Chapter 6

Prenatal features of Ebstein’s anomaly

L.A. Lisowski, P.M. Verheijen, Ph. Stoutenbeek, E.J. Meijboom
The Thoraxcentre Journal 2001; 13; 57-60.
In press Prenatal Diagnosis
Abstract

Objectives
A meta-analysis of the literature on Ebstein’s anomaly and a comparison of the results in a tertiary level referral center for pediatric cardiology and cardiac surgery. Included is a review of the diagnosis, management and outcome in cases of Ebstein’s anomaly.

Methods
A diagnosis of tricuspid valve anomaly was made in 14 fetuses. Isolated Ebstein’s anomaly occurred in 4 patients. One patient had Ebstein’s anomaly associated with discordance of the great arteries, congenitally corrected transposition of the great arteries. Tricuspid valve dysplasia was encountered in 10 fetuses.

Results
In the group with Ebstein’s anomaly (n=4) two fetuses died in utero at a gestational age of 29 and 36 weeks. Parents opted for compassionate care in one fetus that died at an age of 2 days. One patient with congenital corrected transposition of the great arteries is alive at an age of 9 years after receiving pulmonary artery banding, a partial cavopulmonary connection and a Damus-Kay-Stansel operation. In this group two fetuses had hypoplasia of the lungs, of which one had a chromosomal anomaly (trisomy 18).

Conclusion
Patients with a prenatal diagnosis of Ebstein’s anomaly or dysplasia of the tricuspid valve represent the most serious component of the spectrum of Ebstein’s malformation. The very poor outcome is representative for this selected population and cannot be compared to patients in which the anomaly is detected in later life. Parental counseling of these patients can therefore not be based upon the natural history of these older patients. Prenatal diagnosis provides opportunities for in-depth counseling of the parents before the medical and emotional complexities associated with the neonatal intensive care setting are encountered. Surgical procedures of tricuspid valve repair or replacement are offered for this anomaly, but this option is almost exclusively provided for patients with a diagnosis in later life, as very few patients survive the neonatal period.
Introduction

Anatomy
Dysplastic malformations of the tricuspid valve (TV) include a wide range of morphologic features. The pathological spectrum of dysplasia of the tricuspid valve starts with deformation of the leaflets and the tension apparatus, but without downward displacement, an arrangement primarily described as dysplasia, and ranges to lesions in which the primary lesion is downward displacement of the proximal attachment of the posterior and septal leaflets, known as Ebstein’s anomaly (EA). Although the anatomical spectrum varies, the clinical expression is similar and the outcome depends primarily on the severity of the tricuspid insufficiency, rather than the anatomical substrate.

Prevalence
The prevalence of Ebstein’s anomaly and tricuspid valve dysplasia (TVD) is approximately 0.5-1.0 % of patients with congenital heart disease. Patients with Ebstein’s anomaly may present at any age, including the prenatal period. Most cases are sporadic, but familial occurrence has been documented. Fetal echocardiography is a very sensitive (91.6%) and specific (99.9%) tool for antenatal diagnosis of congenital heart disease in high-risk pregnancies. The experience with prenatal detection of structural congenital heart defects is still increasing and the methods of prenatal examination become more sensitive. Therefore more lesions of this kind, even the milder cases, will be detected in utero which might improve the overall outcome and will raise questions about the management of the fetus during pregnancy and in immediate postnatal life.

Indications for intrauterine evaluation

Fetal factors
Fetal factors for reference include fetal arrhythmias, fetal hydrops and/or hydramnion, but most patients with an in utero diagnosis are referred because of an abnormal four-chamber view on a routine prenatal ultrasound. This abnormal four-chamber view is not infrequently associated with the existence of non-immune hydrops fetalis and associated arrhythmias.

Maternal factors
Maternal factors for referral include: a history of congenital heart disease in the previous offspring of the mother, gestational diabetes and teratoge-
nic exposure to drugs, mostly lithium therapy, during pregnancy.\textsuperscript{6,9-17} The latter forms a special indication for referral. A direct teratogenic effect of lithium on the atrioventricular junction is thought to facilitate the development of Ebstein’s anomaly.\textsuperscript{6} While initial information regarding the teratogenic risk of lithium treatment was derived from retrospective reports, more recent epidemiological data indicate that the teratogenic risk of first trimester lithium exposure is lower than previously suggested. An incidence of 2-8\% of the occurrence of Ebstein’s anomaly has been reported with lithium use during pregnancy, whereas the normal incidence of EA is 1 in 20,000 births.\textsuperscript{19} Finally, one study reported that the development of polyhydramnios in the last trimester could be explained by lithium crossing the placenta and causing fetal polyuria, which results in the detected polyhydramnios.\textsuperscript{20} As a general rule most authors state that the administration of lithium should be avoided during pregnancy at least during the first trimester and, if used, the patients should definitely have a timely fetal echocardiographic investigation.

**Echocardiographic features**

As cardiac structural anomalies and functional problems in the fetus can be detected by prenatal echocardiography from 16 weeks gestation, a systemic assessment of the four-chamber view can pick up more than half of the intracardiac abnormalities such as Ebstein’s anomaly and tricuspid valve dysplasia.\textsuperscript{22-23} The echocardiographical examination is dominated by the enlarged right atrium and the dilated atrioventricular annulus. In Ebstein’s anomaly the degree of the tricuspid valve displacement divides the right ventricle in a proximal or inlet portion, which is atrialized, and the distal trabecular portion, which makes up the remaining functional ventricle. The wall of the atrialized portion is usually thinner than that of the functional right ventricle.\textsuperscript{24,25} Early presentation is more frequently associated with cardiac lesions, usually pulmonary stenosis or atresia. Serious underdevelopment of pulmonary tissue, caused by either primary pulmonary hypoplasia or secondary pulmonary dysplasia is frequently encountered.

**Associated abnormalities**

**Intracardiac abnormalities**

Other intracardiac malformations reported in Ebstein’s anomaly are atrial septal defects, ventricular septal defect, pulmonary stenosis or atresia, mitral valve prolapse, endocardial fibroelastosis and less frequently the rare combination of Ebstein’s anomaly with ventricular L-loop, corrected transposition of the great arteries.\textsuperscript{26-28} One study reported cardiac rhabdo-
myomata. Fetal rhythm disorders such as supraventricular tachycardia (SVT) and atrial flutter (AF) are also frequently encountered.

Extracardiac abnormalities
Other extracardiac malformations reported in Ebstein’s anomaly are hydrops fetalis associated with the presence of SVT or AF. The presence of tuberous sclerosis was seen in one case-report. Other anomalies described associated with Ebstein’s anomaly are the Holt-Oram syndrome, a dominantly inherited syndrome of skeletal abnormalities. The association of Ebstein’s anomaly and chromosomal abnormalities, such as Down syndrome, is extremely unusual.

Pathophysiology
The pathophysiology is similar in both groups of the anomaly of the tricuspid valve. The natural history depends on the varying degrees of severity of incompetence of the tricuspid valve, the presence or absence of an atrial septal defect, the degree of impairment of right ventricle function and associated clinical findings. Although the right ventricular abnormalities might be explained by hemodynamic stress in utero, abnormalities of the left ventricular free wall, which are also sometimes encountered, suggest that either genetic or non-hemodynamic environmental factors are involved in the morphogenesis of this condition.

The fetal and neonatal period however are dominated by the extent and pathophysiology of the pulmonary hypoplasia. Once the crucial neonatal phase is survived and pulmonary problems prove to be surmountable, the outlook becomes more comparable to that of older children and adults and is usually associated with an excellent outcome.

Intrauterine course and mode of delivery
Spontaneous intrauterine death is reported, as high as 48%, and 35% of those who were live-born died despite vigorous medical and, when necessary, surgical management, of a combination of hypoxia and severe congestive heart failure. Early detection of tricuspid valve disease has led parents to the option of termination of pregnancy in view of the poor postnatal course of the anomaly. For those deciding to continue the pregnancy no advantage of a cesarean section has been proven and a normal delivery is therefore suggested.
Postnatal interventions and outcome

The diagnostic potential and importance of fetal echocardiography during prenatal evaluation of cardiac malformations allows for adequate perinatal planning and management, with an obvious impact on morbidity and mortality. Some report a policy of induction at term and immediate surgical intervention when Ebstein’s anomaly was diagnosed prenatally. Despite these efforts most patients with a prenatal diagnosis surviving the fetal period die of a combination of pulmonary and cardiac insufficiency shortly after birth. The prognosis of Ebstein’s anomaly during fetal life is not influenced by criteria described for postnatal life but is primarily related to the hypoplastic lungs and to factors that control the volume load of the left ventricle. Previous studies have indicated that in cases with dilation of the chambers of the right heart, pulmonary atresia and an intact ventricular septum the prognosis is even worse. The degree of cardiomegaly may provide useful information about secondary lung compression or cardiac failure and therefore assists in giving an accurate prognosis for postnatal survival. When surgical intervention becomes necessary, it is essential to make a detailed assessment of both valvular and ventricular abnormalities (Figure 1 and 2).

Experience

Prenatal diagnosis of Ebstein’s anomaly or tricuspid valve dysplasia was established in 14 patients at the University Medical Center Utrecht in the Netherlands between January 1, 1988, and July 31, 2001. The diagnosis of EA was based on two-dimensional echocardiographic evidence of a downward displacement of the septal leaflet of the TV, as seen in the apical four-chamber view. If the TV inserts on the ventricular septum more than 8 mm/m² below the insertion of the mitral valve, the diagnosis can be made. In case of TVD only an abnormal thickened and irregular TV but no apparent downward displacement is seen on echocardiography.

In these 14 patients with a dysplastic tricuspid valve Ebstein’s anomaly was only documented in four. One fetus with Ebstein’s anomaly died in utero at a gestational age (GA) of 29 weeks and another with associated hypoplasia of the lungs and trisomy 18 died at a GA of 36 weeks. Parents opted for compassionate care in one fetus that died at an age of 2 days. In another fetus parents chose for surgery in which Ebstein’s anomaly was associated with a congenitally corrected transposition of the great arteries. This patient received a pulmonary artery banding at one week of life, later a partial cavopulmonary connection (PCPC), and at a later stage a Damus-Kay-Stansel operation. This patient is still alive at an age of 9 years.
Figure 1

[A] Fetal chest with enlarged heart.
LA = Left atrium, LV = Left ventricle, RA = Right atrium, RV = Right ventricle.

[B] Fetal chest with Ebstein’s anomaly and the typical downward displacement of the tricuspid valve.

[C] Fetal chest with Ebstein’s anomaly and hypoplastic lungs.

Figure 2

[A] Ebstein’s anomaly with downward displacement of the tricuspid valve and enlarged right atrium compressing the left atrium.

[B] Dysplastic tricuspid valve syndrome with downward displacement of the tricuspid valve but with enlarged right atrium compressing the left atrium.
Discussion

Patients with Ebstein’s anomaly may present at any age, including the prenatal period. Patients with an in utero diagnosis were most commonly referred because of an abnormal routine prenatal ultrasound. Fetuses may also be referred for an associated arrhythmia, gestational diabetes, a history of maternal lithium ingestion, and a history of congenital heart disease in the offspring.

Ebstein’s anomaly and dysplasia of the tricuspid valve can both be easily recognized during routine prenatal ultrasonography, since it tends to produce significant cardiomegaly and regurgitation. These structural abnormalities should prompt the need for an in-depth fetal echocardiographic evaluation and search for associated malformations.

The clinical presentation of Ebstein’s anomaly varies for the different age groups. In utero patients may develop significant right ventricular outflow tract obstruction, congestive heart failure, cardiomegaly, pulmonary hypoplasia and hydrops fetalis. Presentation in utero is associated with a significant risk of death, which can be predicted by the echocardiographic appearance and presence of associated lesions. Early presentation was frequently associated with other cardiac lesions, usually pulmonary stenosis or atresia. The high incidence of intrauterine death in our series is in accordance with other studies. Neonatal survivors mostly present with cyanosis and heart failure.

The poor prognosis of the fetus is mainly due to the incompetence of the tricuspid valve, leading to right atrial enlargement and subsequently pulmonary hypoplasia or cardiac failure. Some authors have suggested that a myocardial problem and not pulmonary artery atresia or stenosis is the leading pathologic factor for the incompetence of the tricuspid valve. The dominating problem in the perinatal age group, the reduction in size of the lungs, may simply be a consequence of the dilation of the chambers of the heart. During the crucial fetal period of development, the lungs have no space to grow since the heart occupies the larger part of the thoracic cavity. The possibility exists that if cardiac dilation could be avoided by therapeutic measures during fetal life, the lungs would grow normally, giving a much better prognosis.

Patients presented with Ebstein’s anomaly in utero should be monitored on a regular basis for the development of arrhythmias and effusions. Some fetal arrhythmias can be managed by maternal administration of antiarrhythmic agents. The presence of enlarging effusions and hydrops are
poor prognostic signs and may be an indication for premature delivery after administration of steroids to maximize lung maturity.

Once a fetus survives the perinatal period, further management depends on the severity of the tricuspid valve anomaly. If it is technically possible, the preferred surgical procedure is repair rather than replacement of the tricuspid valve and closure of the atrial septal defect under cardiopulmonary bypass. Variations on this theme have been proposed by others. In milder cases the full-term neonate presenting with cyanosis might benefit from treatment with prostaglandine E1 to maintain ductal patency.

Conclusion

Ebstein’s anomaly remains a severe and frequently fatal disorder in the fetus, with gross echocardiographic abnormalities, readily detectable by routine obstetrical ultrasound. In Ebstein’s anomaly visualization of an apical displaced septal tricuspid leaflet has been shown to be the most diagnostic feature. There is much overlap between valvular dysplasia and Ebstein’s anomaly, and therefore the two conditions can be readily confused with each other on the echocardiogram. Differentiation is very important, but sometimes difficult. Knowledge of the natural history and the observed poor outcome in continuing pregnancies, allows us to counsel parents on the course of the disease in the fetus and possible management during fetal life. In general, the earlier the patient presents with the malformation, the poorer the prognosis. Fetal and neonatal presentation is typically associated with a dismal outcome secondary to the almost always occurring pulmonary hypoplasia.
References

Chapter 6


Ebstein’s anomaly