Congenital nephrotic syndrome and the heart: Lest we forget!

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Abstract:

Congenital nephrotic syndrome is defined by the presence of nephrotic range proteinuria, hypoalbuminemia and edema, with onset in the first three months of life. It is usually secondary to genetic mutations of the components of the glomerular filtration barrier, although infective causes must be ruled out. Congenital heart disease is extremely rare in congenital nephrotic syndrome, accounting for less than 20% of cases and is mostly associated with podocin mutation. We report a two month girl, presenting with anasarca in the first two months of life and was diagnosed to have congenital nephrotic syndrome. Infectious causes including malaria, cytomegalovirus, toxoplasmosis, syphilis, human immunodeficiency virus and rubella were ruled out. In view of a systolic murmur, echocardiography was done which revealed ostium secundum atrial septal defect and branch pulmonary artery stenosis. Genetic analysis showed homozygous single base pair duplication in exon 20 of the NPHS1 gene (chr19:36332624dupG; Depth: 216x) resulting in a frameshift and premature truncation of the protein 6 amino acids downstream to codon 937 (p.Ser937GlnfsTer6; ENST00000378910.5). This is the first case of NPHS1 (nephrin) mutation associated with congenital cardiac disease along with congenital nephrotic syndrome.

Introduction

Congenital nephritic syndrome defined as proteinuria leading to clinical symptoms soon after birth up to 3 months. Congenital nephrotic syndrome of Finnish type originally referred to severe form of proteinuria typically seen in Finnish newborn without providing albumin substitution and nutritional support the classic pictures of hypoproteinemia develop like as generalized edema ,abdominal distention, ascites, umbilical hernia, and widened cranial sutures and fontanelles it considered as autosomally recessive disease which happen more frequent in Finland (1 in 8200 live birth) with severe proteinuria beginning from fetal period leads to complications due to protein deficiency. They are premature in 80% (before the thirty-eight week) with a mean birth weight of 2600 grams (1500 to 3500) diagnosed within the first week in 82%. Congenital nephrortic syndrome has been associated with many minor functional disorders like as hypothyroidism, hypotonia, central nervous system or metabolic disorders mainly dyslipidemia. Minor cardiac findings such as hypertrophy and mild pulmonary stenosis have been reported in one fourth of the Finnish type. In this study, we try to find this incidence as our cases.

Materials and methods:

During 4 years from September 2006 to January 2010, six cases of congenital nephritic syndrome diagnosed in our referral centre, our criteria include diagnosing before month 3, hypoalbuminemia (serum albumin below 2.5 gram/deciliter) and proteinuria more than 50 milligram/kilogram/day as cut point of nephrotic range proteinuria. Cases associated with hepatosplenomegaly and positive intrauterine infections omitted from our study. Echocardiography was performed and the type of structural defects and parameters about shunt characters, regurgitation and their gradients were reordered. Their valvular structures were assessed in detail by using standard left lateral decubitus position by Vingemed system with 2.5 megahertz probe in the apical four chambers image. The right and left atrium diameter were measured at the levels of mitral and tricuspid annulus valve in millimeter which means the distance from the lateral wall of the right atrium to the interatrial septum and from the lateral wall of the left atrium to the interatrial septum moderate tricuspid regurgitation (gradient between right atrium and right ventricle 35-50 millimeter of mercury) and severe (pressure gradient between right atrium and right ventricle above 50 millimeter of mercury) considered in our study for report. The pulmonary valve was structurally assessed in parasternal short axis image.

Results:

During 4 years from September 2006 to 2010, six cases of congenital nephrotic syndrome referred to our hospital as a referral hospital. Two out of 6 cases diagnosed before age of 2 months and 4 out of 6 before third months. All presented with ascite, paleness, edema mostly died before age of 4 months due to sepsis and acute renal failure. Serum albumin in all cases were below 2 g/dl (mean: 1.3 gram/deciliter), they were born in term or near term pregnancy (mean: 34 week of gestational age and 2900 gram weight of birth), the parents were not consanguine mostly. Tricuspid regurgitation in moderate grades was seen in 3/6. Pulmonic stenosis were seen in 3/6 , in one case it was valvular in other case it was sub pulmonic stenosis and in third it was in peripheral branches of pulmonary arteries that was missed in first try. Left ventricular hypertrophy and mitral regurgitation was observed in 2 cases

Conclusion:

Congenital nephritic syndrome is a rare event in Iran but co-morbidity with cardiac malformation is common, multiple cardiac malformation may happen in non-consanguine families consecutively in siblings. Pulmonary valve stenosis may happen in all part of sub valvular, valvular and peripheral branches of pulmonary arteries which may be ignored. Left ventricular hypertrophy with or without mitral regurgitation occurred in 2 out of 6 cases, half of patients may have moderate tricuspid regurgitation backed to some predisposing factors like as pulmonary hypertension ,embolism or pulmonic stenosis as a structural predisposing factors it may happen between 15 to 50th.days after birth.