Hypoplastic left heart syndrome

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Abstract

Hypoplastic left heart syndrome is a rare congenital heart defect in which the left-sided heart structures are underdeveloped, such that the left ventricle is unable to support the systemic circulation. It is almost always lethal without surgical treatment, and if left untreated would account for around 25–40% of neonatal cardiac deaths in the United Kingdom. Complex neonatal surgery to enable the right ventricle to support the circulation (the Norwood Procedure) has transformed management of the condition, but requires three staged procedures during early childhood. Management of these patients into adulthood will offer new challenges. Transplantation for this condition remains rare, and is reserved for those in which conventional treatment has failed. In this review article, we discuss epidemiology, genetics, morphology, pathophysiology, prenatal diagnosis, modes of clinical presentation, and management strategies in this challenging condition.

Keywords hypoplastic left heart syndrome; norwood; univentricular heart

Introduction

Hypoplastic left heart syndrome (HLHS) is a complex congenital heart defect in which one or more of the left-sided cardiac structures are underdeveloped such that the heart is unable to support the systemic circulation. It is a fatal condition without intervention, which usually needs to be undertaken in the first few days after birth. Prior to the 1980s there was no treatment for the condition and it was viewed as being universally lethal until 1982. Surgical treatment was first undertaken in the UK in the early 1990s and now several congenital heart units in the UK have established programmes to treat affected children.

Surgical management focusses on utilizing the right ventricle to support the systemic circulation. A series of staged operations then gradually redirect the systemic venous drainage directly into the lungs to create a circulation that is driven by a single (right) ventricle. This extraordinary series of procedures essentially creates a circulation in series rather than the normal situation of a circulation in parallel, driven by two ventricles.

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These staged operations are the definitive way of managing HLHS and often referred to as the 'Norwood' strategy after the surgeon who first described them. The heart can never be 'normal' as there is functionally only one developed ventricle, so these operations are often referred to as being 'palliative' in the sense that they do not correct the heart condition back to a normal (biventricular) circulation. The term 'palliative' can be misleading in this context and should not be confused with the commoner use of the word in the setting of palliative care.

Primary cardiac transplantation is, in theory, an alternative treatment strategy but neonatal heart donors are essentially unknown in the UK and very rare around the world. Neonatal heart transplantation is therefore not a practical option in most countries, although a handful of centres have pursued this approach – accepting that many patients will die while awaiting a suitable organ. Given the success of the Norwood strategy, most units opt for this 'staged palliation' approach and only consider transplantation as a secondary option in children or adults who run into heart failure later in life.

The 'Norwood strategy' is undertaken through three stages: (i) the Norwood operation on neonates; (ii) superior cavopulmonary anastomosis at 6–8 months of age; and (iii) total cavopulmonary connection between 18 months and 5 years of age (most commonly around 4 years). HLHS continues to be one of the highest risk lesions in children with congenital heart disease and, although surgical outcomes continue to improve, survival is currently around 65% at 5 years of age and 55% at 10 years of age. Despite these encouraging outcomes, many affected children may have developmental issues and a need for lifelong medical attention for ongoing health problems, both of which can place considerable strain on families. Counselling is essential for parents to make an informed decision and comfort care should be considered as an alternative pathway.

Epidemiology

HLHS is rare, occurring in about one in every 5000 live births, comprising approximately 2–3% of all children with congenital heart defects, and equating to approximately 150 affected children born in the UK per year. The condition is found worldwide with no particular ethnic or geographical preponderance, nor is there any described association with maternal age or parity. It is slightly more common in males. Despite the low incidence, the condition is of considerable significance because of its serious natural history – without treatment it would be responsible for 25–40% of all neonatal cardiac deaths, being fatal within a few weeks from birth in 95% of cases.

Pathophysiology

Genetics

As yet, no causative gene for HLHS has been found and most children with HLHS do not have chromosomal anomalies. There are, however, associations with Turner's syndrome (monosomy X), Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13). The chromosomal abnormality with the most consistent incidence of HLHS is the terminal deletion of the long arm of chromosome 11 (Jacobsen syndrome), comprising between 5 and 10% of affected individuals. A candidate gene in this region, *ETS-1*, has been implicated in cardiac development in non-

mammals and in mice. Other genes that have been associated with HLHS include *GJA1* (chromosome 6), *NKX2* on chromosome 5, and somatic mutations in the *HAND1* gene, also on chromosome 5.

A small, but well-recognised, risk of recurrence in future pregnancies exists. This is around 2–4%, although in families with two affected children the recurrence risk is considerably greater, estimated at 25%. This finding alone suggests that HLHS has a genetic component, although it is likely to be more complex and multifactorial in nature.

Physiology

In HLHS, the left side of the heart cannot support the systemic circulation. Survival is only possible where the systemic circulation is supported by the right ventricle via right-to-left flow through the ductus arteriosus (Figure 1). Without intervention the duct closes during the first few days after birth, exposing the left heart insufficiency, with subsequent failure of the systemic circulation. In addition, pulmonary venous return can only reach the systemic circulation by crossing the atrial septum (through a patent foramen ovale) to reach the right side of the heart. Thus the circulation relies on two shunts, with resultant obligate mixing of pulmonary venous and systemic venous return, creating a cyanotic condition. Without ductal flow the situation is incompatible with life: a duct-dependent systemic circulation.

Morphology

The cardiac morphology of HLHS is heterogeneous. The condition cannot simply be called left ventricular hypoplasia as the left heart consists of components (i.e. the mitral valve, left ventricular cavity, left ventricular outflow tract, aortic valve, ascending aorta, and aortic arch) that are all inter-related in their development and function. No single component can be considered in isolation as all may be involved in the condition. More than one and frequently all components are underdeveloped to varying degrees.

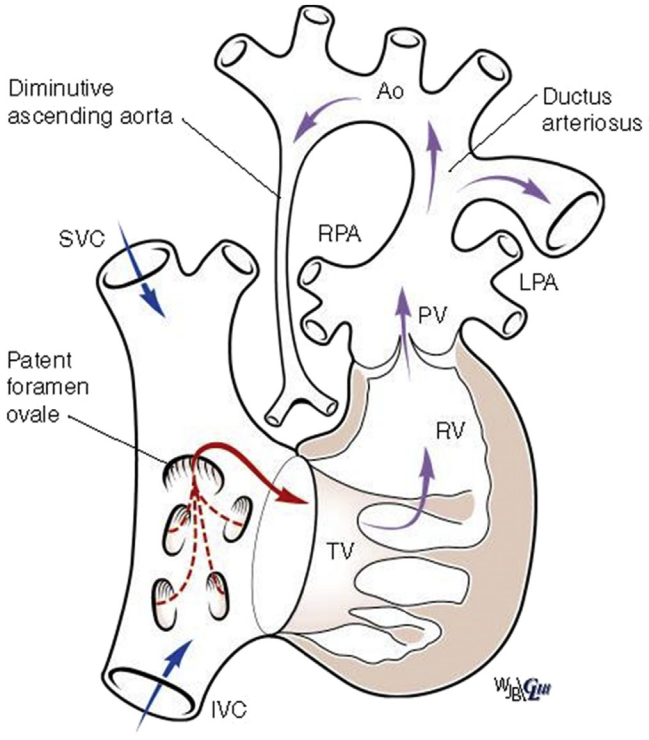

Figure 1 Hypoplastic left heart syndrome.

Establishing the morphological subtype has prognostic significance, particularly in aortic atresia and mitral stenosis, in which there is inflow to but no outflow from a small, hypertensive left ventricular cavity. This subtype has been shown to have poorer outcomes than others, perhaps related to associated coronary anomalies.

Other cardiac abnormalities can occur together with HLHS in about 7·5% of all cases. Examples are transposition of the great arteries, atrial isomerism, and total anomalous pulmonary venous drainage. These additional abnormalities may require additional surgical procedures and might affect outcome, but HLHS remains the dominant lesion and thus governs the management of these more complex patients.

Presentation and diagnosis

The clinical presentation of HLHS varies depending on the flow through the obligate shunts. Often, babies are born in good condition by virtue of a patent ductus and the systemic circulation being supported by the right heart. At one end of the spectrum, if the patent foramen ovale and the ductus are widely open, then cyanosis may not be clinically obvious and abnormal findings on examination would suggest a large patent ductus (continuous murmur and wide pulse pressure) and little else. However, these patients have uncontrolled pulmonary blood flow and a large volume load on the circulation due to the shunts. As the pulmonary vascular resistance falls pulmonary blood flow increases and babies typically develop signs of congestive heart failure with increasing tachypnoea and hepatomegaly, and cardiomegaly and pulmonary congestion on the chest radiograph. This situation may progress into respiratory distress, increasing acidosis, and circulatory collapse.

At the other extreme, babies may have significant pulmonary venous congestion and are cyanosed and tachypnoeic from birth secondary to a restrictive patent foramen ovale or even intact atrial septum. Severe restriction at the atrial septum leads to profound cyanosis, rapid decompensation, and may be incompatible with life. Survival depends on the degree of restriction and some patency of the mitral and aortic valves to allow at least some blood to leave the left heart.

Within the spectrum, babies may have a moderate sized ductus and aortic coarctation with weak or absent femoral pulses and congestive heart failure because of the combination of high pulmonary blood flow and high systemic afterload. These signs may only become apparent a few days after birth as the ductus begins to close. The degree of cyanosis is variable and arterial saturations can be maintained in the 90s, with mixing of the circulation masked to some extent by high pulmonary blood flow.

A plain chest radiograph can reveal cardiomegaly with pulmonary plethora and oedema, but is not diagnostic. An electrocardiogram (ECG) is generally non-specific, usually demonstrates a normal rhythm, and can show evidence of right ventricular hypertrophy with tall R-waves in the anterior chest leads. Echocardiography is the key to confirming the diagnosis and