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A Case of Noonan's Syndrome with Primary Pulmonary Hypertension*)

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ABSTRACT

A case of Noonan's syndrome with primary pulmonary hypertension is reported. The patient has multiple anomalies (small mandible, high arched palate, low set ears, hypertelorism, and webbed neck). He has normal karyotype. Cardiac examinations show pulmonary hypertension, right ventricular hypertrophy, high RPEP/RVET and no other shunt diseases.

We consider that this is the first reported case of Noonan's syndrome with primary pulmonary hypertension

INTRODUCTION

Cardiovascular malformation is a well-known complication in patients with Noonan's syndrome. Congenital heart disease is present in 55% of these patients, the most common abnormalities are pulmonary valve stenosis, atrial septal defect, hypertrophic cardiomyopathy, and patent ductus arteriosus[1,5].

Other infrequent cardiac lesions include truncus arteriosus, tetralogy of Fallot, ventricular septal defect, Ebstein's malformation, and aortic stenosis[5].

Primary pulmonary hypertension is very rare in patients with Noonan's syndrome and in other diseases. It is the purpose of this communication to describe a patient with Noonan's syndrome and primary pulmonary hypertension; to our knowledge this association has not been reported.

CASE REPORT

A 2-month-old male was referred to us for evaluation of multiple anomalies and a slightly enlarged heart on chest X-ray film. He was the first child of young, unrelated, healthy parents. He was born at term and the delivery was normal. At birth his length was 54 cm and weight 4, 200 g.

There is no consanguinity in the family. No other members of the family have anomalies or heart disease.

On admission, length was 57 cm, weight 4, 680 g, and head circumstance 38. 4 cm. Abnormal findings were small mandible, high arched palate, low set ears, hypertelorism, and webbed neck. Heart sound were clear and no heart murmurs were audible. There was no hepatosplenomegaly or lymphoadenopathy. Blood count and urinalysis were normal. Other laboratory investigations including liver and renal tests, electrolytes and serum amino acids were normal. Thyroid function tests showed a normal T_4 (7. 8 μg/dl) and TSH (11. 1 μU/ml). Antithyroid antibodies were absent. Chromosomal analysis revealed a normal 46, XY karyotype.

Radiologic examinations of the skull and bones were normal. Chest X-ray films showed a slightly enlarged pulmonary artery and right

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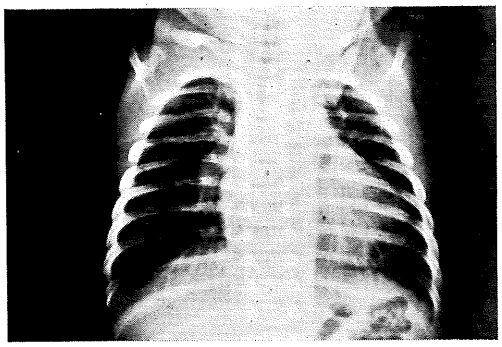

Fig. 1. Chest roentgenogram

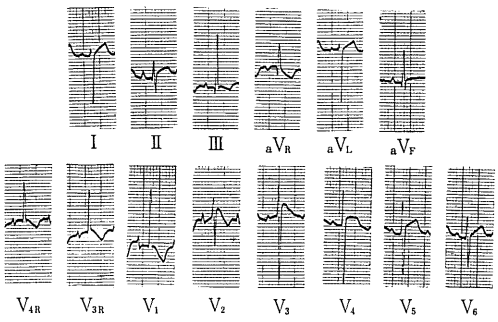

Fig. 2. ECG

Table 1. Cardiac catheterization data

SITE			PRESSURE (mm/Hg)	
SVC			2	
RA			0	
RV			52/1	
PA			67/35	47
LA			4	
LV			109/5	
% O_2 saturation of FA			80.1%	
% O_2 saturation of RA			56.7%	
RV volume	EDV	27 ml		
	ESV	8 ml		
	EF	70%		
LV volume	EDV	13 ml		
	ESV	5 ml		
	EF	64%		
Left to right shunt		0%		
$P_p/P_s=0.61$				
$Q_p/Q_s=1.00$				

ventricle. The cardio-thoracic ratio was 0.63 (Fig. 1).

An electrocariogram showed a mean frontal plane axis of 150 degrees with a monophasic R wave in V_{4R}, V_{3R} and V_1, a tall R wave (taller than 1 mV) in V_{4R}, V_{3R} and V_1, and a RS pattern in V_6 (Fig.2).

An echocardiogram showed high RPEP/RVET (0.40) and no other abnormalities. The RPEP/RVET did not fall when the patient breathed 100% O_2 (RPEP/RVET=0.33).

The pressure recorded at the time of cardiac catheterization are shown in Table 1. Pulmonary artery end-systolic pressure was 67 mmHg, end-diastolic pressure 35 mmHg, and left atrial mean pressure was 4 mmHg. A right ventricular cineangiogram showed no shunt anomalies or pulmonary valve abnormalities. A transseptal left atrial cineangiogram was normal.

A phonocardiogram showed single second sound. Myocardial biopsy showed slight interstitial fibrosis. A myocardial imaging by $^{201}TlCl$ revealed thick right ventricle muscle.

The clinical manifestation and cardiac examinations led to a diagnosis of Noonan's syndrome with primary pulmonary hypertension.

DISCUSSION

Noonan's syndrome is clinically similar to Turner's syndrome, but the chromosomes are normal in the former, and in the latter a sex chromosome abnormality is present[4]. The anomalies in Noonan's syndrome are short stature, webbing of the neck, cubitus valgus, sexual infantalism, congenital heart disease, etc[4,5].

Congenital heart disease is present in 55% of cases of Noonan's syndrome, right-sided cardiac malformations being most frequent, especially pulmonary stenosis, pulmonary branch stenosis, atrial septal defect, hypertrophic cardiomyopathy, and patent ductus arteriosus[1,5].

The case present in this report is of interest because it documents probably for the first time, the occurrence of primary pulmonary hypertension in Noonan's syndrome.

Primary pulmonary hypertension is very rare in children, and its origin is unknown. It is charecterized by hypertension of the lesser circulation and right cardiac failure. Primary pulmonary hypertension places a burden on the right ventricle and pulmonary artery with resultant right ventricular hypertension and dilatation of the pulmonary artery. The cardiac output is frequently decreased, and right heart failure develops[6].

It is difficult to determine the true incidence of this condition. Wood[7] cited it as 0.17% of

10,000 patients with heart disease surveyed clinically. The female to male ratio is usually estimated at between 3 : 1 and 4 : 1 in adults; among children the sexes are equal[7]. It may well be that primary pulmonary vascular obstruction is a different disease in children than in adults.

The differential diagnosis from Eisenmenger syndrome is made by cardiac catheterization, which demonstrates the site, direction and magnitude of the shunt which results in pulmonary hypertension.

The predominant symptoms include exertion intolerance and fatigability. Peripheral cyanosis may be present, as in our patient. If right heart failure is present, hepatosplenomegaly and edema occur. The heart is slightly to moderately enlarged (right ventricular hypertrophy). The roentgenogram reveals a prominent pulmonary and right atrial hypertrophy. In some patients this may not be excessive, in spite of maximal pulmonary arterial hypertension. Cardiac catheterization reveales right ventricular and pulmonary hypertension with normal pulmonary arterial wedge pressure. Cardiac output is low, and the course of the catheter is not unusual[3]. Cineangiograms show the dye lingering in the right heart chambers and sometimes lack or arborization of the pulmonary vascular trees. These cardiac manifestations were present in our case.

The definite diagnosis of primary pulmonary hypertension is made by lung biopsy or autopsy. Lung biopsy shows (1) plexogenic pulmonary arteriopathy, (2) recurrent pulmonary thromboembolism, and (3) pulmonary veno-occlusive diseases[2]. These findings are irreversible, and in our case we did not do lung biopsy.

In conclusion, we consider that this is the first reported case of Noonan's syndrome with primary pulmonary hypertension.

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