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Harlequin Ichthyosis (HI) Associated with Atrial Septal Defect (ASD) and Choanal Atresia

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Abstract

Harlequin ichthyosis (HI) is a severe form of congenital ichthyosis with autosomal recessive inheritance. Incidence of harlequin ichthyosis is 1 in 3,00,000 live births. We report a case of HI associated with bilateral choanal atresia and atrial septal defects, which is a rare association in this skin disorder. A-month-old preterm male baby born out of consanguineous marriage presented with features of armour-like scales and erythema all over body, ectropion, eclabium and fissures over flexures. The patient was born with a colloidion membrane at birth. The baby was operated for bilateral choanal atresia soon after birth because he developed cyanosis upon breast feeding which improved on crying. Upon flexible nasal endoscopy, diagnosis of membranous type of choanal atresia was confirmed by ENT (ear, nose, throat) surgeon. Heart auscultation revealed a murmur in our patient. Electrocardiogram and 2D Echocardiography was reported as atrial septal defect (4.5 mm OsASD). The patient was started on acitretin (1 mg/kg/day) and emollients after complete evaluation and is currently on regular follow up. Harlequin ichthyosis is linked to mutation of ABCA12 gene. It is often associated with eclabium, ectropion, hypoplastic nose, ears and fingers. Congenital heart diseases are rarely reported with HI in literature. This makes it mandatory to screen HI patients for internal defects.

Key words: Ichthyosis, Lamellar; Chonal Atresia; Heart Septal Defects, Atrial; Infant, Premature; Consanguinity; Skin Abnormalities; Comorbidity

Introduction

Harlequin ichthyosis (HI) is the most severe form of congenital ichthyosis inherited in an autosomal recessive manner. It is characterized by mutation in ABCA12 gene. It occurs in 1 in 3 lakhs live births (1). Babies with HI are often preterm and are covered with thick armour-like scales all over body. The rigid skin severely restricts mobility of joints and may result in deformities of face. Eclabium, ectropion, hypoplastic fingers/toes, hypoplastic ears and nose are common associations of HI. Choanal atresia and congenital heart disorders are extremely rare associations of HI. In this article, we illustrate a rare case of a preterm male baby with harlequin ichthyosis associated with bilateral choanal atresia and atrial septal defect.

Case Report

A-month-old preterm male child presented to us with armour like scales all over the body, ectropion, eclabium, hypoplastic pinnae, hypoplastic nose, hypoplastic fingers and toes. There was complete loss of body hair including eyebrows and eyelashes, scanty hairs were present over scalp. Multiple fissures were noted on flexures especially over neckline, axillae, and antecubital fossae bilaterally. The rigidity and fissures lead to restricted mobility along respective joints. The baby, born out of a consanguineous marriage, was born encased in a collodion membrane at birth as per history.

The patient was operated by an ENT surgeon for bilateral choanal atresia (membranous type) post delivery on emergency basis as he was having difficulty in breathing at birth and developed cyanosis while being breast fed, which improved on crying. The baby had a diastolic murmur on cardiovascular examination. Electrocardiogram revealed a right axis deviation. 2D ECHO was suggestive of osteum secundum type of atrial septal defect (OsASD) of size 4.5 mm. The patient

Figure 1. One month old baby showing generalized erythema and scaling with plate like scales over scalp, upper limbs, lower limbs and ectropion

was referred to Pediatric Cardiology Department in view of his OsASD. Currently, the baby is being managed conservatively for his ASD.

Upon examination of other systems (abdominal, neurological, respiratory), no other abnormality was detected. Hemogram, liver and renal function tests, lipid profile, urine microscopy, ultrasound of abdomen and pelvis were found to be within normal limits. The child was started on oral acitretin at a dose of 1 mg/kg/day in two divided doses. Apart from acitretin, topical emollients and antibiotic (2% mupirocin ointment) were introduced for fissures over flexural areas. Detailed skin care regarding maintaining hygiene, including use of syndet bars for bath, frequent application of emollients was explained to the parents on discharge. Currently, the baby is under regular follow up and shows mild improvement in scaling and mobility. Our patient is being managed in collaboration with pediatricians, pediatric cardiologists and otorhinolaryngologists.

Discussion

Harlequin Ichthyosis (HI) is a severe form of congenital ichthyosis caused by mutation in ABCA12 gene which encodes ATP binding cassette protein (subfamily A, member 12). This protein is responsible for skin lipid metabolism (2). Hence, mutation in this gene leads to abnormal membrane transport of skin lipids with abnormal lipid metabolism in skin (2, 3). No systemic associations have been elaborated in literature for this life-threatening ichthyosis. However, a case series by Verma B, et al. demonstrates cardiovascular anomalies associated in seven cases of harlequin ichthyosis (4). According to their report, ostium secundum type of atrial septal defect (OsASD) is the commonest type of congenital heart disease associated with harlequin ichthyosis. Other heart defects associated with HI are patent ductus arteriosus, ventricular septal defects and patent foramen ovale.

Concurrence of bilateral choanal atresia with harlequin ichthyosis and OsASD makes our case unique. There is no documentation of such kind of association with HI in literature.

HI is known for its lethal complications like hypernatremia, sepsis, heat intolerance, ocular complications due to persistent ectropion, joint contractures etc. Before 1980s, the disease was considered fatal. But now, with availability of oral retinoids and intensive care for managing systemic complications, survival rate of harlequin ichthyosis has improved (5). However, the disease still remains a prob-

lem as the babies might survive with recurrent or persistent erythroderma posing a constant threat to life.

Prenatal genetic counselling and amniocentesis for early diagnosis of HI remains the basic strategy to avoid this unsightly congenital birth defect.

Abbreviations

HI – harlequin ichthyosis
OsASD – osteum secundum type of atrial septal defect

Conclusion

Harlequin ichthyosis has ectodermal defects of skin, pinna, nose, eyes and digits. However, a rare association of this disorder with congenital heart disorder makes it crucial to screen all patients for other systemic abnormalities.

Harlequin ichthyosis, a congenital disorder hitherto notorious for its lethality, can now be managed with oral retinoids and proper intensive care.

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Harlekinova ihtioza (HI) združena sa atrijalnim septalnim defektom (ASD) i atrezijom hoana

Sažetak

Harlekinova ihtioza (HI) je težak oblik kongenitalne ihtioze nasleđene sa autosomalno recesivnim nasleđivanjem. Incidencija harlekinove ihtioze je 1 na 300,000 živorođenih beba. Prikazujemo slučaj HI združene sa bilateralnom atrezijom hoana i atrijalnim septalnim defektom što je retka združenost u ovom poremećaju kože. Jednomesečno prevremeno rođeno muško dete, rođeno u braku srodnika, imalo je skrame tipa oklopa od krljušti i eritemu po celom telu, ektropion, eklabium i fisure preko fleksura. Dete je rođeno sa koloidnom membranom i operisano zbog bilateralne atrezije hoana uskoro posle rođenja pošto je došlo do cijanoze nakon dojenja što se popravilo plakanjem. Nakon fleksibilne nazalne endoskopije, otorinolaringolog je potvrdio dijagnozu membranoznog tipa atrezije hoana. Prilikom auskultacije srca, čuo se šum na srcu pacijenta. Elektrokardiogram i 2D ehokardiografija su prikazani kao atrijalni septalni defekt (4,5 mm OsASD). Pacijent je počeo da dobija acitretin (1 mg/kg/dan) i emolijente. Posle kompletne evaluacije i sada je u redovnom procesu praćenja. Harlekinova ihtioza je povezana sa mutacijom ABCA12 gena. Često je združena sa izvrnutim usnama (eclabium), ektropionom, hipoplastičnim nosem, ušima i prstima. Kongenitalna srčana oboljenja su retko opisana sa HI u literaturi. Zbog toga je potrebno pregledati pacijente sa HI i zbog unutrašnjih defekata.

Ključne reči: Lamelarna ihtioza; Honalna atrezija; Atrijalni septalni defekt; Nedonošče; Konsangvinitet; Kožne abnormalnosti; Komorbiditet

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