteng-Ntim *MBBS PGDiP FRCOG is a Consultant Obstetrician and Honorary Senior Lecturer in the Division of Women's Health at St. Thomas' Hospital, London, UK. Conflict of interest: none declared.*

Shazia Nazir *MBBS MRCOG is a Consultant Obstetrician at Maidstone and Tunbridge Wells NHS Trust, UK. Conflict of interest: none declared.*

Tasneem Singhal *MBBS MD MRCOG is a Senior Registrar at the Division of Women's Health, St. Thomas' Hospital, London, UK. Conflict of interest: none declared.*

Jo Howard *MBBS MRCP is a Consultant Haematologist at Guy's and St. Thomas' Hospital, London, UK. Conflict of interest: none declared.*

There are approximately 100–200 pregnancies in women with SCD per year in the UK and pregnancy outcome in this group is currently being assessed by the UK Obstetric Surveillance System (UKOSS).

Background

SCD has its origins in Sub-Saharan Africa and the Middle East; hence it is most prevalent in individuals of African descent as well as in the Caribbean, Middle East, parts of India, Mediterranean and South and Central America. Due to population migration it is now of increasing importance worldwide and there are increasing numbers of affected individuals in Europe and the US.

Definition

SCD is an autosomal recessive disorder, caused by the 'sickle' gene, which affects haemoglobin (Hb) structure. The term SCD refers to homozygous sickle cell disease (HbSS). The heterozygous conditions which occur when HbS is co-inherited with another abnormal haemoglobin, most commonly HbC or β-thalassaemia, giving rise to HbSC or HbSβ thalassaemia. Co-inheritance can occur less commonly with HbD, HbE and HbO-Arab. All genotypes give a similar clinical picture, although with varying severity, for example patients with HbSC tend to follow a milder clinical course than patients with HbSS.

Pathophysiology

Normal haemoglobin

Haemoglobin is composed of the haem, which consists of an iron molecule attached to four pyrrole rings and two pairs of globin chains (two α and two β).

Normally, from 6 months of age, 95–97% of the total haemoglobin is haemoglobin A (HbA) (two α and β chains). The remaining haemoglobin consists of HbA2 (2%: two α and two δ globin chains) and fetal haemoglobin (HbF, <1.5%; two α and two γ globin chains).

Haemoglobin S

This is the predominant haemoglobin in people with sickle cell disease caused by a point mutation in the β-globin chain, causing the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position giving the molecule the structure, $a_2b_2^s$ whereas the alpha chain is normal.

Haemoglobin S combined with normal haemoglobin (A) is known as sickle trait (AS). It is asymptomatic except for a possible increased risk of UTIs and microscopic haematuria.

Erythrocyte changes

In the oxygenated state, the solubility of HbS is nearly equal to that of HbA, and its oxyhaemoglobin form has the ability to function in a physiological manner. In the deoxygenated state, however, its solubility falls to one-fiftieth of that of HbA, resulting in aggregation to form liquid crystals. This causes the erythrocytes to assume the classical 'sickle shape'. Re-oxygenation can restore these erythrocytes to their normal shape.

Repetitive cycles of sickling and polymerization lead to membrane rigidity, and irreversible sickle cells are eventually formed. These permanently damaged erythrocytes are then

© 2012 Published by Elsevier Ltd.

cleared by the reticuloendothelial system. Thus, the average lifespan of the red blood cells of sickle cell patients is 17 days compared with the 120-day lifespan of normal erythrocytes.

Clinical features

Chronic anaemia

One result of this pathophysiology is a chronic compensated anaemia (6.5—9.0 g/dl in HbSS), as the marrow's capacity to generate new red blood cells is limited. Bone marrow aspirate will show erythroid hyperplasia and the blood film will show sickle-shaped red blood cells and polychromasia.

Patients with the milder genotypes (e.g. HbSC) may have higher Hb levels or even within the normal range. So having abnormal, or near-normal haemoglobin does not exclude the diagnosis of SCD.

Painful sickle crisis

The other major clinical feature is recurrent, unpredictable episodes of severe bony pain secondary to vaso-occlusion, which occurs lifelong. These painful episodes (or 'crises') occur with variable frequency and severity. These crises can be precipitated by stress, dehydration, infection and cold damp conditions. There is an increased risk of painful crisis during pregnancy, especially in the latter half of pregnancy and the puerperium. Crises may even occur in women who have previously had very few episodes of sickle pain.

Acute chest syndrome

This life-threatening complication presents with cough, chest pain, dyspnoea, fever, worsening anaemia, leukocytosis, audible crackles and/or bronchial breathing on examination, and a florid infiltrate on the chest X-ray. The patient may need assisted or mechanical ventilation. This is among the most common causes of maternal death. The syndrome arises due to sickling in the lungs, often combined with infection. Aetiology is multifactorial but the pathophysiology is not totally understood. Diagnosis and treatment are often delayed and early detection and treatment may reduce the severity and prevent death. Optimal treatment includes exchange blood transfusion and antimicrobial agents.

Endocrine and metabolic changes

It is currently thought that iron overload is the main underlying cause of endocrine dysfunction in patients with SCD. Increased numbers of transfusions have been associated with greater risk of endocrine organ failure.

Growth failure and delayed pubertal development, gonadal failure, diabetes and carbohydrate intolerance and primary hypothyroidism have been documented. Generally, treatment consists of replacement of particular hormones and improvement of nutritional status.

An unanswered question is whether patients with SCD are prone to endocrine pathology in the absence of iron overload due to crises in the glands. Future work may allude to this.

Other complications

In patients with SCD splenic infarction has usually occurred by 5—6 years of age, leading to a lifelong increased risk of infection, especially due to encapsulated organisms such as Streptococcus pneumoniae and *Haemophilus influenzae*. Occasionally, splenomegaly or splenic sequestration, which is associated with profound anaemia, can occur in adults when splenic auto infarction has not taken place.

Gallstone formation is common in SCD secondary to increased red cell breakdown and can lead to acute cholecystitis. Aplastic crises occasionally occur during pregnancy associated with infection of parvovirus B19, and are characterized by a rapidly falling haemoglobin level secondary to an aplastic bone marrow.

SCD is also associated with chronic organ damage and this can cause renal dysfunction, pulmonary hypertension, chronic lung disease, retinopathy, leg ulcers, cholelithiasis and avascular necrosis. Any of these complications can occur de novo, or worsen during pregnancy. Neurological complications such as stroke or silent infarction are also common in SCD, although there is no evidence that they increase during pregnancy.

Impact on maternal and fetal outcome

SCD is a disease of tremendous clinical variability. Early experience with SCD and pregnancy was a cause for pessimism, and the first report of a successful pregnancy in a woman with SCD was only in 1931. The first major review, in 1941, reported a 50% fetal loss. Since that time, there have been a number of observational reports on maternal mortality rates. The initiation of early aggressive prenatal care has dramatically improved perinatal outcome and reduced maternal mortality to less than 1% (Table 1).

SCD is associated with both maternal and fetal complications. In the mother, there is an increased incidence of acute painful crises in pregnancy, increased antenatal hospitalization, maternal mortality, caesarean rate, infection, thromboembolic events and antepartum bleeding. An increased risk of pre-eclampsia and pregnancy induced hypertension has been seen in some studies but not in others.

Fetal complications include an increased incidence of perinatal mortality, stillbirth, premature labour, fetal growth restriction. Some studies have also seen an increase in spontaneous abortion.

The differences in these studies are probably due to the small size of some of them, and their retrospective nature. In HbSC there are less reported adverse outcomes, but there is evidence of increased painful crises during pregnancy, and increased fetal growth restriction, antepartum hospital admission and postpartum infection.

With improved medical care, the frequency of sickle crises in pregnancy has decreased significantly; but they may still occur and constitute an obstetric emergency. Therefore, it is important for every obstetrician to be familiar with the condition.

Screening

Newborn screening

The United Kingdom Newborn Screening programme functions to provide early identification of conditions for which appropriate, timely treatment can lead to a reduction in the associated mortality and morbidity. Children who have SCD are at increased risk of bacterial infection as neonates. Prophylactic penicillin in children who have the disease decreases the risk of pneumococcal septicaemia by 84%.

A universal newborn screening programme has been implemented in the UK since 2006. All mothers, regardless of ethnic origin, are offered neonatal screening for SCD. The universal

© 2012 Published by Elsevier Ltd.

Download English Version:

https://daneshyari.com/en/article/3967020

Download Persian Version:

https://daneshyari.com/article/3967020

Daneshyari.com