Hypoplastic left heart syndrome: diagnosis and management

Rachel Andrews, Robert Tulloh

The prognosis of hypoplastic left heart syndrome has improved dramatically in recent years with advances in reconstructive surgery. Many cases are now diagnosed antenatally, allowing parents time to make informed decisions about treatment options.

Hypoplastic left heart syndrome (HLHS) is a relatively common form of congenital heart disease, making up approximately 8% of the total, with an estimated birth incidence of 0.1–0.25/1000 live births (Abu-Harb et al, 1994). However, the true incidence will be higher than this, as the risk of spontaneous intrauterine death increases in affected pregnancies. Allan et al (1994) reported a rate of 5% in 161 cases of antenatally-diagnosed HLHS. The condition usually occurs in isolation, with only 3% of cases having other extracardiac anomalies (Cook et al, 1998) and 5% having chromosomal abnormalities (Raymond et al, 1997).

If untreated, the condition is universally fatal, with 95% of babies dying within the first month of life (Stuart et al, 1991). However, the development of reconstructive surgical techniques and heart transplantation has lead to a dramatic improvement in the prognosis of HLHS over the last 20 years. Medium-term survival is now approaching 70% following reconstructive surgery in some centres (Bove, 1999; Mahle et al, 2000a); and is even higher following transplantation (Razzouk et al, 1996; Hehrlein et al, 1998), but the use of transplantation is severely limited by a shortage of donor organs (Stuart et al, 1991). Worldwide, it is the increased availability of reconstructive surgery, together with improvements in surgical technique and intensive care facilities, that has led to the greatest improvement in survival.

This review describes the anatomical features of HLHS and what is known of its aetiology. Presenting features of the condition are discussed, together with advances in diagnostic techniques and their implications. The surgical techniques involved in treating HLHS are outlined, and the outcome in terms of mortality and morbidity is discussed. Finally, possible future developments are considered.

Dr Rachel Andrews is Specialist Registrar in Paediatric Cardiology and **Dr Robert Tulloh** is Consultant Paediatric Cardiologist in the Department of Congenital Heart Disease, Guy's Hospital, Guy's and St. Thomas' NHS Trust, London SE1 9RT

Correspondence to: Dr R Tulloh

ANATOMICAL FEATURES

First described in 1958, the anatomical features of HLHS are severe aortic and mitral valve hypoplasia or atresia, with underdevelopment of the left ventricle and varying degrees of aortic arch hypoplasia. Pulmonary venous blood returning to the left atrium passes through the foramen ovale to mix with systemic venous blood in the right atrium. This is pumped into the main pulmonary artery by the right ventricle, with flow to the descending aorta provided through a patent arterial duct. The head and neck vessels are supplied from retrograde flow around the aortic arch. After birth, if the duct closes, the systemic circulation cannot be supported and the infant will die if untreated.

With this anatomical arrangement, both pulmonary and systemic circulations depend on the right ventricle. The reconstructive techniques pioneered by William Norwood in the early 1980s are based on a staged separation of the pulmonary and systemic circulations, such that the right ventricle becomes solely the systemic pump (Norwood et al, 1983). Although this reduces the load on the right ventricle, it is obviously not designed to pump at systemic pressure, and it remains to be seen how it will fare in the long term.

GENETICS

Grossfeld (1999) reports evidence which support a genetic aetiology for HLHS. As with other forms of congenital heart disease, the recurrence risk when one family member has been affected is somewhat greater than the background risk, maybe as high as 13%. Second, bicuspid aortic valves are 12 times as common in first-degree relatives of infants with HLHS than in the general population. Third, although HLHS usually occurs in isolation, a minority of cases do occur in association with recognized syndromes, notably Turner's syndrome and trisomies 13 and 18.

Evidence from animal models and serial fetal echocardiography in humans points to decreased blood flow through the left ventricle as being a key factor in the development of HLHS. In some cases, decreased flow occurs as a result of mitral or aortic hypoplasia or atresia, but in others there seems to be a primary defect in left ventricular growth, with reduced left ventricular inflow as a result. This heterogeneity makes it likely that there are multiple genes which, when mutated, primarily or secondarily decrease blood flow through the left side of the heart, resulting in HLHS.

Identification of candidate genes by linkage analysis is difficult, as large families with multiple affected members are extremely rare, and the apparent genetic heterogeneity of HLHS means that data from smaller pedigrees cannot be pooled. In view of this, research is currently focussing on syndromes with known deletions or translocations in which HLHS occurs with a higher frequency, e.g. Jacobsen syndrome, in the hope of being able to identify at least some causative genes.

ANTENATAL DIAGNOSIS

With improvements in the resolution of fetal ultrasound, an increasing number of HLHS cases are being picked up on routine antenatal anomaly scans (Simpson, 2000). On the standard four-chamber view of the heart, underdevelopment of the left ventricle may be seen, and if the fetus is lying in a suitable position, it may also be possible to see hypoplasia of the aortic arch. A minority of cases may be detected very early in pregnancy (12–14 weeks) if specialist ultrasound equipment is available. In this situation, there would appear to be a primary failure of development of the left side of the heart. However, cases may also be detected in later pregnancy or postnatally when there has been a normal 20-week scan, or just a mild degree of aortic stenosis. These findings suggest that progressive aortic stenosis and/or coarctation has led to growth failure of a ventricle which was previously appropriately sized.

If HLHS is suspected, an urgent referral should be made for a fetal cardiology opinion at a tertiary centre. If the findings are confirmed, parents can be counselled about the different options: to continue the pregnancy and have surgery, to have palliative care after delivery or to terminate the pregnancy. Elective delivery in a specialist unit can be arranged to minimize separation of mother and baby and avoid the need for an ex-utero transfer. The parents may also be able to meet the surgeon who will be operating on their child and be shown around the unit, providing a coordinated service between fetal cardiology, neonatology, paediatric cardiology and cardiac surgery.

POSTNATAL DIAGNOSIS

Infants with HLHS may appear healthy at birth but rapidly become cyanosed and shocked as the arterial duct begins to close. Besides cyanosis, clinical signs include lethargy, pallor, dyspnoea and weak or absent peripheral pulses. Chest X-ray may show cardiomegaly and increased pulmonary vascularity, but it is often normal. The electrocardiogram may show prominent P waves and signs of right ventricular hypertrophy, but this too is often normal. Saturations are not significantly improved even in 100% oxygen, and a high inspired fractional oxygen concentration (FiO_2) is actually harmful, as it encourages the duct to close.

If the diagnosis is suspected, the infant should be intubated and commenced on an infusion of prostaglandin E_1 or E_2 to maintain ductal patency. Peripheral oxygen saturation, as measured by pulse oximetry, may remain at 50–60% without the infant coming to any harm in the short term. Inotropes may be required in addition, but volume expanders should be used with caution in order not to overload the heart.

Once the infant's condition has been stabilized, the diagnosis can be confirmed on an echocardiogram. *Figure 1* shows a four-chamber view of the heart from an echocardiogram in an infant with HLHS. In this example, a small globular left ventricular cavity can be seen; in other cases, the cavity may be slit-like, or there may be no demonstrable cavity at all. As well as examining the left heart structures and the aortic arch, it is important to ensure that the duct is widely patent, that there is good right ventricular function and that there is unrestricted flow across the atrial septum. If the interatrial communication is very small, obstructing the pulmonary venous return, surgery may need to be performed early.

TREATMENT

There are two surgical options for treatment of HLHS: staged reconstructive surgery or heart transplantation. Where there is donor availability, transplantation provides an essentially nor-

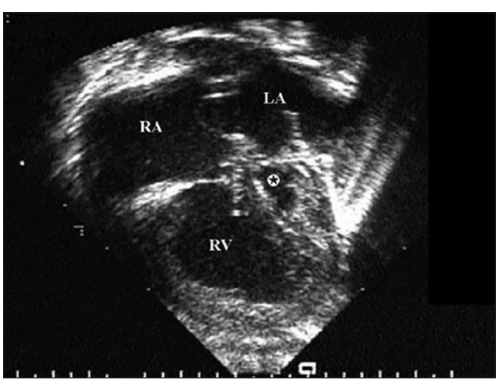

Figure 1. Four-chamber view of the heart from an echocardiogram in an infant with hypoplastic left heart syndrome. The hypoplastic left ventricle is marked with a star. LA = left atrium; RA = right atrium; RV = right ventricle.

mal circulatory physiology in a single procedure. However, the mortality while awaiting transplantation is approximately 25% (Bove, 1999), and there are long-term problems from rejection, infection, lymphoproliferative disease and accelerated atherosclerosis. In the UK, primary transplantation for HLHS is very limited because of a shortage of donors, and the vast majority of babies undergo reconstructive surgery.

Reconstructive surgery for HLHS is performed in three stages (*Figures 2–4*). The first stage, known as the Norwood procedure, is performed within the first few days of life. This consists of reconstruction of the hypoplastic aorta using the proximal main pulmonary artery, removal of the atrial septum and insertion of a systemic–pulmonary artery shunt. The second stage, the hemi-Fontan operation, is carried out between 4 and 12 months and consists of an anastomosis between the superior vena cava and the right pulmonary artery. The third stage, the Fontan operation, is performed at 2–4 years of age and consists of an anastomosis between the inferior vena cava and the right pulmonary artery.

These operations allow complete separation of the pulmonary and systemic circulations, with systemic venous drainage passing directly to the lungs, and the right ventricle acting solely as the systemic pump. The staged approach is necessary as the pulmonary vascular resistance is initially too high for the Fontan circulation. The mortality is lower if the Fontan circulation is created in two stages (hemi-Fontan then Fontan), allowing the right ventricle to adapt gradually to its changing workload (Norwood, 1991; Forbess et al, 1997).

Children undergoing reconstructive surgery need to be assessed regularly both by echocardiography and cardiac catheterization. As well as checking that there has not been any anatomical distortion, particularly of the pulmonary arteries, it is important to assess pulmonary vascular resistance and cardiac function. If right ventricular function deteriorates despite the reduction in workload as surgery progresses, a transplant may be required, although this is unusual. Most children who have undergone reconstructive surgery do not require any long-term medication.

OUTCOME

There has been a steady improvement in survival figures following both reconstructive surgery and transplantation (Hehrlein et al, 1998; Mahle et al, 2000a). There is considerable variation in the survival rates reported by different institutions in the UK and the USA following reconstructive surgery; this is explained partly by differences in patient populations and partly by differences in selection criteria for surgery. Medium-term sur-

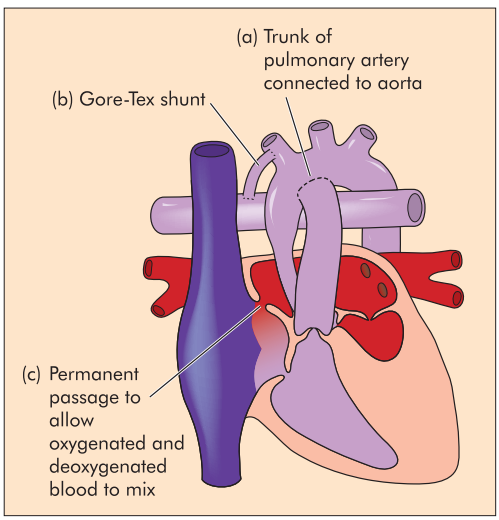

Figure 2. The Norwood procedure.

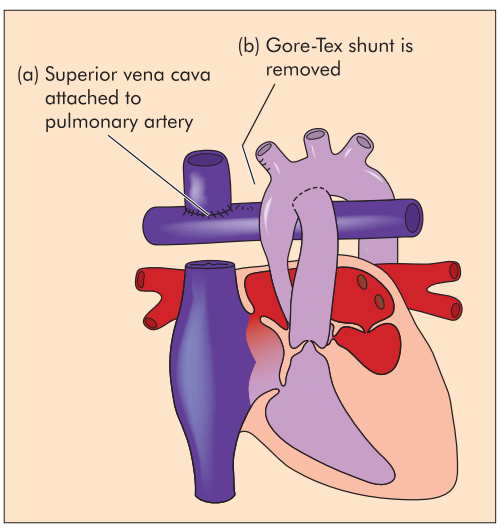

Figure 3. The hemi-Fontan procedure.

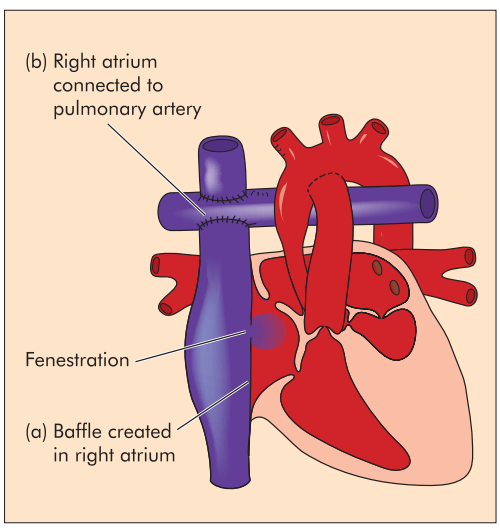

Figure 4. The Fontan procedure.

vival rates vary from 48–70%, with the majority of deaths occurring at stage 1 (Bove, 1999; Ishino et al, 1999; Mahle et al, 2000a; Andrews et al, 2002).

Although mortality following stage 1 is high, the medium-term outlook for survivors is good. In one UK series, only 3 out of 31 children had significant neurological impairment (Andrews et al, 2002). On formal neurodevelopmental testing, Bove (1999) found that most children had normal verbal and performance scores, and Goldberg et al (2000) reported Wechsler intelligence scores in the normal range. However Mahle et al (2000b) reported that although most school-aged survivors had IQ scores within the normal range, mean performance was lower than in the general population, and 18% of patients had IQs of less than 70.

In the long term, there is uncertainty as to how patients with HLHS will fare with a Fontan circulation dependent on the right ventricle as the systemic pump. Worldwide, the oldest patients are now in their late teens, and although there have been concerns about decreased exercise tolerance, this does not appear to be related to ventricular morphology or surgical approach (Joshi et al, 1997). However, it seems likely that some patients will eventually require transplantation.

CONCLUSIONS AND FUTURE DEVELOPMENTS

With increased availability of reconstructive surgery and improvements in surgical techniques, the outlook for infants with HLHS has improved dramatically in recent years. Antenatal diagnosis allows parents to come to terms with the diagnosis and make informed decisions about the pregnancy and subsequent management of their child. Such decisions will be helped by advances in the understanding of the aetiology and natural history of HLHS and the availability of long-term outcome data. It is hoped that continuing improvements in surgical technique will minimize peri- and postoperative mortality and reduce the risk of complications in the medium and long term.

Likely future developments include use of magnetic resonance imaging to assist or even replace cardiac catheterization in the evaluation of children with HLHS; it is less invasive, quicker and can provide the same information. Mechanical hearts, such as the Jarvik 2000 (Westaby et al, 2000), may provide an alternative to transplantation in fully grown patients with a failing Fontan circulation. Ultimately, identification of the genes responsible for HLHS will lead to earlier diagnosis and possible prevention of the condition. HM

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KEY POINTS

- Overall surgical survival for babies with hypoplastic left heart syndrome is about 70%.
- Antenatal diagnosis allows parents time to make informed decisions.
- If the diagnosis is suspected after birth, a prostaglandin E_1 or E_2 infusion should be used and the inspired oxygen level kept low to maintain duct patency.
- Surgery is performed in three stages over 3–4 years, with the highest mortality occurring at stage 1. Most survivors have a good quality of life and function within the normal intelligence range.