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CASE REPORT

# A Rare Cause of Chylothorax: Hennekam Syndrome

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Abstract

Hennekam syndrome was defined as a syndrome characterized by a new autosomal recessive, severe lymphedema in legs, face and genitalia with intestinal lymphangiectasia, various face anomalies and severe mental retardation. A 21 years old male patient was examined due to bilateral pleural effusion. There were edema in both legs and eyelids, swelling in the scrotum and operation scar, broad forehead and face, depressed nasal bridge, epicanthal folds and micrognathia in the physical examination. Chylothorax was diagnosed due to level of pleural triglyceride (650 mg/dL). Lymphatic flow delayed in both lower extremities in lymphoscintigraphy. The patient was diagnosed as Hennekam syndrome due to face anomalies, lymphedema, epilepsy, chylothorax and mild mental retardation.

**KEY WORDS:** Hennekam syndrome, lymphedema, pleural effusion, chylothorax

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## INTRODUCTION

Hennekam syndrome (HS) has been firstly described by Hennekam et al. in 1989. HS is transmitted as an autosomal recessive trait and characterized by severe lymphedema in legs, face and genitals as well as intestinal lymphangiectasia, several facial abnormalities and severe mental retardation. Most important findings of HS are the occurrence of lymphangiectasia and the accumulation of the lymphatic fluid in the body cavities by leaking out of the vessel as a result of a developmental defect in the lymphatic vessels. While the lymphangiectasia is most commonly seen in intestines, extremities and genital area, pleura, pericardium, thyroid gland and kidneys may also be rarely affected [1-3]. Given that it is a rarely seen syndrome and due the presence of rare pulmonary involvement, the case was presented after having his consent.

## CASE PRESENTATION

The patient who has been operated for hydrocele one week ago, was admitted to hospital with complaints of cough, fever and epileptic seizure. He was treated with antibiotic and anti-epileptic therapy due to pulmonary infection and epileptic seizure. Patient, who had relieved complaints after the antibiotherapy, admitted to our center with the complaints of increased cough, production of white sputum and exertional dyspnea that have lasted for the last 2 days. Medical history showed that the patient had congenital epilepsy and lymphedema that has been lasting for the last 12 years and he was operated for hydrocele 1 week before.

The patient's general status was good and he was conscious, oriented and cooperative. In his physical examination, there were edema in both legs and in the eyelids, swelling and operation scar in his scrotum, large front and face, broad nasal root, epicanthic folds and micrognathism (Figure 1). His posteroanterior (PA) lung radiography showed an opaque appearance consistent with pleural fluid that covered bilateral costodiaphragmatic sinuses, being marked in the right side (Figure 2). In the fluid obtained by thoracentesis performed for the etiology of pleural effusion, total protein was 3 gr/dL (5.9 gr/dL in the serum), albumin was 1.6 gr/dL (3.2 gr/dL in the serum), glucose was 107 mg/dL (89 mg/dL in the serum), lactate dehydrogenase (LDH) was 248 U/L (325 U/L in the serum), triglycerides were 650 mg/dL, cholesterol was 62 mg/dL and white blood cell (WBC) was 700 pg (lymphocyte rate, 72.5%). Patient was thought to have chylothorax due to triglyceride level of 650 mg/dL in the pleural fluid. In thoracic computerized tomography (CT), paratracheal, precarinal and subcarinal lymph nodes, the largest having a dimension of 7 mm, pleural effusion and atelectasis areas adjacent to pleural effusion were observed. In the abdominal CT, hepatomegaly was observed. Acid-resistant bacillus (ARB), Tbc polymerase chainreaction (PCR) and Tbc culture were done using pleural fuid to exclude tuberculosis (Tbc) resulted

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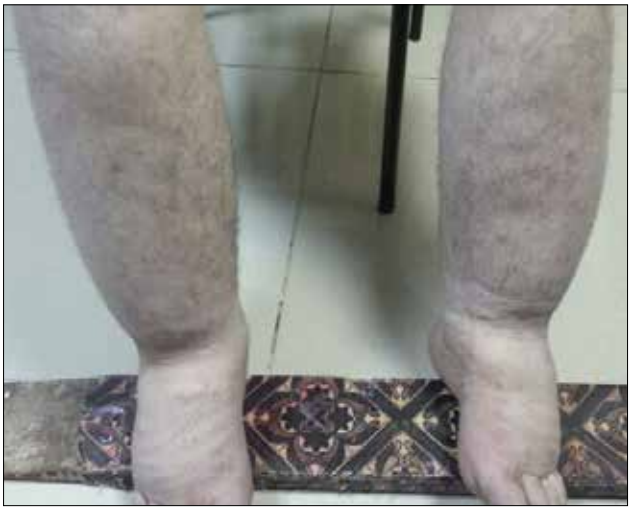

**Figure 1.** Presentation of swelling and edema in both lower extremities of the patient

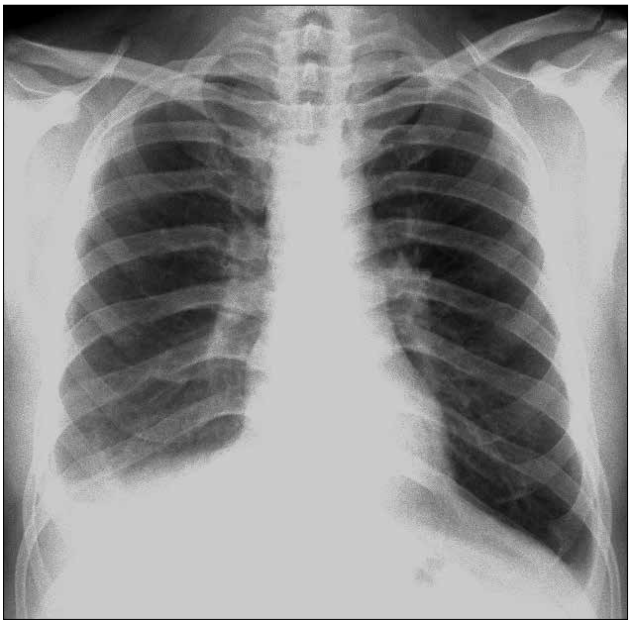

**Figure 2.** Chest X-ray consistent with bilateral pleural effusion markedly seen on the right side

negative and adenosine deaminase (ADA) level was found to be 25.50 U/L. CD3 and CD20 investigated in the pleural fluid upon the suspicion of lymphoma were 55% and 20%, respectively and this result was considered as normal. Intelligence test performed in collaboration with the psychologist, IQ score was found as 70-80, which was interpreted as "borderline deficiency". Lymhoscintigraphy of the patient with swelling in both legs revealed the activity in the lymph nodes located in the inguinofemoral area with very low intensity in the images obtained at 1st hour. In the late spot images obtained at 3rd hour, it was found that the lymph nodes located in the inguinofemoral area were well-enhanced and there was a delay in the lymphatic flow in both lower extremities.

Upon the detection of chylothorax, the patient was given an oral diet poor in lipid and rich in protein. During the follow-up, due to the lack of a decrease of pleural fluid, oral therapy was discontinued and intravenous somatostatine infusion with a dose of 400 mcg/h was initiated. The patient was diagnosed with HS due to the presence of facial abnormalities, lymphedema, epilepsy, pleural effusion (chylothorax) and mild mental retardation. Subsequently, the case was presented along with the literature after obtaining the consent of the patient.

**DISCUSSION**

HS has been described by Hennekam et al. in 1989 as a syndrome with autosomal recessive inheritance trait characterized by intestinal lymphangiectasia and severe mental retardation as well as severe lymphedema in legs, face and genitals. During this syndrome, due to lymphatic developmental defect, lymphangiectasia occurs and lymph fluid leaks out of the vessel and deposits in the body cavities. Edema is seen mainly in the extremities and genitals and rarely in pleura and pericardium [1-3].

In our case, HS was predominantly considered due to the presence of the signs such as bilateral epicanthus, hypertelorism, broad nasal root, large nasal bridge, small mouth, lymphedema in legs, hydrocele and pleural effusion. In some cases, facial appearance may not be typical and these cases that are especially heterozygous are considered as HS variant [3].

In the cases accompanied by intestinal lymphangiectasia, hypoproteinemia, hypogammaglobulinemia and lymphocytopenia may be seen. As HS is a developmental disorder of the lymphatic system, dilatation and malformation of the lymphatic ducts are observed. Thereby, in the affected area of the body, lymphatic drainage is impaired and lymphatic fluid is accumulated in the related ducts [3]. Amount of chylous fluid resulting from the extremities is normally ignored.

In the HS, lymphedema is generally congenital and, occasionally, it is markedly unilateral and generally progressive. Although lymphangiectasia is most commonly seen in the face, extremities, genitals and intestines, it may also be seen in the pleura, pericardium, thyroid gland and kidneys [4]. Facial anomalies include midfacial hypoplasia, broad nasal root, hypertelorism, epicanthus, long filtrum, gingival hypertrophy, small mouth and low ears. Facial signs are suggested to result from lymphatic occlusion that affects the early migration of the neural crest tissue [4].

In the cases with recurrent gastroenteritis and respiratory tract infection, hypogammaglobulinemia is commonly seen [4]. Other findings that may be observed in HS include mild growth and developmental retardation, sensorineural or conductive hearing loss, glaucoma, atrial or ventricular septal defect, oligodontia, cryptorchidism, hydronephrosis, horseshoe kidney, vesicoureteral reflux, delayed bone age, coronal craniosynostosis, scoliosis, small hands and feet, erysipelas, hirsutism, focal parietal pachygyria, convulsions, hyperactivity and, as laboratory findings, hypoglobulinemia and hypoalbuminemia. Presence of pachygyria may explain the mental retardation and seizures observed in the cases [5]. Cellulitis and erysipelas may be seen as the complications of lymphedema. Given the eventual additional findings, our case did not show clinical and laboratory findings. As our knowledge, in the literature, chylothorax was reported in one

infant with HS to date [6]. Pleural involvement is very rare and in our country, a 38-month-old infant was diagnosed with HS due to pericardial effusion [7].

Differential diagnosis includes congenital lymphedema syndromes of, Turner's syndrome, Noonan syndrome and Milroy disease. Furthermore, lymphedema may be accompanied by intestinal lymphangiectasia, cerebrovascular anomalies, ptosis, yellow nail dystrophia, distichiasis and cholestasis. Lymphedema may also result from acquired scars (fibrosis, philariasis and inflammation resulting from trauma, surgery, tumor and radiation) [7].

Chylothorax is managed by decreasing the intake of dietary fat and by increasing the protein ratio in the diet. In case of persisting chylous fluid, somatostatin or octreotide is given. In addition to dietary modifications and medical therapy, the methods such as drainage and surgery (such as ductus thoracicus ligation, flap closure and fibrin adhesion) may be used [8]. In one case, despite the use of these methods, chylous fluid persisted and, therefore, an alpha-1 adrenergic agonist, midodrine, was used. It was seen that midodrine decreased the lymphatic fluid flow by leading to vasoconstriction in the lymphatic system [8].

In our case, chylothorax was thought to be congenital. Patient was initially given a diet poor in lipid and rich in protein and, upon the lack of any regression of chylous fluid, oral intake was discontinued and somatostatin infusion was initiated. Upon the observation of regression of fluid in the follow-up, the patient was discharged.

Our case with borderline retardation and without fluid accumulation to an extent to require a re-intervention after the pleural drainage was presented to highlight that congenital lymphedema and recurrent pleural effusions should be included in the differential diagnosis of HS.

**Informed Consent:** Written informed consent was obtained from patient who participated in this case.

**Peer-review:** Externally peer-reviewed.

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**Conflict of Interest:** No conflict of interest was declared by the authors.

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