

# Spontaneous Chylothorax in a Patient with Noonan Syndrome. Treatment with Prednizone

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Noonan syndrome is a relatively common cardiofascial syndrome which is usually diagnosed in childhood. We report on the case of a 29 year old adult patient with this syndrome who presented in respiratory distress due to spontaneous chylothorax. He was treated with thoracocentesis and prolonged evacuation of the fluid, medium chain triglyceride diet and oral prednizone. The cardiologist may be the first doctor to encounter a patient with Noonan syndrome and a high index of suspicion is needed to make the correct diagnosis and treat all possible complications of the syndrome.

**N**oonan syndrome constitutes a relatively common hereditary syndrome with characteristic facial features and cardiovascular manifestations, with a large variety of clinical features<sup>1</sup>. Congenital heart diseases are present in 50% of cases and congenital pulmonary stenosis, valvular or subvalvular, is the most common<sup>2</sup>. In less than 20% of cases we also observe dysplasia of the lymph vessels<sup>2</sup>.

The case we present refers to a young adult male, 29 years old, with Noonan syndrome, spontaneous chylothorax and bilateral lymphedema.

## Case description

A young adult male, 29 years old, came to our outpatient department complaining of progressively aggravated dyspnea both on exertion and at rest and lower limb edema. Dyspnea was not accompanied by orthopnea nor paroxysmal nocturnal dyspnea. The patient had a history of surgical pulmonary valve correction, at the age of 4, due to congenital stenosis. At the age of 2 and 6 years old, the patient underwent unsuccessful operations for orchiopexy, due to cryptorchism of the right and left testis, respectively. Six years ago, he underwent percutaneous valvuloplasty of the

pulmonary valve due to restenosis. Two years ago he was admitted to a large hospital due to dyspnea and malleolar edema. During his hospitalization there, atrial fibrillation and pleural effusion in the left hemithorax, were observed. He was hospitalized for a long period and underwent a transoesophageal echocardiography, cardiac catheterization and coronary angiography. The final diagnosis was myocarditis and the treatment included digitalis, furosemide, ACE inhibitors and oral anticoagulants, which lead to mild symptom improvement without any reduction of the edemas nor of the pleural effusion. Three months ago, the patient presented extensive right lower limb edema because of viral etiology lymphedema and was prescribed antibiotics. Within one month, the edema extended to the left lower limb, while at the same time his pre-existing dyspnea was aggravated.

Clinical examination showed normal height and normal communication ability of the young adult. During the examination of the head, we observed hypertelorism with big, fixed eyes, wide forehead, low position of the ears and low position of the hair. The jugular veins were not dilated. There was a scarred incision on the sternum from the previous cardiac surgery, while also apparent were the post-



**Figure 1.** Posteroanterior chest roentgenogram on admission showing large left pleural effusion and a small right one. Increased interstitial markings at the right lower lobe represent pulmonary lymphangiectasia.

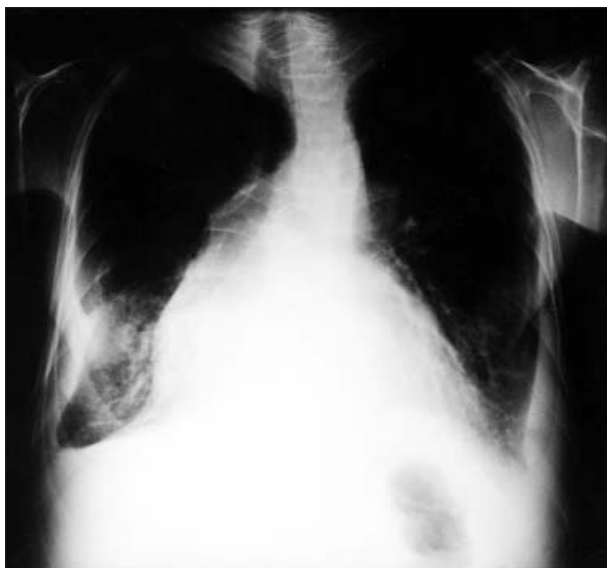


**Figure 2.** Posteroanterior chest roentgenogram after thoracocentesis and catheter drainage.

operative scars bilaterally above the inguinal canals. Giant edemas were observed in the lower limbs, originating from the buttocks without presenting pits upon pressure. Arterial pressure was 105/80 mmHg and breathing rate 28/minute. Lung auscultation revealed dull sounds on the lower 2/3 of the left hemithorax accompanied by absence of the vesicular murmur. Heart auscultation showed arrhythmic tones with normal intensity and timbre with a 2/6 systolic and diastolic murmur at the auscultation site of the pulmonary valve. The electrocardiogram showed atrial fibrillation with 90 heart beats/min. and a morphology of incomplete right bundle branch block. Chest X-rays showed large pleural effusion on the left with displacement of the trachea and the mediastinum to the right, small pleural effusion on the right and increased interstitial markings at the lower lobe of the right lung, compatible with lymphangiectasias (Figure 1). The trans-thoracic echocardiography showed a left ventricle with normal dimensions and wall thickness and hyper-contractility. Thickened mitral and aortic valves were also observed with mild regurgitations. The pulmonary valve was intensely echogenic, without satisfactory imaging. Continuous Doppler examination revealed mild valve stenosis with maximum pressure gradient 28 mmHg while color Doppler scan showed valve regurgitation. We were not able to record tricuspid valve regurgi-

tion. The right ventricle presented mild dilation with paradoxical movement of the inter-ventricular septum of the volume overload type. The inferior vena cava had normal dimensions with complete folding of its walls during non-forced breathing, indicative of low central venous pressure. General blood examination and biochemical markers were within normal limits. Diagnostic paracentesis of the left hemithorax showed the existence of a thick, milky fluid. The examination of the pleural fluid showed the presence of triglycerides at a concentration of 353 mg/dl indicating chylothorax.

Noonan's syndrome diagnosis was set based on the patient's history, clinical and paraclinical findings. The next day the patient was treated with thoracocentesis and drainage tube (Billow #32), removing 3.5 liters of chylous exudate (Figure 2). At the same time, the patient was started on complete hypercaloric, low fat, parenteral feeding. The lymphedema receded immediately while the daily drainage rate, in the next four days, was on average 900 ml chylous fluid per day. From the fifth day onwards, the fluid became less thick and the quantity fell to 300 ml approximately per day, but without further reduction trends. We administered oral prednisone on the 28<sup>th</sup> day of hospitalization at a dose of 1mg/kg of body weight. Three days following the start of prednisone treatment, the drainage tube stopped draining fluid and 2



**Figure 3.** Posteroanterior chest roentgenogram showing resolution of significant effusions 8 months after admission to the hospital.

days later it was removed. The patient left the hospital with a low-fat diet and replacement with a pharmaceutical preparation rich in medium chain triglycerides. The prednizone treatment was progressively cut-off within a three month period. Eight months after the beginning of the treatment and while the patient's diet had returned to its previous form, the patient remained asymptomatic, without recurrence of the lymphedema and a small pleural effusion on the left (Figure 3).

## Discussion

Noonan syndrome is a relatively common hereditary syndrome that affects both genders equally<sup>1</sup> with characteristic facial features and cardiovascular manifestations, with an incidence of 1 out of 1000 births. In half of the cases it is inherited with the predominant autosomal character while the other half cases regard sporadic incidents<sup>1</sup>. Noonan's syndrome patients present a characteristic image with hypertelorism and big, fixed eyes, large forehead, low position of the ears and of the hair, sternum deformity and bilateral cryptorchism in male patients. Cardiovascular disorders are seen in 50% of cases and congenital pulmonary stenosis, valvular or subvalvular, is the most common one<sup>2</sup>. It is suggested that patients with this disease are always examined for this syndrome. The valve folds are thick and dysplastic

even in the absence of significant stenosis. The majority of patients also manifest thickening of the mitral, the aortic and of the tricuspid valve with mild regurgitations. Other cardiovascular disorders include atrial septal defect (1/3 of patients), ventricular septal defect (10%), patent ductus arteriosus (10%) and hypertrophic cardiomyopathy (30) that may affect both ventricles.

Lymph vessel dysplasia is present in less than 20% of Noonan's syndrome patients<sup>2</sup> and in most cases it is manifested with lymphedema of the dorsal surface of the hands and feet, upon birth, that recedes through the years. Rarely, there is severe extended lymphovascular dysplasia<sup>3</sup>, manifested with chylothorax, chyloperitoneum, lymphedema, subalimentation and lymphopenia, particularly of T-helper lymphocytes<sup>4-9</sup>.

The presence of spontaneous chylothorax in Noonan's syndrome patients is rare and has been described in all age groups<sup>10</sup>. In children and in adult patients it may be asymptomatic or be manifested with dyspnea. Searching in literature, we only encountered 16 such cases, including the present one<sup>3, 11-20</sup>. Chylothorax in Noonan's syndrome patients has been treated from time to time with drainage and repeated thoracocentesis, with prolonged drainage, using a Billow drainage tube, or with the creation of pleuroperitoneal shunt<sup>21</sup>, with reduction of the lymph production with a low-fat diet or complete parenteral feeding, with surgical modification of the lymph drainage through pleurodesis, pleurectomy or ligation of the major thoracic duct<sup>22</sup>. From references in literature, 7 patients responded to a low-fat diet and/or parenteral feeding, two patients died despite the treatment with diet and surgical operation, one responded to steroid treatment, while for the rest of the patients there was no mention of the treatment. Only one of the papers we reviewed tackled the subject of failure of combined dietary and surgical treatment<sup>20</sup>. In this case, prednizone was administered for a period of 3 months without recurrence of the effusion within a period of 8 months. We decided to follow the same strategy, leaving aside surgical treatment due to the low success rates, indicated in previous papers.

Glycocorticoids' effect on the lymph flow is not known. What is known is that endogenous glycocorticoids reduce the quantity of proteins in the tissues, increasing the degradation rate of extra-hepatic proteins. Amino acids that are released constitute a substrate for the increase of hepatic protein synthesis<sup>23</sup>. The increase of the plasma's osmotic pressure causes the immediate shift of the fluids from the interstitial

tissue to the blood, reducing the volume of the lymph. This may help reduce the lymph flow for a time period sufficient to restore normal lymph drainage.

As a conclusion, the present case is of special interest for the following reasons: 1) the presence of spontaneous chylothorax is a rare manifestation of the syndrome and 2) it is the first described case of successful treatment of chylothorax with a combination of prolonged drainage, low-fat diet and prednisone administration without any attempt at surgical treatment. Cardiologists may be the first doctors to encounter a Noonan's syndrome patient, due to the frequent co-existence of congenital heart diseases. High suspicion combined with the characteristic clinical and paraclinical findings suffice to set the diagnosis and to lead to a successful treatment of the possible complications of the syndrome.

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