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Isolated Pulmonary Valvular Stenosis –Noonan Syndrome – A Case Report

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Abstract

Noonan syndrome is an autosomal dominant dysmorphic characterized by hypertelorism, a downward eyeslant, and low-set posteriorly rotated ears. Other features include short stature, a short neck with webbing or redundancy of skin, cardiac anomalies, epicanthic fold, deafness, motor delay, and a bleeding diathesis. In this case report a 20 years male presented with severe pulmonary stenosis with classical sketetal abnomalities.

Key words :Autosomal dominant, pulmonary stenosis

Introduction

Noonan Syndrome (NS) is a relatively common congenital genetic condition which affects both males and females equally[1]:550. It used to be referred to as the male version of Turner's syndrome[2]; however, the genetic causes of Noonan syndrome and Turner syndrome are distinct. The principal features include congenital Heart Malformation, short stature, learning problems, indentation of the chest, impaired blood clotting, and a characteristic configuration of facial features. The syndrome is named after Dr Jacqueline Noonan. It is believed that between approximately 1 in 1,000 and 1 in 2,500 children worldwide are born with NS. It is one of the most common genetic syndromes associated with congenital heart disease, similar in frequency to Down syndrome. However, the range and severity of features can vary greatly in patients with NS. Therefore, the syndrome is not always identified at an early age.This case is diagnosed and managed in BSMMU.

Discussion

Noonan Syndrome (NS) is a relatively common congenital genetic condition which affects both males and females equally[1]. 550. It used to be referred to as the male version of Turner's syndrome[2]. however, the genetic causes of Noonan syndrome and Turner syndrome are distinct. The principal features include congenital Heart Malformation, short stature, learning problems, indentation of the chest, impaired blood clotting, and a characteristic configuration of facial features. The syndrome is named after Dr Jacqueline Noonan.NS may be inherited in an autosomal dominant pattern with variable expression.Recurrence in siblings and apparent transmission from parent to child has long suggested a genetic defect with autosomal dominant inheritance and variable expression. A person with NS has up to a 50% chance of transmitting it to a child. The fact that an affected parent is not always identified for children with NS suggests several possibilities:a parent could carry the gene without being affected (incomplete penetrance) manifestations are variably expressed and could be so subtle as to go unrecognized (variable expressivity) .a high proportion of cases represent new, sporadic mutations or Noonan syndrome is heterogeneous, comprising more than one similar condition of differing cause , some not inherited . In most of the families with multiple affected members, NS maps to chromosome 12q24.1. In 2001, it was reported that approximately half of a group of patients with Noonan syndrome carried a mutation of the PTPN11 gene at that location, which encodes protein tyrosine phosphatase SHP-2[3]. The SHP2 protein is a component of several intracellular signal transduction pathways involved in embryonic development that modulate cell division, differentiation, and migration, including that mediated by the epidermal growth factor receptor. The latter pathway is important in the formation of the cardiac semilunar valves. It has recently been shown that activating mutations in SOS1 also give rise to NS[4]. Shp2 and SOS1 both have roles as positive regulators of the Ras/MAP kinase pathway suggesting that dysregulation of this pathway may play a major role in the genesis of this syndrome[5]. Additional mutations in KRAS[6].and RAF1[7].genes have been reported to cause Noonan syndrome in a smaller percentage of individuals with the syndrome. Chromosomal abnormalities, such as a duplication of chromosome region 12q24 encompassing gene PTPN11 can result in an apparent Noonan syndrome [8]. Differing cause, some not inherited .In our case showed short stature, triangular shape in face, webbed neck, low hairline at the

Case Summary

20-yrs. old boy with Noonan syndrome. Note the typical webbed neck

Mr. Anowar Hossain a 20 years old cultivator from B. Baria has presented to us in the cardiac OPD with the complaints of Shortness of breath after exertion which was not associated with chest pain or seasonal variation of cough , not history suggestive of paroxysmal nocturnal dyspnea or orthopnea.He also complains poor appetite , nausea and occassionl vomiting. He also noticed episodic palpitations after exertion and relived after rest. There was no h/o weight loss.

His parients ,brothers and sisters are alive and healthy. No consanguineous marriage o f his parents. He has no family history of down syndrome and Marfan syndrome. His examination showed short stature, triangular shape in face, webbed neck, low hairline at the nape of the neck ,widely set eyes (hypertelorism), proptosis (bulging eyes), depression of breast bone (pectus excavatum) Shiled chest and widely apart nipple, winging of the scapula ,low sets ears,

Deeply grooved philtrum (top lip line), Microganthia (undersized lower jaw), High arched palate, Malalinghed teeth, articulation difficulties ,Cubitus valgus, Flat feet , Clumsiness, poor coordination, motor delay,Mental retardation, learning disabilities.

His pulse 84/min ,regular ,symmetrically palpable all peripheral pulse, BP was 110/80 mm Hg ,RR 16/min. JVP *was not raised* , Patient is mildly anaemic, not ecteric, cyanosis, clubbing and oedema not present. Apex beat located in Lt 5th ICS normal in character, RV heave present , P2 was absent, S1 is audiable all the cardiac area & normal, pulmonary component of S2 is soft in pulmonary area.

Spectral doppler of PS

Thrill present on the pulmonary area. There is a ejection systolic murmur grade 4/6 on the pulmonary area radiates towards the lt side of the neck. Other systemic examination reveals no abnormalities. His investigation showed serum creatine 1mg/dl, Hb-14.7gm/dl, ECG showed RAH & RVH with strain pattern. Echo 2D –M mode, colour & spectral doppler showed main pulmonary artery narrowed then poststenotic dilation of main pulmonary artery, Left pulmonary artery dilated .RA,RV dilated , mosaic flow from RV outflow to pulmonary artery during systole, Pressure gradient of PV is146mm Hg ..USG of KUB regions showed rt sided pelvis dilated and are cystic lesion (6.6 x6.8) cm size. CxR P/A view showed RV type of hypertrophy. Cardiac catheterization RV graphy showed, RV pressure 130 mm Hg, PA – pressure 80 mm Hg and pressure gradient 50 mm Hg . Balloon valvuloplasty attempted but unsuccessful patients awaits for valvotomy at convenent time. If unsuccessful than valve replacement

nape of the neck,widely set eyes (hypertelorism), proptosis (bulging eyes), depression of breast bone (pectus excavatum) Shiled chest and widely spaced nipple, winging of the scapula, low sets ears, Deeply grooved philtrum (top lip line), Microganthia (undersized lower jaw), High arched palate, Malalinghed teeth, articulation difficulties, Cubitus valgus, Flat feets, Clumsiness, poor coordination, motor delay, Mental retardation and learning disabilities.Almost all males of noonan syndrome patient present Cryptorchidism (Undescended testis) but our patient has no Cryptorchidism .Noonan syndrome is a genetic defectt with autosomal dominant inheritance and variable expression. But our reported patient no parients and other family member are affected. So this is a new case and sporadically manifested .2/3 of patients have one of the following heart defects, Pulmonary Valvular Stenosis (50 %), Septal defects, Atrial 10%) or ventricular (less common), and Cardiomyopathy. Our reported patients has severe pulmonary valvular stenosis. Noonan syndrome is a rare case. This is the first reported case in Bangladesh .

Conclusion

Noonan syndrome is a relatively common congenital genetic condition which affects both males and females equally. Despite identification of four causative genes, the diagnosis of noonan syndrome is still based on clinical features. In other words, it is made when physician feels that a patient has enough of the features to warrant the label indicating association. The patient can be tested for mutations in the PTPN11, SOS, or KARS gens, however absence of a mutation will not exclude the diagnosis as there are more as yet undiscovered genes that cause NS. The principal values of making such a diagnosis are that it guides additional medical and developmental evaluations, it excludes other possible explanations for the features , and it allows more accurate recurrence risk estimates.

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