Journal of Rare Cardiovascular Diseases 2013; 1 (4): 139–143
www.jrcd.eu

Ebstein anomaly (RCD code: IV-1D.1b)

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Abstract

Ebstein anomaly (EA) is a rare congenital malformation of the heart that is characterized by apical displacement of the septal and posterior tricuspid valve leaflets, with atrialization of the right ventricle and variable degree of malformation and displacement of the anterior leaflet. Patients can have a variety of symptoms related to the anatomic abnormalities of EA and their hemodynamic effects or associated structural and conduction system disease. Most frequently cyanosis, palpitations, fatigue and dyspnea can be observed. In severe forms edema and ascites. Treatment of EA is complex and depends of the severity of the disease itself and the effect of accompanying congenital structural and electrical abnormalities. Options of treatment include medical therapy, radiofrequency ablation, and surgical therapy. Main aim of the surgical therapy is to correct the underlying tricuspid valve, right ventricular abnormalities and any associated intracardiac defects if exist. Palliative procedures and cardiac transplantation can be considered in most sever EA patients.
JRCD 2013; 1 (4): 139–143

Key words: Ebstein anomalny, tricuspid valve plasty

Background

Ebstein's anomaly is a rare cardiac defect. It accounts for 0.5%–1% of all congenital heart defects in an equal proportion of males and females (1).

The anomaly affects the tricuspid valve (TV), right ventricle (RV) and right atrium (RA). EA is a complex of congenital heart diseases that includes:

- right atrium (RA) enlargement and varying degrees of tricuspid valve insufficiency, which may be clinically "mute" or else the symptoms may appear at various age, both in children and adults;
- apicardial displacement of the septal and posterior cusps – which are partially or completely attached to the myocardium;
- the anterior cusp is normally attached to the annulus, yet it is markedly (sail-like) enlarged and its mobility is varied; chorda tendinae of anterior cusp may obscure blood inflow to the RV cavity and/or RV outflow to the main pulmonary artery (MPA);
- the division of RV into the proximal, "atrialized" (aRV) and distal, functional part (fRV); aRV may vary in size and demonstrate different degrees of contractility impairment and thinning of the wall (2);

The complex of the above presented heart defects was first described by Wilhelm Ebstein in 1866. In the same year, Ebstein autopsied a 19-year-old male and described lesions he observed in his heart, which involved the tricuspid valve, right ventricle and right atrium (3). Ante mortem, the patient presented with dyspnea, heart rate disorders and cyanosis. Similar anatomopathological lesions were described only 20 years later (4). The term "Ebstein's disease" was coined by Arnstein in 1927. For years, nobody suspected the defect might be diagnosed intravitally. Only in the years 1951–1952 were the first reports published (Van Lingen) that described angiographically confirmed clinical lesions appearing in Ebstein syndrome (5,6), although initial suggestions associating the clinical features with the cardiac pathology described by Ebstein were formulated in 1949 (7). Since that time, the complex of the above-described heart defects is commonly termed "Ebstein's syndrome" or "Ebstein's anomaly".

The defect develops in consequence of impaired delamination of TV cusps and chorda tendinae from the endocardium in the inlet part of RV. Impaired embryological development of these structures occurs between 8 and 12 weeks of fetal life (8). The causes of impairment of TV cusps development are not fully understood. Some authors suggest that the cause of abnormalities may be viral infections or fetal exposure to lithium in the third trimester of pregnancy (9-11). Familial incidence of the defect was observed, what was confirmed in studies on familial incidence of some gene mutations (12). Certain genetic researches indicated that EA is geneti-

Conflict of interest: none declared.

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cally heterogeneous defect which could be associated with some chromosomal microdeletions (13).

Clinical features

Clinical features depend on the degree of Ebstein's anomaly intensity and on the nature of concomitant heart defects. The most severe forms will be manifested in the early days or at times hours after birth and usually are life-threatening and require prompt intervention.

In fetal life, TV is to a considerable degree a systemic valve and its competence determines whether a fetus will be carried to term and how soon after birth the neonate will develop cardiac insufficiency.

Some patients with Ebstein's syndrome may suffer from no ailments whatsoever. They live to adulthood if the defect does not cause any significant hemodynamic alterations in the circulatory system. In such individuals, the defect may not be detected intravitally or else be detected accidentally (14).

Morphology

Apicardial displacement of the TV annulus determines the division of the right ventricle into the proximal, atrialized part of RV (aRV) and distal, functional RV part (fRV). The atrialized RV part is situated between the tricuspid annulus and displaced attachments of the septal and posterior cusps. Most commonly, this is a thin-walled region with paradoxical movements during a systole despite the fact it has ventricular action potential. In advanced forms of the defect, the condition is manifested internally as an aneurysm situated in this region.

The functional RV cavity is situated distally to the TV cusp attachments. The size of fRV depends on the degree of defect intensity; fRV may be thin-walled not because of distensions but rather because of a lower number of muscle fibers as compared to normal RV (15). The ventricular septum often demonstrates paradoxical movements and protrudes to the left.

The RA size corresponds to the degree of TV and RV pathology. Most commonly, RA is markedly enlarged in association with TV regurgitation and RV dysfunction.

Various degrees of left ventricle (LV) dysfunctions are observed. The pronouncedly enlarged right heart compresses the septa, displacing them to the left and compressing both LA and LV. Such phenomena impair both the diastolic and systolic LV function. The compressed left heart assumes the shape of a "banana" attached to a giant right heart. Impaired mobility of the LV free wall is seen in 67% of patients. Some patients present with mitral valve (MV) prolapse and both MV cusps thickening (16-18).

In the most severe forms of Ebstein's syndrome, the giant right heart exerts a destructive effect not only on the LV function, but also on the function of other organs situated in the chest. A markedly enlarged heart that occupies almost the entire chest cavity compresses the lungs as early as in fetal life. Some fetuses that present with so much advanced cardiomegaly die in utero due to circulatory failure. Immediately after birth, the surviving fetuses develop circulatory and respiratory failure associated with pulmonary hypoplasia, as their lungs were considerably compressed throughout the entire fetal life. Such children require early intubation, intensive pharmacotherapy and prompt surgical intervention.

Concomitants defects

In 60–85% of patients with Ebstein's syndrome, there is a communication between the atria manifested as the patent foramen ovalis (PFO) or a small ostium secundum atrial septal defect (ASD II). One-third of Ebstein's anomaly patients present with varying degrees of pulmonary stenosis. Other concomitant defects include ventricular septal defects, tetralogy of Fallot, patent ductus arteriosus, transposition of great arteries, coarctation of the aorta and congenital mitral stenosis (19). Very rarely EA coexists with other complex heart defects, such as congenitally corrected transposition of great arteries or hypoplastic left heart syndrome. Wolff–Parkinson–White syndrome (WPW) is noted in 14% of EA patients, deteriorating the clinical course and prognosis (20-22).

Diagnosis

Depending on the severity of the defect, the majority of EA patients may manifest symptoms at any age and of any intensity. In moderate forms, the prodromal symptoms may be breathlessness and dyspnea combined with limited physical ability. Cyanosis is present in more than one-half of patients and severe cyanosis in one-third (23). It may be already manifested in young children and be intensified with age. Palpitations and a sense of irregular heartbeat are relatively frequent in EA patients. These symptoms accompany arrhythmias. Individuals with EA also more frequently suffer from WPW syndrome and supraventricular tachycardia and tachyarrhythmia. One-third of patients demonstrate butterfly-shaped redness of the face.

On auscultation, one notes a wide spitted first heart sound associated with a delayed TV closure. Occasionally, EA patients are referred to as exhibiting the so-called "multiple heart sounds". The third and fourth sounds may be present, what could be erroneously interpreted as the gallop rhythm. If the closure of the pulmonary valve is delayed, the second sound is splitted. A loud holosystolic murmur is heard at the left sternal margin due to TV insufficiency.

Electrocardiography (ECG) demonstrates a broadened, high P wave, an extended PQ interval, a dextrogram and right bundle branch block. Oftentimes, features of WPW syndrome are present, such as supraventricular tachycardia, atrial fibrillation and atrial flutter. Cardiac rhythm abnormalities are seen in approximately 65% of EA patients.

Depending on the degree of defect intensity, chest X-ray demonstrates either an image of a normal cardiac silhouette through a characteristically enlarged rugby ball-shaped contour to a giant cardiac silhouette, which occupies the major part of the chest. In such instances, the lungs are significantly compressed and demonstrate a sparse vascular pattern.

Echocardiography (ECHO) is decisive in diagnosing EA. The most specific echocardiographic index is apicardial displace-

ment of the septal TV cusp. A precise evaluation of the degree of displacement is possible through comparison to the MV annulus in the apical four-chamber view. The so-called "displacement index" of the septal TV cusp can be then determined by calculating the quotient of the septal cusp displacement expressed in millimeters and body surface area expressed in square meters. The value of the index above 8 mm/m^2 in combination with other echocardiographic findings decides on the diagnosis of EA (24,25). Echocardiographically demonstrated anatomical details of the defect that are of a diagnostic and prognostic importance include:

- the size and mobility of the anterior TV cusp, assessment of its subvalvular apparatus, the number and size of perforations in the cusp, the relation of chorda tendinae and their attachments to RV inflow and outflow;
- the size, mobility and degree of adherence to the myocardium of the septal and posterior cusps combined with assessment of the septal cusp displacement;
- the degree of TV annular enlargement;
- the size, mobility and contractibility of aRV;
- the size of fRV cavity and the thickness and function of its muscle coat;
- assessment of the size and function of fRA;

the presence of concomitant defects and assessment of blood flow and possible shunts.

In case of doubt, data originating from a transthoracic examination should be supplemented by a transesophageal echocardiography (TEE). ECHO provides information that is sufficient for establishing the diagnosis, evaluating the risk and planning appropriate treatment. In complex cases, with concomitant other heart and vascular defects, angiography continues to be helpful as it provides images of the regions of interest and allows for performing hemodynamic examinations necessary for making decision on the selection of treatment. In case of need, diagnostic details may be provided by multi-slice computed tomography (Angio-CT) or by magnetic resonance angiography (mRA) allowing for evaluation of cardiac cavities (26).

Systematics

The first widely accepted proposal of classification of the defect was presented by Carpentier in 1988 (2). The degree of advancement (A-D) in the classification depends on tricuspid valve cusp mobility (predominantly of the anterior cusp) and on the degree of RV atrialization and contractability.

A helpful indicator while selecting treatment and assessing risk is the GOSE index (Great Ormond Street Ebstein ECHO) proposed by Celermajer in 1992 (27). The index is calculated during echocardiography as the ratio of RA area + aRV area to the sum of RV+LA+LV. Depending on the value of the ratio, four grades are distinguished. A score associated with a good prognosis is lower than 1, while scores above 1 indicate a poor prognosis. Score 4 is believed to be lethal in 100% of cases.

Surgical treatment

The first, unfortunately failed attempt at surgical treatment of Ebstein's anomaly was made in 1950. The procedure was a palliative Blalock–Taussig systemic-pulmonary shunt. Only in 1959 did Gasul successfully perform the Glenn shunt. In 1962, Barnard and Schrire successfully implanted a tricuspid artificial ball valve (28). The first successful TV plasty in an EA patient was performed by Hardy following the concept developed by Hunter and Lillehei (29). In 1982, Danielson proposed a right atrioventricular outlet plasty consisting in a horizontal plication of the atrialized part of RV, reducing the TV annulus size and TV plasty with formation of a monocusp tricuspid valve coapting to the ventricular septum. To increase tightness, the papillary muscles of the anterior cusp are approximated to the ventricular septum by pledgeted mattress sutures. A new TV annulus is stabilized by insertion and suturing in place of a Carpentier ring.

In 1988, Carpentier published a report describing his method of performing TV plasty in Ebstein's anomaly (2). The procedure consists in detaching the anterior TV cusp from the annulus, dissecting the cusp free from the free RV wall, lengthening and mobilizing its chorda tendinae. The atrialized part of RV is then vertically plicated, the TV annulus is reduced in size and stabilized by means of an artificial ring and the previously detached anterior cusp is rotated clockwise and sutured into the "new" TV annulus, forming a monocusp valve coaptating to the ventricular septum.

Both in the Danielson and Carpentier method, a single large cusp is left in the tricuspid valve; during its function, it coaptates to the ventricular septum. In consequence, various degrees of residual regurgitation are seen and the incompetence tends to intensify with time. The intensifying insufficiency is in a great measure associated with asymmetric, turbulent blood inflow to RV through the new atrioventricular ostium. Reports were published that stressed the necessity of forming the second TV cusp to achieve normal coaptation and function of the valve (20,30-32).

The idea of forming the second TV cusp to improve the valvular function was introduced by da Silva (33). In his plasty, he detached from the annulus all the cusps that were possible to mobilize, including the rudimentary forms. He reduced the TV annulus in size using interrupted sutures, and rotated the detached valve clockwise and sutured it to the new annulus, thus creating a "bicuspid" valve consisting of the anterior cusp and another cusp formed from the septal and posterior cusps. The type of plasty was termed by its authors the "cone procedure". What is a novelty in the method is that the annulus of the new tricuspid valve does not require stabilization with an artificial ring. Good results of the procedure inspired various authors to devise modifications of the "cone procedure", preserving its major principles (34-37).

"Bicuspid" plasty allows for achieving better late results as compared to "monocusp" plasty in patients with Ebstein's anomaly. However, in extreme EA forms, the septal and posterior cusps are often completely missing, what rules out the formation of another TV cusp coaptating to the anterior cusp. For the group of patients with the most severe types of EA, Perier proposed in 2006 a method of bicuspid TV plasty consisting in forming one cusp from the native anterior TV cusp, while the other TV cusp is created from au-

togenic pericardium, with its free margin being fixed with artificial chorda tendinae. The atrialized part of RV is vertically plicated. The "new" TV annulus is stabilized through insertion and suturing in of a Carpentier-Edward ring (classic) (38).

Failures following TV plasty procedures were predominantly associated with RV insufficiency, especially when the proper right ventricle cavity was considerably reduced in size and thin-walled. The idea of RV volume decompression by means of the bidirectional Glenn anastomosis (BDG) appeared in the literature of the nineties. BDG also increases LV preload, decreases RA pressure and increases pulmonary flow. Combining BDG with TV plasty or TV valve implantation has considerably improved surgical results in EA.

In 2008, the team from the Mayo Clinic (Rochester) presented their experience based on the material of 539 patients with EA belonging to various age groups and after various types of surgical treatment, including implantation of artificial valves. The authors demonstrated comparable late results after TV plasty procedures and implantation of artificial TV valves both with low – few percent mortality rate (39). Nevertheless, after artificial valve implantation, often bothersome anticoagulation treatment is necessary and with passing time, a reoperation is almost always required, hence the continuous search for new possibilities of performing a successful TV plasty in patients with various forms of EA.

A separate group of patients with Ebstein's anomaly consists of newborns and infants that require early interventions. Children at this age hospitalized due to circulatory and respiratory failure associated with Ebstein's anomaly are usually in critical condition. In the most severe forms of the defect, when the right heart provides a significant obstacle for LV output, of assistance is a single-ventricle solution, with RV being "switched off". The commonly accepted management is that proposed by Starnes consisting in closing off the inflow to RV by means of a patch with a 3–4 mm perforation, resection of a part of the RA wall and handling the PA inflow by a systemic-pulmonary anastomosis. This is the first stage of surgical treatment of a single ventricle heart. The subsequent stages lead to the Fontan operation. According to guidelines of European Society of Cardiology surgical repair should be performed in symptomatic patients, ASD/PFO closure should be also performed at the time of valve repair (40).

Conclusions

Ebstein anomaly is a rare disease which can appear with different anatomical severity and various clinical features so every patient needs to be individually evaluated and recommended to eventual surgical correction.

In recent years, there new correction techniques for Ebstein anomaly with low postoperative mortality rates have appeared, which opens up new possibilities for adjustment through even in advanced forms.

References

1. Watson H. Natural history of Ebstein's anomaly of tricuspid valve in childhood and adolescence. An international co-operative study of 505 cases. Br Heart J. 1974;36:417–27
2. Carpentier A, Chauvaud S, Mace L, et al. A new reconstructive operation for Ebstein's anomaly of the tricuspid valve. J Thorac Cardiovasc Surg 1988;96:92–101.
3. W. Ebstein. Über einen sehr seltenen Fall von Insufficienz der Valvula tricuspidalis, bedingt durch eine angeborene hochgradige Missbildung derselben. Archiv für Anatomie, Physiologie und wissenschaftliche Medicin, Leipzig, 1866, 238–254.
4. Mann RJ, Lie JT. The life story of Wilhelm Ebstein (1836–1912) and his almost overlooked description of a congenital heart disease. Mayo Clin Proc 1979;54:197.
5. Soloff LA, Stauffer HM, Zatuchni J. Ebstein's disease: report of the first case diagnosed during life. Am J Med Sci. 1951 Nov; 222:554–61
6. Van Lingen B, McGregor M, Kaye J et al. Clinical and cardiac catheterization findings compatible with Ebstein's anomaly of the tricuspid valve: a report of two cases. Am Heart J. 1952;43:77–88
7. W.E. Medd, M.B. Matthews, W.R.R. Thursfield, Ebstein's Disease Thorax 1954; 9:14.
8. Nora J, Nora A, Toews W. Lithium, Ebstein's anomaly, and other congenital heart defects. Lancet 1974; 4:594–595.
9. Cohen L, Friedman J, Jefferson J, et al: A reevaluation of risk of in utero exposure to lithium. JAMA 1994; 271:146–150.
10. Emanuel R., O'Brien K., Ng R. Ebstein's anomaly: Genetic study of 26 families. Br Heart J 1976; 38:5–7.
11. Rosenmann A, Arad I, Simcha A, Schaap T. Familial Ebstein's anomaly. J Med Genet 1976; 13:532–535.
12. Postma AV, van Engelen K, van de Meerakker J et al. Mutations in the sarcomere gene MYH7 in Ebstein anomaly.Circ Cardiovasc Genet. 2011;4:43–50.
13. Digilio MC, Bernardini L, Lepri F et al. Ebstein anomaly: Genetic heterogeneity and association with microdeletions 1p36 and 8p23.1. Am J Med Genet A. 2011;155A:2196–202.
14. Radford DJ, Graff RF, Neilson GH. Diagnosis and natural history of Ebstein's anomaly. Br Heart J. 1985;54:517–522.
15. Anderson KR, Zuberbuhler JR, Anderson RH, et al. Morphologic spectrum of Ebstein's anomaly of the heart: a review. Mayo Clin Proc. 1979;54:174–80
16. Daliento L, Angelini A, Ho SY, et al. Angiographic and morphologic features of the left ventricle in Ebstein's malformation. Am J Cardiol. 1997;15:1051–1059
17. Monibi AA, Neches WH, Lenox CC, et al. Left ventricular anomalies associated with Ebstein's malformation of the tricuspid valve. Circulation. 1978;57:303–306
18. Cabin HS, Roberts WC Ebstein's anomaly of the tricuspid valve and prolapse of the mitral valve. Am Heart J. 1981;101:177–180
19. Kirklin/Barratt-Boyes. Cardiac Surgery. Morphology, Diagnostic Criteria, Natural History, Techniques, Results, and Indications. Third Edition. Churchill Livingstone. 2003.
20. Danielson GK, Driscoll DJ, Mair DD, et al. Operative treatment of Ebstein's anomaly. J Thorac Cardiovasc Surg. 1992;104:1195–11 202
21. Chauvaud SM, Brancaccio G, Carpentier AF, Cardiac arrhythmia in patients undergoing surgical repair of Ebstein's anomaly. Ann Thorac Surg. 2001;71:1547–1552
22. Khositseth A, Danielson GK, Dearani JA, et al. Supraventricular tachyarrhythmia's in Ebstein's anomaly: management and outcome. J Thorac Cardiovasc Surg. 2004;128:826–833.
23. Giuliani ER, Fuster V, Brandenburg RO, Mair DD. Ebstein's anomaly: the clinical features and natural history of Ebstein's anomaly of the tricuspid valve.Mayo Clin Proc. 1979;54:163–173.
24. Shiina A., Seward J., Edwards W. Two-dimensional echocardiographic spectrum of Ebstein's anomaly: Detailed anatomic assessment. J Am Coll Cardiol 1984; 3:356–370.
25. Gussenhoven E, Stewart P, Becker A. Offsetting" of the septal tricuspid lealfet in normal hearts and in hearts with Ebstein anomaly: Anatomic and echographic correlation. Am J Cardiol 1984; 54:172–176.
26. Głowacki J, Miszalski-Jamka K, Pawlak S et al. The new diagnostic tool – congenital heart diseases and the great arteries imaging using multislice computed tomography – case presentations. Kardiol Pol. 2009;67:459–63.

27. Celermajer DS, Dodd SM, Greenwald SE et al. Morbid anatomy in neonates with Ebstein's anomaly of the tricuspid valve pathophysiologic and clinical implications. J Am Coll Cardiol 1992; 19: 1049–1053.
28. Barnard CN, Schrire V. Surgical Correction Of Ebstein's Malformation With Prosthetic Tricuspid Valve. Surgery. 1963;54:302–308.
29. Hunter SW, Lillehei CW. Ebstein's malformation of the tricuspid valve; study of a case together with suggestion of a new form of surgical therapy. Dis Chest. 1958;33:297–304
30. Dearani JA, O'Leary PW, Danielson GK. Surgical treatment of Ebstein's malformation: state of the art in 2006. Cardiol Young. 2006; 16(suppl 3):12–20.
31. Wu Q, Huang Z. Anatomic correction of Ebstein anomaly. J Thorac Cardiovasc Surg. 2001;122:1237–1238.
32. Hetzer R, Nagdyman N, Ewert P, et al. A modified repair technique for tricuspid incompetence in Ebstein's Anomaly. J Thorac Cardiovasc Surg. 1998;115:857–868.
33. da Silva, JP, Baumgratz JF, da Fonseca L et al. The cone reconstruction of the tricuspid valve in Ebstein's anomaly. The operation: early and midterm results. J Thorac Cardiovasc Surg 2007;133:215–223
34. Komoda T, Komoda S, Nagdyman N, et al. Combination of a Hetzer operation and a Sebening stitch for Ebstein's anomaly. J Thorac Cardiovasc Surg 2007;55:355–359.
35. Malhotra SP, Petrossian E, Reddy VM et al. Selective right ventricular unloading and novel technical concepts in Ebstein's anomaly. Ann Thorac Surg 2009;88:1975–1981.
36. Nagdyman N, Ewert P, Komoda T. et al. Modified repair in patients with Ebstein's anomaly. J Heart Valve Dis 2010;19:364–370.
37. Ullmann MV, Born S, Sebening C, et al. Ventricularization of the atrialized chamber: a concept of Ebstein's anomaly repair. Ann Thorac Surg 2004;78:918–925.
38. Perier P, Pająk J, Rycaj J, et al.Double leaflet reconstruction of tricuspid valve in Ebstein's anomaly by use of autologous pericardium.Interact. Cardiovasc. Thorac. Surg. 2009; Suppl: 2, S79-S80
39. Brown ML, Dearani JA, Danielson GK et al. The outcomes of operations for 539 patients with Ebstein anomaly. J Thorac Cardiovasc Surg. 2008;135:1120–1136,
40. Baumgartner H., Bonhoeffer Ph., De Groot N.M.S et al. Guidelines for the management of grown-up congenital heart disease (new version 2010) European Heart Journal (2010) 31, 2915–2957