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Case Report

Ebstein's Anomaly, Possible Newly Implicated Drug Aetiology? A Case Report

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ABSTRACT

Ebstein's anomaly is a congenital malformation of the heart that is characterized by downward displacement of an abnormal tricuspid valve into the right ventricle. It is rare, with an incidence of 1 in 200,000 live births. Etiology is unknown. Our patient was exposed to artemether-lumefantrine, ciprofloxacin, and ibuprofen (not previously linked with Ebstein's anomaly) at about four weeks of gestation. An obstetric scan at 33 weeks' gestation, was the first clue to the diagnosis.

Keywords
Ebstein's anomaly; Atrial septal defect (ASD); Nonsteroidal anti-inflammatory drugs (NSAIDs).

INTRODUCTION

Ebstein's anomaly is a congenital heart disease characterized morphologically by apical displacement and malformation of the tricuspid valve, dilation of the right atrium, small right and left ventricles, and usually an atrial septal defect (ASD).[1]

A striking aspect of Ebstein's anomaly is its varying clinical presentation based on the age at which it is detected. Its mode of presentation ranges from hydrops fetalis in utero and cyanosis in the newborn, a murmur or heart failure in an infant, an arrhythmia in an adolescent to incidental detection of an ASD in the elderly, all based on the degree of affectation of the tricuspid valve and other associated cardiac defects.[1]

In this case report, we describe Ebstein's anomaly in a Nigerian neonate, highlighting its spectrum of presentation across all age groups, highlighting the presentation, known etiology and its prognosis. Permission was granted by the mother to publish this case report.

CASE REPORT

A.B. a female neonate was delivered *via* spontaneous vaginal delivery to a 35-year-old para 4+0 to a Hepatitis B positive but human immunodeficiency virus (HIV) negative mother at a gestational age of 38-weeks. At approximately four weeks of gestation, mother developed fever, headache, right hypochondriac abdominal pain with malaise for which she used a 3-day adult course of artemether-lumefantrine, a 5-day course of ciprofloxacin 500 mg twice daily and ibuprofen 400 mg three times a day for 8-days. She presumed she had malaria, and commenced the self-treatment, although she did not undergo any laboratory testing to confirm her own assumption. She was subsequently diagnosed with pregnancy dated at 6-weeks gestation.

An obstetric scan at 33-weeks' gestation, revealed cardiomegaly and a dilated right atrium. There is no known family history of heart defects. She was referred to our facility and presented at 38-weeks in labor. Appearance, pulse, grimace, activity and respiration (APGAR) scores were 4 and 8 at the first and fifth-minutes respectively. Her weight was 2,670 g. She however remained centrally cyanosed despite regular respiratory excursions and administration of supplemental oxygen. Oxygen saturation was 66% in room air and 76% on intranasal oxygen.

Peripheral pulses and blood pressure (BP) were normal. The apex beat was displaced at the fifth left intercostal space and the trachea was central. Precordium was normoactive and there

was a systolic murmur, grade 3/6 was heard in the left lower sternal border. Heart rate was 158 beats per minute.

Chest radiography revealed cardiomegaly with a cardiothoracic ratio (CTR) of 0.7 (Figure 1). A QRS axis of 120°, tall *p* waves in lead V1, suggesting right atrial enlargement and low voltage QRS complexes in the left precordial leads, Figure 2. Echocardiography revealed a markedly dilated right atrium and a small left atrium. The tricuspid valve was displaced apically by 16 mm into the right ventricle with severe tricuspid regurgitation with a gradient of 30 mmHg. A large Secundum ASD 25 mm, with a right to left shunt, an intact ventricular septum. The pulmonary valve was stenosed. A diagnosis of an Ebstein's anomaly with a large Secundum ASD was established in the neonate. She was managed in the neonatal unit with anti-failure medication until her demise in the 2nd week of life.

Figure 1. *Chest Radiograph of Patient Showing Cardiomegaly*

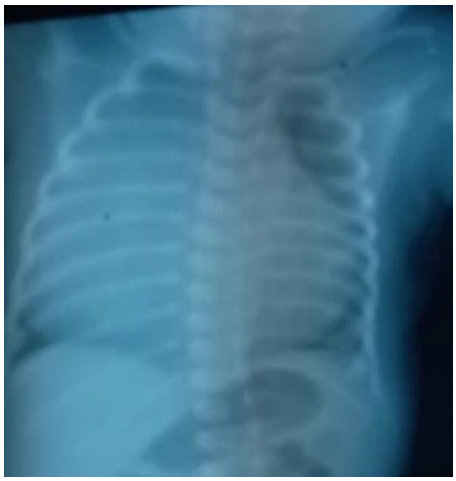


Figure 2. *Electrocardiograph of Patient*

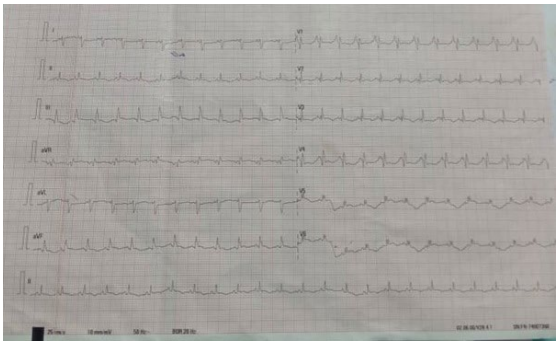
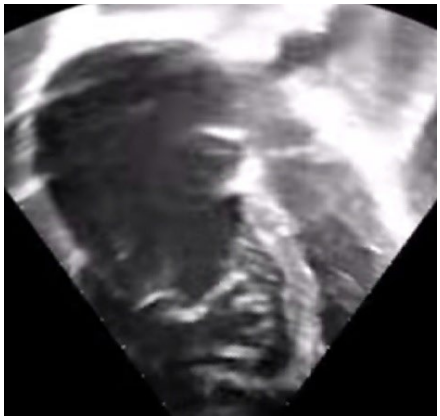


Figure 3. *2D-Echocardiography Showing a Markedly Dilated Right Atrium and a Small Left Atrium. The Tricuspid Valve was Displaced Apically by 16 mm into the Right Ventricle*



DISCUSSION AND CONCLUSION

Ebstein's anomaly was first described by Wilhelm Ebstein in 1866. Its characterized by malformation and downward displacement of the insertion of the septal and posterior leaflets of the tricuspid valve into the right ventricle. This valve displacement results in an enlarged right atrium due to the "atrialized" portion of the right ventricle and accompanying tricuspid regurgitation. The right ventricle is usually small and dysfunctional. The left ventricular size is usually normal, but it may be compressed by a dilated right ventricle. The left ventricle is also dysfunctional and maybe fibrotic.[1]

Ebstein's anomaly occurs in 1 in 200,000 live births it accounts for about <1% of all congenital heart diseases. In a series in Lagos by Animasahun et al[2] it accounted for 0.3% of all cyanotic congenital heart diseases.

The cause of Ebstein anomaly is unknown. Studies have linked the use of lithium for bipolar disorders in pregnant mothers and the use of benzodiazepines and marijuana to its occurrence.[3] There are also reports of genetic mutations leading to Ebstein's anomaly.[4] Artemether lumefantrine is safe in pregnancy and not linked to adverse outcomes in the foetus.[5] However, Schiebler et al6 in the United States reported a case of Ebstein's anomaly that occurred following a history of malaria in the mother in the sixth-week of pregnancy.[6] Maternal febrile illness in the first trimester of pregnancy has been considered a risk factor for the development of right obstructive heart defects.[7]

Fluoroquinolones are not linked with cardiac malformation.[8] Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with some cardiac malformations but not with Ebstein's anomaly.[9] The mother had hepatitis B, which has not been linked with congenital heart diseases.[10]

The clinical presentation of Ebstein's anomaly is varied depending on the patient's age. In fetal life, cardiomegaly is the usual mode of presentation like in our patient. In newborns, cyanosis, heart failure, or murmur in infant, while arrhythmias or an incidental finding of an ASD is the presentation in adolescence and adulthood. The earlier the age at presentation, the worse the prognosis.[1]

In the newborn, symptomatology is due to ineffective ventricular output and severe tricuspid valve regurgitation. Massive cardiomegaly may lead to compression of the adjacent lungs leading to lung hypoplasia.[11]

Medical management is the mainstay of treatment in the first month of life. There's an increased risk of mortality of up to 36% if the surgery is done in the neonatal period. Supplemental oxygen, no more than a 21% fraction of inspired oxygen (FiO_2) may be used to ensure oxygen saturation of 75 and 85%.[11] Some neonates with severe Ebstein's anomaly and the normal pulmonary valve will benefit from closure of their ductus as this will improve forward flow across the pulmonary valve and decrease right ventricular pressure. Medications such as anti-failure, anti-arrhythmic drugs, and aspirin can be used from the neonatal period in those with severe Ebstein's anomaly to manage complications.

There's a high-risk of mortality from Ebstein's anomaly in the neonatal period and beyond. The causes of death include heart failure, hemodynamic instability, arrhythmias, and peri-operative complications.[9] Management in the neonatal period is daunting for the healthcare team even in the developed world. If new medications are linked to its occurrence, they need to be documented.

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To the parents of this newborn who gave consent write this case report to improve knowledge. We say thank you.

AUTHOR CONTRIBUTION

AA was the project leader, participated in the design and supervision, and manuscript writing. OA participated in manuscript writing, FL and ED participated in the conceptualization, design, supervision, and critical review of the manuscript. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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