J Cardiovasc Disease Res., 2018; 9(3):154-155
A Multifaceted Peer Reviewed Journal in the field of Cardiology
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Case Report

Cardiac Abnormalities in Harlequin Ichthyosis: First Case Study

Bhupendra Verma*, Anand Mohan, Amrita Singh, Ashwani Kumar Saxena

Department of Cardiology, Shree Krishna Hospital, Kashipur, Uttarakhand, INDIA.

ABSTRACT
Harlequin ichthyosis is the most severe form of congenital ichthyosis and inherited in an autosomal recessive manner. The disease is marked by severe thickened and scaly skin on the entire body. It is a lethal disease, but patients can very rarely survive for several months or years. We present here cardiac abnormalities in a full term baby with Harlequin ichthyosis. To our knowledge, this is first case study to report associated cardiac abnormality in such patients. Further case studies are required to ascertain the findings and explore the cardiac involvement in this extremely rare disorder.
Key words: Harlequin ichthyosis, Congenital ichthyosis, Cardiac abnormalities, Ostium secundum atrial septal defect (OsASD), Patent ductus arteriosus (PDA).

Correspondence
Dr. Bhupendra Verma
Consultant Interventional Cardiologist, Shree Krishna Hospital and Heart Centre, Kashipur-244713, Udham Singh Nagar, Uttarakhand, INDIA.
Ph.no: +91- 8110086705
E-mail address: bhupendra.269@gmail.com

Submission Date: 03-07-2018;
Revision Date: 20-08-2018;
Accepted Date: 18-09-2018.
DOI : 10.5530/jcdr.2018.3.34

INTRODUCTION

Harlequin ichthyosis (HI) is the most severe form of congenital ichthyosis, with the incidence of one in 300,000 births. It is an autosomal recessive disorder associated with mutations in gene ABCA12.[1] HI is characterized by a thick, scaly, armor-like covering that severely restricts movement and results in deformities of the face, head and extremities.[2] Antenatal diagnosis in suspected cases can be confirmed using electron microscopy of fetal skin biopsy and DNA-based diagnosis with chorionic villus sampling or amniocentesis.[3] HI is associated with preterm birth and often leads to death due to neonatal complications such as fluid loss and septicemia.[4] In the past few years, however, the prognosis of HI infants has improved due to advances in neonatal intensive care and targeted oral retinoids.[5]

The improved survival makes it imperative to better understand the phenotypic expression of the disease. We present a case full term baby with HI where detailed echocardiography was done to delineate the cardiac abnormalities.

CASE REPORT

A female baby weighing 2100 g was born at full term gestation to a 27 years primigravida woman. Caesarean section was done due to obstetrical indication and the pregnancy was uneventful. The mother has not undergone any antenatal check-up due to poor socio-economic status. There was no family history of any inherited skin disorder.

The baby didn't cry at birth though she was continuously moaning. Her skin was covered with thick yellowish scales like armor with deep erythematous fissures all over the body. The limbs and fingers were held in rigid flexion and were oedematous. Further she had eclabion with a fixed, open mouth and thick lips, hypoplastic nose with two nostrils, hypoplastic ears with closed pinna, severe ectropion (everted eyelids), absent eyebrow, eyelashes and absent nails (Figure 1). The heart rate and respiratory rate were normal and she was maintaining saturation on room air. The baby was sent to the neonatal intensive care unit for further management.

A detailed echocardiography was done on 5th day in view of continuous murmur in left infraclavicular area. It showed a small patent ductus arteriosus (PDA), 1.5mm in size with left to right shunt (Figure 2). There were no features of left ventricular volume overload. Further she had a large ostium secundum type atrial septal defect (OsASD), measuring 6.9 mm with left to right shunt. There was mild dilatation of RA and RV (Figure 3). Pulmonary venous drainage was normal. No other significant abnormality was noted.

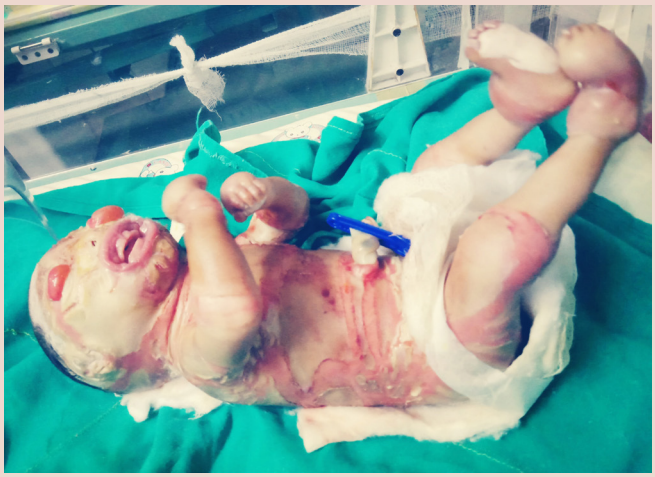

Figure 1: The baby with Herlequin Ichthyosis. Note the characteristic featues described in text. The entire body is covered with thick yellowish scales like armor with deep erythematous fissures. Bleeding is seen in features. The limbs and fingers are held in rigid flexion. Further note eclabion with a fixed, open mouth and thick lips, hypoplastic, hypoplastic ears with closed pinna, severe ectropion (everted eyelids). The eyebrow, eyelashes and nails are also absent.

Conservative management was given with nasogastric feeding, intravenous antibiotics, emollients and retinoids. However, the baby died on the 7th day.

DISCUSSION

Harlequin Ichthyosis (HI) is the rarest and the most severe form of congenital ichthyosis, with the incidence of one in 300,000 births. It is inherited in an autosomal recessive manner and associated with mutations in gene ABCA12.[1] Babies with harlequin ichthyosis are covered in thick, rigid, armor-like plates of highly keratinised skin separated by deep fissures. The rigid skin results in deformation of facial features and

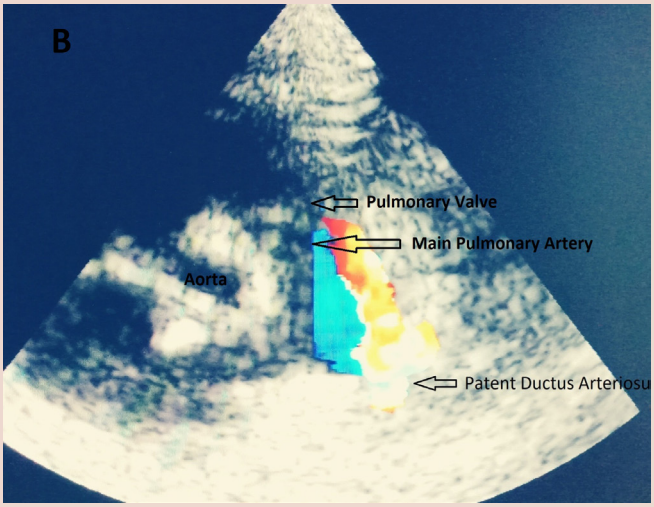

Figure 2: Small patent ductus arteriosus (PDA), 1.5mm in size with left to right shunt.

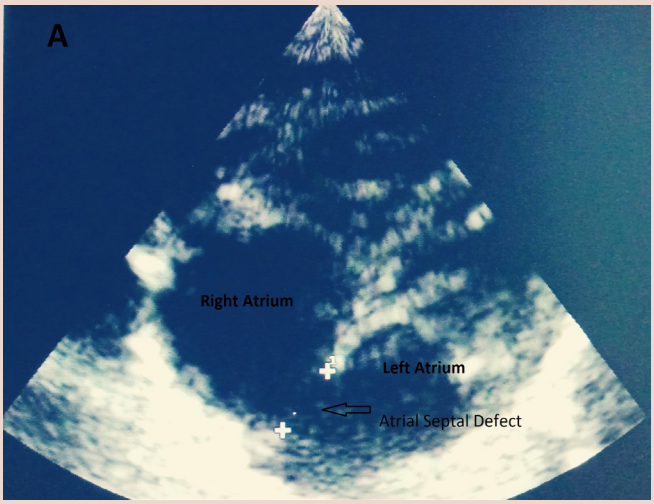

Figure 3: Large ostium secundum type atrial septal defect (OsASD), measuring 6.9 mm with left to right shunt. There is mild dilatation of RA and RV.

microcephaly. Children surviving beyond few weeks eventually shed these plates and develop generalized scaling erythema of the skin. External auditory meatus and nostrils appear rudimentary and immature. In addition, ectropion, lack of development of the external parts of the nose and ears, eclabium and open mouth, hypoplastic fingers, anonychia and flexion deformity of the joints are some other clinical features of the HI.[2]

Babies are at risk for life-threatening complications in the postnatal period including respiratory distress, dehydration, electrolyte imbalance, temperature instability, feeding problems and bacterial infections, often with fatal consequences.[3] In addition, patients with HI have respiratory failure as a result of restricted chest expansion and skeletal deformities. Feeding problems may result in low blood sugar, dehydration and kidney failure.[6]

Prenatal diagnosis would be the first step for early detection of the disease. Therefore, obtaining the family history, consanguinity between the parents and the presence of other skin disorders in offspring would be very helpful for early diagnosis of the disease.[2] Antenatal diagnosis in suspected cases can be confirmed using electron microscopy of fetal skin biopsy and DNA-based diagnosis with chorionic villus sampling or amniocentesis.[4,7] 3D or 4D ultrasound examination may be helpful in identifying fetuses with harlequin ichthyosis as early as the second trimester in families with a known history of harlequin ichthyosis.[8]

There is no cure for this condition and only supportive treatment can be given to prolong life. The mortality of HI is high and most of the babies die within a few weeks of birth because of secondary complications such as sepsis, respiratory failure, infections and poor nutrition and electrolyte imbalances. In the past 20 years, however, the prognosis of HI infants has improved due to advances in neonatal intensive care and targeted oral retinoids.[5,9] The patients' quality of life improves with supportive cares. It has been reported that the survival rate varies from 10 months to 25 years with supportive treatment depending on the severity of the condition. A survival rate of 56% has been reported with early prescription of oral retinoids and is expected to further increase with improved neonatal intensive care and treatment options.[10] Recurrence of this condition in the next pregnancy is 25%. Each sibling of an affected individual has a 25% chance of being affected.

With increasing survival rate in these patients it becomes imperative to study the spectrum of disease in further details. This would help in better comprehensive management of the disease. To best of our knowledge cardiac involvement has never been studied, not surprisingly to the shear rarity of the syndrome.

The detailed echocardiographic examination in our patient revealed a hemodynamically insignificant patent ductus arteriosus (PDA) and large ostium secundum atrial septal defect (OsASD). Further disease course could not be studied due to early demise of the baby. Since this is first case study, this association is merely a speculation as of now. Further studies are required to confirm or refute this observation. The current case adds to the collective clinical knowledge of this rare skin disorder.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Cite this article : Verma B, Mohan A, Singh A, Saxena AK. Cardiac Abnormalities in Harlequin Ichthyosis: First Case Study. J Cardiovasc Disease Res. 2018; 9(3):154-5.