Case Report

Isolated hemosiderosis of liver in an infant with hypertrophic cardiomyopathy

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Abstract

Cardiomyopathy in newborn period is very rare. Cardiomyopathy with hepatic involvement causes early death. We report a case of isolated hepatic hemosiderosis with associated hypertrophic cardiomyopathy (HCM) without any evidence of cardiac hemosiderosis in a 50-day-old infant who had been symptomatic since birth.

Key words: Hepatic hemosiderosis, hypertrophic cardiomyopathy, isolated hepatic hemosiderosis

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INTRODUCTION

Cardiomyopathy refers to diseases of the heart muscle associated with varying degree of cardiac dysfunction. World Health Organization (WHO) has defined cardiomyopathies as "heart muscle diseases of unknown cause", to distinguish cardiomyopathy from cardiac dysfunction due to hypertension, ischemic heart disease, or valvular disease which are mostly secondary to problems of metabolism.[1] The estimated incidence of pediatric cardiomyopathy in two large regions of the United States, that is, New England and the central southwest region (Texas, Oklahoma, and Arkansas) of the United States (1996 and 1999) was 1.13 cases per 100,000 children.[2]

We report a case of hypertrophic cardiomyopathy (HCM) in an infant with isolated hepatic hemosiderosis.

CASE REPORT

A 50-day-old male presented with incessant cry and respiratory distress. Blood pressure was 90/50 mmHg, heart rate 178/min, and respiratory rate - 60/min. He had normal heart sounds and grade III systolic murmur over precordium. Liver was palpable 5 cm and spleen 2 cm below costal margin. Musculoskeletal, neurological, and dermatological system examination was unremarkable.

He was the second baby born to third degree consanguineous parents and was antenatally diagnosed to have HCM by ultrasonography. He was a term baby and required oxygen for few hours after a normal delivery. He had a systolic murmur on the precordium without any signs of congestive cardiac failure. Later, he was discharged on day 8 of life after collecting a blood sample to determine alpha acid glucosidase level. He was not on regular follow-up and this time he was readmitted at 50th of life in a sick condition. The first male baby was born preterm and died in a hospital at 3 months of age due to acute respiratory distress without fever or seizure (cause not known).

Thyroid function test, hematological parameters, renal function tests, and serum electrolytes (Na^+, K^+, Ca^{++}) were normal and blood culture was sterile. Echocardiogram (ECG) demonstrated sinus tachycardia, normal PR interval, deep Q in Lead II, III, and aVF (6 mm). Chest radiograph showed cardiothoracic ratio of 92% and prominent bronchovascular markings. Two-dimensional (2D) ECG revealed left ventricular hypertrophy (LVH) with asymmetry, right ventricular hypertrophy (RVH), 5 mm patent foramen ovale (PFO) with right to left shunt, left ventricular outflow tract (LVOT) gradient. His serum troponin T level was within normal limits. Acid alpha-glucosidase activity in lymphocytes with

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acarbose as inhibition was normal. He did not respond to resuscitation and expired after 18 h.

Postmortem liver tissue showed dark brown granular coarse pigments within hepatocytes [Figure 1a]. Perl's stain for iron was positive [Figure 1b]. This showed hepatic hemosiderosis with no evidence of storage disease. Myocardium showed hypertrophy of myofibrils with mild disarray, interstitial fibrosis without any vacuolization in fibers [Figure 2]. Perl's stain for iron was negative. Histopathological images (HPI) of liver and heart are shown in Figures 1 and 2.

DISCUSSION

HCM may be idiopathic or secondary to critical aortic stenosis, coarctation of aorta, inborn error of metabolism, that is, glycogen storage disease, mucopolysacharidosis (MPS).[2]

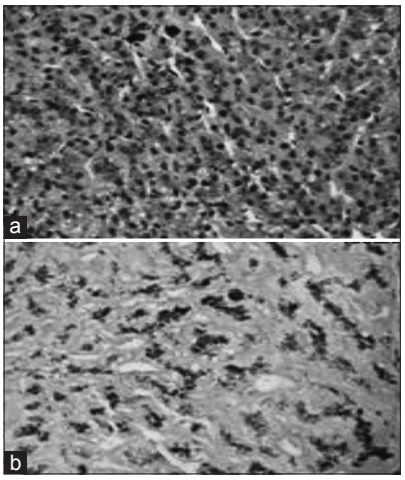

Figure 1: (a) Histopathological images (HPI) of liver showing dark brown granular coarse pigments within hepatocytes and Kupffer cells. (b) Pearls stain shows prussian blue staining of the hemosiderin granules

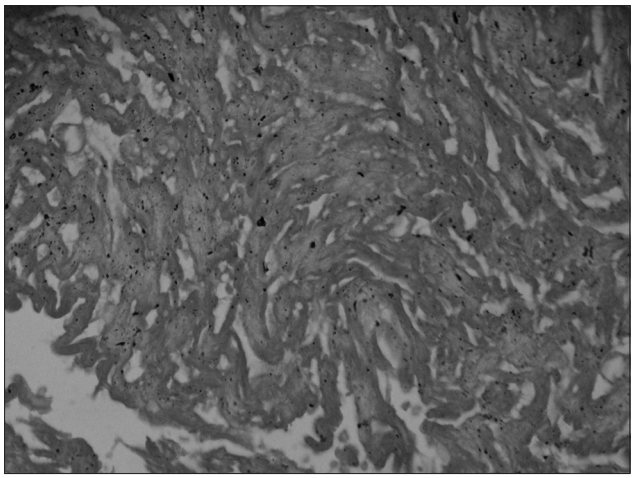

Figure 2: HPI of heart showing hypertrophy of myofibrils with mild disarray and interstitial fibrosis

Histologically idiopathic HCM shows varying degrees of myocardial fibrosis with electron microscopic evidence of disarray of myofibrils and myofilaments.[3]

Transient HCM is due to maternal diabetes and antenatal or postnatal exposure to steroids.[4] Normal level of alpha acid glucosidase enzyme in this case ruled out storage disorder (glycogen storage disease type II (GSDII)). HCM is typically an isolated cardiac lesion in newborn.

Without any cardiac deposits of iron or histopathological evidence of liver cell failure makes neonatal hemochromatosis unlikely.[5] Normal serum troponin levels reasonably ruled out myocarditis. Rare conditions like aceruloplasminemia and atransferrinemia may cause hepatic hemosiderosis. Familial or primary HCM is the most common genetic cardiovascular disorder, occurring in $\approx$ 1/500 individuals.[6] In this case, it is most likely a familial HCM as the elder sibling had similar respiratory distress leading to death. To date, isolated hepatic hemosiderosis in newborn has not been reported.

Though iron overload cardiomyopathy/iron overload conditions (both hemochromatosis and hemosiderosis) involve almost all the visceras in advanced stage of the disease, this was surprisingly not so in this case. The heart of this child had no evidence of excessive iron deposit either in myocyte or in interstitium. HCM is not usually associated with hemosiderosis. Rather hemosiderosis is associated with dilated cardiomyopathy.

Three genetic defects account for most cases of HCM, that is, beta major histocompatibility complexes (MHC), myosin-binding protein C, and troponin T genes. Ninety percent of beta MHC gene defect will demonstrate left ventricular hypertrophy.[7] Prenatal molecular diagnosis of HCM is possible. Tissue Doppler derived early transmitral left ventricular filling velocity (E/septalEa) ratio predicts adverse outcomes (death, cardiac arrest, and ventricular tachycardia).[8] ECG evidence of Q wave >3 mm deep and/or >0.04 s in at least two leads other than aVR is sensitive and specific in identifying cases for a positive diagnosis on genotyping.[9] Magnetic resonance imaging (MRI) is becoming increasingly popular in evaluation of HCM. Disopyramide, alone or with a beta-blocker is useful in treatment of LVOT obstruction.[3] Surgical myectomy is a standard therapy for LVOT obstruction refractory to medical therapy.

Advances in precision of noninvasive assessment leads to safe and effective therapies to control the progression of HCM and prevents death. In conditions with iron overload, early diagnosis and chelation of excess iron may delay and prevent multiorgan failure and prolong life. Standard treatment currently includes dietary management,

phlebotomy, and chelating agents aimed at keeping a target serum ferritin below 20 ng/ml.[10]

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