Successful Ocreotide and Medium-Chain Triglyceride Therapy for Cylothorax in a Patient with Noonan Syndrome: Case Report

Noonan Sendromlu Bir Olguda Oktreotid ve Orta Zincirli Yağ Asitleri Kullanılarak Şilotoraksın Başarılı Tedavisi

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ABSTRACT Noonan syndrome (NS), is an autosomal dominant disorder commonly seen in childhood and is characterized by short stature, congenital heart defects and facial abnormalities (especially in adults) along with thoracic deformity. Lymphatic dysplasia can be seen with this syndrome causing chylothorax by development of fistulas between thoracic duct and pleural space or it can directly occur by malformation of thoracic lymphatic vessels. Hence, chylothorax can also be seen. Herein, we present a case with this syndrome and chylothorax secondary to possible lymphatic dysplasia. We achieved a great success with ocreotide and medium chain trigliserides in the management of chylothorax and hence suggest this therapy to other clinicians.

Key Words: Noonan syndrome; chylothorax

ÖZET Noonan sedromu (NS), otozomal dominant geçişli, çocukluk çağında görülen, kısa boy, konjenital kalp hastalığı, yüz anomalisi (özellikle erişkinde) ve toraks deformitesiyle seyreden bir hastalıktır. Lenfatik bozukluk Noonan olgularının %20'den azında görülür. Böylelikle şilotoraks da gözlenebilir. Burada lenfatik displazi sonucu şilotoraks gelişen bir Noonan olgusunu sunuyoruz. Bu olguda octreotid ve orta zincirli yağ asitleriyle şilotoraks tedavisinde büyük başarı sağlanmıştır. Bu nedenle diğer klinisyenlere de bu tedavi yaklaşımını önermekteyiz.

Anahtar Kelimeler: Noonan sendromu; şilotoraks

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CASE REPORT

A 57-year-old man* presented with large pleural effusion on the right side. He was suffering from chest pain and increasing dyspnea for the previous month. He was 150 cm tall and had a mild mental retardation. Facial features included hypertelorism, down-slanting palpebral fissures, bilateral ptosis and strabismus, and low-set and posteriorly rotated ears. A short neck, kyphoscoliosis and widely spaced nipples were evident as well as an anterior chest deformity with pectus carinatum superiorly and pectus excavatum inferiorly (Figure 1). Breath sounds were seriously diminished on the right hemi-thorax and grade 5/6 pansystolic murmur was heard on the mitral focus.

* Informed consent was obtained from the patient for publishing his data in the scientific journal as a case report.

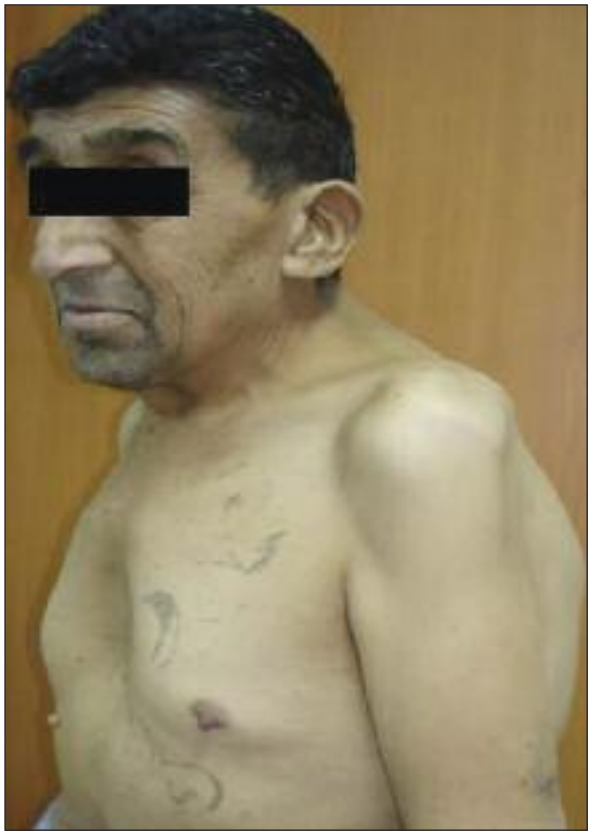
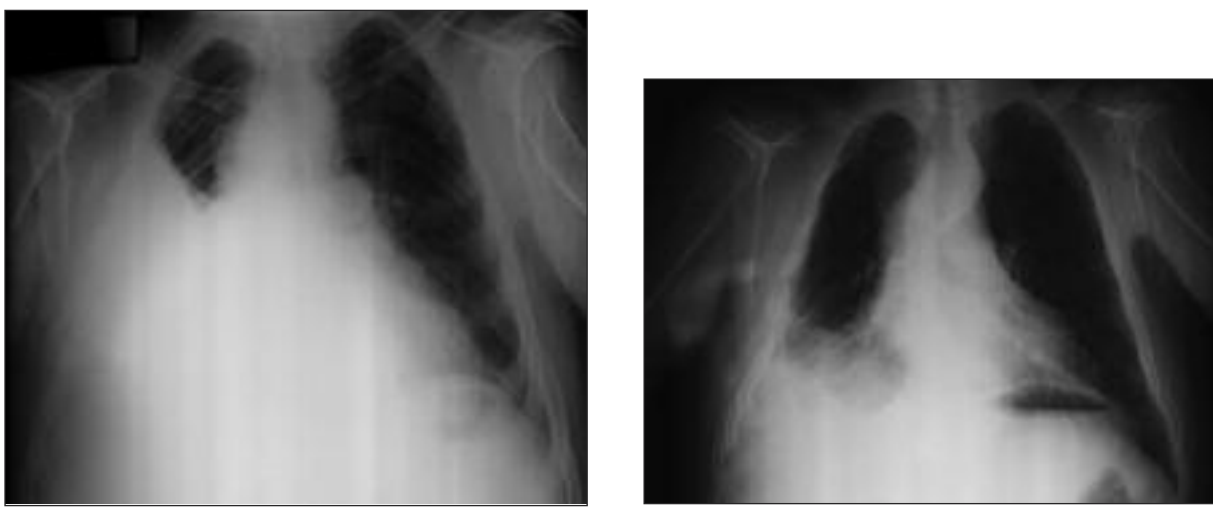


FIGURE 1: Typical appearance of face and thorax.

Chest X-ray (Figure 2a) revealed massive right-sided pleural effusion that proved to be chylothorax on biochemical analysis; total cholesterol level was 53 mg/dL, triglyceride 514 mg/dL, glucose 96 mg/dL, protein 4,1 mg/dL, and lactate dehydrogenase 145 IU/L without any bacterial overgrowth. Chylous fluid (1000 mL) was drained by a pleural catheter daily for 21 days, until the treatment was started was. Other routine biochemical investigations, lymphoscintigraphy and positron emission tomography were unremarkable. Echocardiography revealed mitral valve prolapsus and minimal incompetence of mitral, aortic and tricuspid valves inconsistent with cardiac oscultation sounds; we could not hear the sounds of those abnormalities most probably due to thoracic deformity or large pleural collection. Pulmonary gradient was 30 mmHg without any evidence of pericardial effusion. At the time of diagnosis computerized tomography of thorax and abdomen revealed that arcus aorta was right-sided in the upper mediastinum and the aorta was tortious in the abdomen. The left subclavian artery had a paraesophageal localization (Figure 3). The patient he was transported to surgical department for video assistant thoracoscopic surgery. Pulmonary embolism was diagnosed while the patient was being monitored preoperatively in thoracoscopic surgery department. The operation was postponed because of the pulmonary embolism and the patient was transferred back to our clinic for anticoagulant treatment. He was stable with this medication when we maintained an effective INR level without any change of cardiac sounds orchest x-ray findings.

Diagnosis of Noonan Syndrome (NS) was estab-



A B

FIGURE 2: A. Chest X-ray before therapy showing massive chylothorax. **B.** Chest X-ray after therapy with significant resolution of pleural fluid

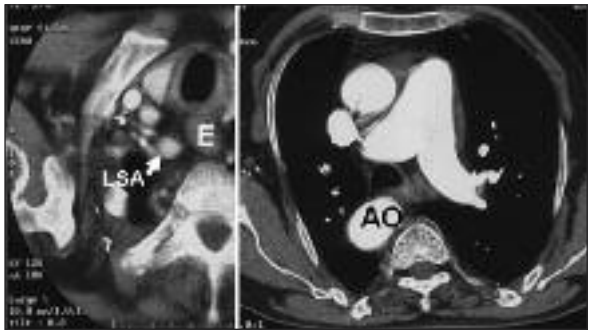


FIGURE 3: At the time of diagnosis, thorax CT showing paraesophageal location of left subclavian artery, right sided arcus aorta in upper mediastinum and tortuous abdominal aorta.

lished on the basis of chylothorax and specific morphological features. Octreotide was started on day 22, initially with 3.5 μg/kg per hour and increased daily by 1 μg/kg per hour to 6.5 μg/kg per hour. Then it was switched to subcuteneous ocreotide (100 μg every 8 hours) with an obvious clinical improvement. Additionally, an oral diet containing medium-chain triglycerides (MCT) was begun. The chylous fluid drainage was abruptly decreased to 100 mL/day on the first month after initiation of octreotide therapy and then chylothorax resolved immediately (Figure 2b). He was discharged in a good condition on the 40th day of admission. Six months later he was doing well without any complaints or effusion.

DISCUSSION

NS, is an autosomal dominant disorder commonly seen in childhood and is characterized by short stature, congenital heart defects and facial abnormalities (especially in adults) along with thoracic deformity.[1] Facial features of NS include short and webbed neck, widely spaced nipples, mild mental retardation, bleeding diathesis and lymphatic dysplasia which more commonly is observed in neonates and infants as dorsal limb lymphedema.[2] Missense mutations of PTPN11 gene on chromosome 12 are found in approximately 50% of the patients.[3] The present patient was not tested for mutations in PTPN11 gene, but the clinical scoring system suggested by van der Burgt et al in 1994 supported the diagnosis (Table 1).[4] His face was suggestive of the disease due to hypertelorism, down-slanting palpebral fissures, bilateral ptosis, strabismus and, low-set and posteriorly rotated ears. He had a short stature below 3rd centile, a characteristic chest deformity, lymphatic dysplasia and mild mental retardation. Additional features including short neck, widely spaced nipples and cardiovascular abnormality were supportive for the diagnosis.[5,6]

The mechanism causing chylothorax is lymphatic obstruction as a result of pulmonary lymphatic dysplasia, and it can account for development of fistulas between the thoracic duct and the pleural space. Malformation of thoracic lymphatic vessels causing chylothorax seems to be more frequent than anticipated. Lymphatic abnormalities occur in less than 20% of NS patients;[7] however, how mutations of PTPN11 cause lymphatic dysplasia in these patients is yet unknown.[2]

To date there is no accepted treatment protocol for cylothorax. Conservative approach commencing low-fat/high-protein diet supplemented with MCT, and total parenteral nutrition are the

TABLE 1: Noonan Syndrome Clinical Scoring System* (van der Burgt et al., 1994)

Number	Features	Group A	Group B
1	Facial	Typical face	Suggestive face
2	Cardiac	Pulmonary valvular stenosis and/or typical ECG	Other defect
3	Height	Below 3rd percentile	Below 10th percentile
4	Chest wall	Pectus carinatum/excavatum	Broad thorax
5	Family history	First degree relative with definite Noonan syndrome	First degree relative with suggestive Noonan syndrome
6	Other	All three (for males): mental retardation, cryptorchidism, lymphatic dysplasia	One of mental retardation, cryptorchidism, lymphatic dysplasia

*: Definite diagnosis requires 1A, one of 2A-6A or two of 2B-6B. It has also been mentioned that 1B plus two of 2A-6A or three of 2B-6B can confirm the diagnosis. Our patient has the features of 3A, 4A, 1B, 2B and two of 6B competible with the diagnosis (shown in bold).

best choices along with pleural drainage. MCT are directly absorbed into the circulation allowing a reduction of lymphatic flow and healing of the damaged lymphatic vessels. Suggested medical therapy also includes a long-acting somatostatin analog, ocreotide. It acts directly on vascular somatostatin receptors and minimizes lymph fluid excretion by its vasoconstrictor effect.[8] Moreover, by increasing splanchnic arteriolar resistance and decreasing gastrointestinal blood flow, octreotide indirectly reduces lymphatic flow.[9] Side effects such as cutaneous flush, nausea, loose stools, transient hypothyroidism, elevated liver function tests, strangulation-ileus, transient abdominal distension, temporary hyperglycaemia and necrotising enterocolitis were reported. Potential adverse effects are fluid retention, hyponatremia, gastralgia, headache, nausea, vomiting, tympanites, and epistaxis.[10] Surgical interventions, such as pleuroperitoneal shunting, pleurodesis, or direct ligation of the thoracic duct can be also be performed.[8]

We did not observe any therapy-related complications, The patient recovered quickly after the treatment beginned. Our findings suggest that, parenteral octreotide and oral MCT are effective, rather noninvasive, and safe agents. So they might be considered for treatment of chylothorax secondary to NS, and surgery might be reserved as a last option. It worths stressing that lymphatic dysplasia is among main clinical features of NS and this syndrome should be kept in mind in patients with suggestive features.

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