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Cardiac Findings in Congenital Nephrotic Syndrome

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ABSTRACT

Introduction: Congenital nephrotic syndrome is a severe debilitating problem associated with extra renal manifestation such as diverse cardiac findings. ***Methods:*** During four years, 6 cases diagnosed as congenital nephritic syndrome in base of definitive criteria their documents reviewed and echocardiographic evaluation has been done for all with or without cardiac sign or symptoms, results gathered and expressed as incidence. ***Results***: All cases have some grades of structural or functional defects from simple form like as tricuspid regurgitation to complex defects. It may be run in consecutively in siblings of a family from non consanguine parents. ***Conclusion*:** Pulmonary stenosis may occur in all parts subvalvualr, valvular and peripheral parts of pulmonary artery, left ventricular hypertrophy and mitral regurgitation observed in some, moderate tricuspid regurgitation observed in half of cases due to pulmonary hypertension or right ventricular hypertrophy due to pulmonary stenosis.

Introduction

Congenital nephritic syndrome defined as proteinuria leading to clinical symptoms soon after birth up to 3 months.[1] 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[2,3] 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%.[2,4-7] 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. [6] 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

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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 (4/6). 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 as Table 1.

Table 1.Cardiac findings, age of diagnosis and sex of patients show most cases are male or diagnosed lately (third month) in 4/6, tricuspid regurgitation as a sign of pulmonary hypertension can be seen in 3/6 as much as pulmonic stenosis in all its parts

Case	Sex /days of presentation	Cardiac findings
1	Male/40 days	Moderate pulmonic stenosis ,Closed ventricular septal defect
2	Male/50 days	Severe subpulmonic stenosis, atrial septal defect, severe right ventricular hypertrophy, moderate tricuspid regurgitation.
3	Female/50 days	Left ventricular hypertrophy, mild mitral regurgitation
4	Female/49 days	Mitral regurgitation , moderate tricuspid regurgitation
5	Male/15 days	Mitral regurgitation, moderate tricuspid regurgitation
6	Male/ 8 days	Ventricular hypertrophy, peripheral pulmonary stenosis

Discussion

Cardiac malformation along steroid resistant nephrotic syndrome due to podocin mutation that have some function in cardiac development has been reported in many cases [8] but its cardiac association described once earlier in a family consisted of four sisters who developed steroid resistant congenital nephritic syndrome developed clinical sign of right ventricular outflow tract obstruction.[9] In two of the girls, confirmation of right ventricular strain was obtained from electrocardiography and chest radiography. In one of the girls subpulmonary right ventricular outflow tract obstruction was demonstrated at postmortem examination. Report of minor cardiac malformation in one fourth of Finnish patient with mild functional pulmonary hypertrophy and stenosis, in other report from Malta severe pulmonary stenosis and subaortic stenosis described.[10,11] As our study heart association are common in congenital nephritic syndrome as it seems not being incidental as in two consecutive siblings complex heart structural defects mainly pulmonic stenosis observed from non consanguine parents although in other studies cardiac evaluation often reveal ventricular hypertrophy but structural defects are rare[12] but in 6 consanguineous Arabs family cardiac anomalies were observed due to podocin synthesis deficiency[8] in another study 2 out of 12 patients had cardiac anomalies mainly mild mitral regurgitation and left ventricular hypertrophy [13] but as our study some grades of heart defects can be seen nearly in all, and multiple structural defects can be seen in lesser generally in familial form, right ventricular hypertrophy happened in 1 out of 6 and left ventricular hypertrophy in 2 out of 6 patients but the most important finding is pulmonic valve stenosis (valvualr or subvalvular) or it may be happened in peripheral part of pulmonary artery that may be missed at first without paying attention precisely. Tricuspid regurgitation is another common problem attributed to increased pulmonary hypertension in nephrotic syndrome that may be seen in 7/8 of steroid resistant nephrotic syndrome with prolonged disease[14] and in moderate to severe form is suggestive for pulmonary embolism as a complication of nephrotic syndrome.[15] As our study tricuspid regurgitation observed in 3/6 cases may happened in age as low as 15th days.

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.

Ethical issues: None to be declared.

Conflict of interests: The authors declare no conflict of interests.

References

1. Mauch TJ,Vernier RL,Burke BA.Nephrotic syndrome in first year of life .In Holliday MA,Barrat TM,Avner ED,eds.pediatricnephrology, 2ed. Baltimore: lippincott,1994:788-802.
2. Ahvenainen EK, Hallman N, Hjelt L. Nephrotic syndrome in newborn and young infants. **Ann Paediatr Fenn** 1956; 2:227-41.

3. Norio R. Heredity in the congenital nephrotic syndrome. A genetic study of 57 fnnish families with a review of reported cases. **Ann Paediatr Fenn** 1966; 27:1-94.

4. Huttunen NP. congenital nephritic syndrome of finnish type. study of 75 patients. **Arch dis child** 1976; 51:344-8.
5. Hallman N, Norio R, Rapolo J. Congenital nephritic syndrome .**Nephron** 1973; 11:101-10.
6. Patrakka J, Kestilä M, Wartiovaara J, Ruotsalainen V, Tissari P, Lenkkeri U, et al. Congenital nephrotic syndrome (NPHS1): features resulting from different mutations in Finnish patients. **Kidney int** 2000; 58:972-80.
7. Holmberg C, Antikainen M, Rönnholm K, Ala-Houhala M, Jalanko H. Management of congenital nephrotic syndrome of t he Finnish type. **Pediatr Nephrol** 1995; 9:87-93.
8. Frishberg Y, Feinstein S, Rinat C, Becker-Cohen R, Lerer I, Raas-Rothschild A, et al. The heart of children with steroid-resistant nephrotic syndrome: Is it all podocin? **J Am Soc Nephrol** 2006; 17:227-31.
9. Fournier A, Pauli A, Ducoulombier H, Cousin J, Sion G. [Nephroanemic syndrome in young infants (7 c ases)]. **Pediatrie** 1967;22:685-97.
10. Guez S, Giani M, Melzi ML, Antignac C, Assael BM. Adequate clinical control of congenital nephrotic syndrome by enalapril. **Pediatr Nephrol** 1998; 12:130-2.
11. Holmberg C, Tryggvason K, Kestila M, Jalanko H. Congenital nephrotic syndrome. In: Avner E, Harmon WE, Niaudet P, editors. Pediatric nephrology. Baltimore: Lippincott; 2004. p. 503–16.
12. Aula P, Rapola J, Karjalainen O, Lindgren J, Hartikainen AL, Seppala M. Prenatal diagnosis of c ongenital nephrosis in 23 highrisk families. **Am J Dis Child** 1978;132:984-7.
13. Caridi G, Dagnino M, Carrea A, Massella L, Amore A, Emma F, et al. Lack of cardiac anomalies in children with NPHS2 mutations. **Nephrol Dial Transplant** 2007; 22:1477-9.
14. Du ZD, Cao L, Liang L, Chen D, Li ZZ. Increased pulmonary arterial pressure in children with nephrotic syndrome. **Arch Dis Child** 2004; 89:866-70.
15. Goldhaber SZ, Elliott CG. Acute pulmonary embolism: part I: epidemiology, pathophysiology, and diagnosis. Circulation 2003; 108:2726-9.