RESEARCH PAPER

Unusual Presentation of Nephrotic Syndrome: Transudative Chylothorax in Membranous Nephropathy

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ABSTRACT

Background: Chylothorax occurs when the pleural cavity is filled with lymphatic fluid, and the main causes are trauma, cancer, or disruption of the lymphatics. The event of transudative chylothorax is super rare, and only a few cases have been recorded related to nephrotic syndrome or membranous nephropathy.

Case Presentation: A 73-year-old man was suffering from a gradual rise in experiencing difficulty to breathe, wheezing, coughing up mucus, lack of breath control, and pain in the left chest area for the past 15 days, along with a month of generalized swelling. The physician examined him and discovered that the patient had a significant amount of fluid disorder in his lower limbs and abdominal wall which was of the type that leaves an impression when pushed (pitting edema). A chest X-ray revealed an accumulation of fluid beneath the right lung (sub-pulmonic pleural effusion). The fluid was diagnosed via therapeutic thoracentesis to be white, like milk. The analyzed fluid was characterized as an ordinary effusion with elevated triglycerides levels (>110 mg/dL) and chylomicrons confirming the presence of chyle in the thorax (chylothorax). The laboratory evaluation reported low protein levels in the body (serum protein 5.56 g/dL), high protein content in urine (3+ albumin), and raised thyroid-stimulating hormone level (13.216 μU/mL). A contrast CT with enhancement demonstrated a thrombus in the left interlobar artery which had gone out into the sub-segmental branches. A PET scan was done ruling out the possibility of a malignant tumor being the cause of the condition. The immunological testing results indicated that the patient had generated auto-antibodies against the phospholipase A2 receptor (anti-PLA2R) and previously kidney pathology was diagnosed as membranous nephropathy by renal biopsy. The man was treated with corticosteroids and immunosuppressive therapy. After initiation of the treatment, the majority of the pleural effusion and swelling all over the body had disappeared.

Conclusion: The case presented highlights that, although unusual, transudative chylothorax might still be seen in patients who have nephrotic syndrome as a result of membranous nephropathy. It is very important for the physicians to be aware of this uncommonly connected, and to carry out a very careful clinical evaluation, then order the necessary biochemical analyses, and finally do the appropriate imaging for accurate diagnosis and prompt management.

Keywords: Chylothorax; Hypoproteinaemia; Nephrotic syndrome; Membranous nephropathy; Transudate; Thromboembolism

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INTRODUCTION

Chylothorax refers to the presence of chyle, a white, oily lymphatic fluid that is rich in fats, in the pleural cavity abnormally due to the rupture, obstruction, or penetrating of the thoracic duct or its branches [1]. The milky appearance of chyle is one of its main attributes, and it also consists of very high levels of triglycerides, lymphocytes, and chylomicrons, which are all indicators of the fluid being derived from the intestines' lymphatic system. Chylothorax is primarily characterized as an exudative pleural effusion by the application of Light's criteria and is most often caused by a traumatic incident or cancer, for example, lymphoma or surgery in the mediastinum [2]. Non-traumatic reasons that might be overlooked include the presence of congenital anomalies in the lymphatic system, infectious agents, or inflammation, which can also

result in the occurrence of chylothorax.

Chylothorax of transudative type, in contrast with the usual exudative type, is very uncommon, and it is hard to come up with the right diagnosis. This kind of chylothorax is rare and therefore, characterized by low concentrations of proteins and lactate dehydrogenase, but at the same time, pleural fluid contains chylomicrons and high triglycerides [3]. Transudative chylothorax is believed to occur via systemic changes in hydrostatic and oncotic pressures rather than through direct lymphatic injury, which eventually results in the passive spilling of chyle into the pleural cavity. Cirrhosis, congestive heart failure and nephrotic syndrome have intermittently been cited in the literature as conditions associated with reported cases [4]. The extreme rarity of transudative chylothorax frequently leads to it being overlooked or misclassified and consequently, the diagnosis and treatment are delayed. Nephrotic syndrome is a medical term that denotes a condition with a bundle of signs comprising loss of protein in urine, lower albumin level in blood, raised levels of lipids, and generalized edema. In adults, membranous nephropathy (MN) is still one of the principal causes of primary nephrotic syndrome, therefore it contributes to a significant number of cases globally [5]. In fact, MN (minimal change nephropathy) is the one that usually leads to the immune system-mediated destruction of the glomerular basement membrane and more often than not, is associated with the detection of circulating antibodies to the phospholipase A2 receptor (anti-PLA2R). The severe hypoproteinemia (profound hypoalbuminaemia) that is invariably associated with MN results in a major drop of the plasma's oncotic pressure thus allowing the fluid to flow into the body's compartments that are less perfused than interstitial and serosal spaces and the pleural cavity .Besides the problem of fluid imbalance, MN is considered as a disease with a hypercoagulable state at the same time. Because of the many overlapping reasons, nephrotic syndrome patients are at a greater risk of venous thromboembolism, one of the main reasons being the loss of some anticoagulant proteins through urine, the liver's increased production of procoagulant factors, the increased activity of platelets, and the impaired functioning of the endothelium [6]. One of the complications from blood clot formation is renal vein thrombosis and pulmonary embolism which contributes a lot to the morbidity and mortality of these patients. A thrombus in the veins can aggravate the lymphatic congestion problem and result in the pleural space being invaded by chyle.

The incidence of transudative chylothorax in patients suffering from membranous nephropathy is exceptionally uncommon and more or less very few instances have been recorded in the writings. The precise cause of this relationship remains vague, yet it is likely that several factors are involved such as very low albumin levels, increased venous and lymphatic pressures, and impaired fat metabolism. Clinically this rare scenario is a challenge since chylothorax is often considered exudative and trauma or cancer related which may lead to extensive and sometimes unnecessary investigations. The limited number of reported cases indicates that clinicians need to be more vigilant and to perform careful pleural fluid analysis in order to arrive at the correct diagnosis. The detection of transudative chylothorax in nephrotic syndrome case facilitates the application of specific management directed at renal pathology treatment instead of invasive procedures on the pleura. This case report showcases a case of rare transudative chylothorax associated with membranous nephropathy aggravated by venous thromboembolism, thus, stressing the need for thorough clinical evaluation and the recognition of uncommon pleural fluid expressions in nephrotic syndrome.

CASE PRESENTATION

A 73-year-old man who previously had no serious diseases went to the hospital because he had been suffering for 15 days from breathlessness that got worse lying down, coughing with sputum, and pain in the left part of the chest. Moreover, he had been having a problem of swollen body for a month. At first, he seemed to be having trouble breathing and was swollen all over the body, but his vital signs were stable. The examination of the body showed the swelling that left marks when pressed and that it affected the legs and the belly, which made the doctor think of a disease that affects the whole body. A radiograph of the chest showed a right sub-pulmonic pleural effusion. The liquid was milky white just drained through the needle puncture, which made the doctor suspect chylous effusion. The analysis of the pleural fluid proved triglycerides >110 mg/dL and positive chylomicrons, making the diagnosis of chylothorax. Light's criteria unexpectedly exhibited a transudative profile, which is a rare occurrence in case of chylothorax.

The initial biochemical analysis revealed hypoproteinaemia in the patient, which was due to nephrotic-range protein loss, and proteinuria. Thyroid hormone tests showed an extremely high level of TSH, which indicated an underlying case of hypothyroidism. The chest imaging with contrast-enhanced CT revealed a thrombus in the left interlobar pulmonary artery that extended to the sub-segmental branches, thus confirming the diagnosis of venous thromboembolism. A PET/CT scan ruled out any underlying cancer as a cause of chylothorax. Based on all the findings, the patient underwent autoimmune and renal work-up. Serum anti-PLA2R antibodies were found to be so high that they could only be interpreted as suggestive of the disease process and the patient's renal biopsy confirmed the diagnosis of membranous nephropathy, thereby establishing nephrotic syndrome as the cause of both the transudative effusion and the hypercoagulable state. Consequently, the patient was placed on corticosteroid therapy and immunosuppressants following the standard protocols for membranous nephropathy. The administration of anticoagulants was started for the thrombus in the pulmonary artery. In addition, diuretics, optimization of thyroid function, and regular monitoring of renal parameters were among the supportive measures taken. During the subsequent follow-up periods, the patient

showed gradual resolution of the pleural effusion and improved in terms of generalized edema, which was parallel to the stabilization of proteinuria and the improvement of oncotic balance.

Table 1: Baseline Laboratory Investigations

Parameter	Value	Reference Range
Serum Protein (g/dL)	5.56	6.0 – 8.0
TSH (µU/mL)	13.216	0.34 – 5.6

Table 2: Pleural Fluid Analysis

Parameter	Value	Interpretation
Appearance	Milky White	Chylous
Triglycerides (mg/dL)	>110	Chylous effusion
Protein Ratio (Pleural/Serum)	<0.5	Transudative

Test Report Status **Final**	Results	Biological Reference Interval	Units
EIA - AUTO IMMUNE			
ANTI-PHOSPHOLIPASE A2 RECEPTOR (PLA2R) IGG,SERUM			
ANTI-PHOSPHOLIPASE A2 RECEPTOR (PLA2R) IGG	**921.06 High**	< 14.00 NEGATIVE 14.00 – 20.00 BORDERLINE > or =20.00 POSITIVE	RU/ml
METHOD : ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA)			

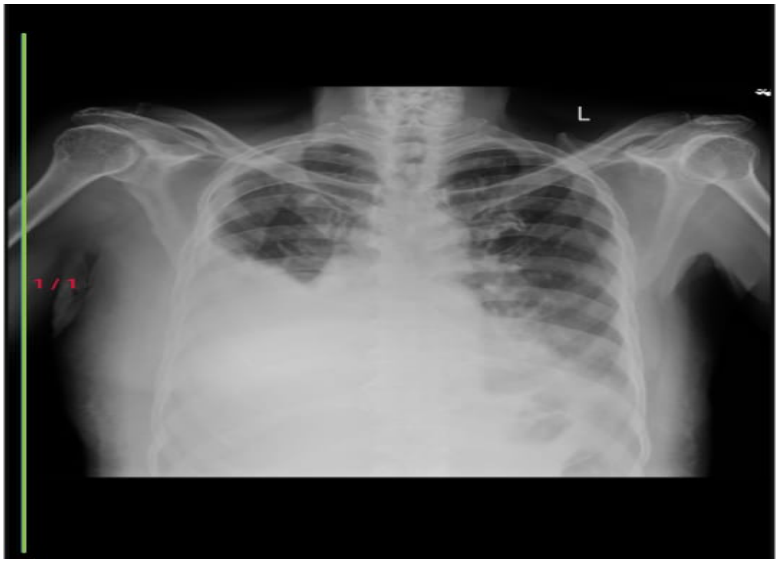

Figure 1: Chest X-ray showing right sub-pulmonic pleural effusion.

Figure 2: Photograph of milky pleural fluid

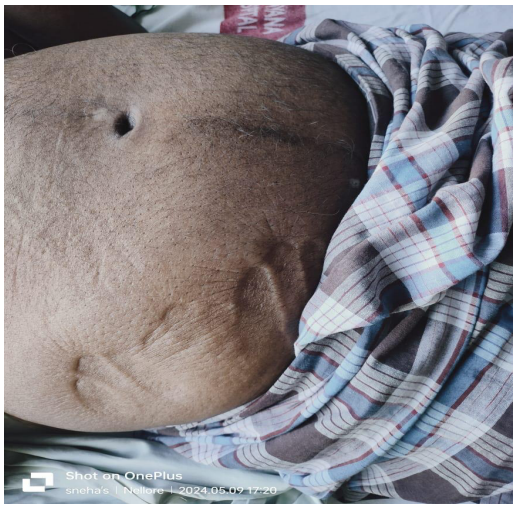

Figure 3: Pitting edema of abdominal wall

DISCUSSION

Chylothorax has been traditionally portrayed as an exudative pleural effusion that develops either due to the tearing or blocking of the thoracic duct; the major reasons being malignancy, trauma, or surgeries. A pivotal study by McGrath et al. noted that more than 75% of the cases of chylothorax revealed exudative features as per Light's criteria, with lymphoma being the most frequent cause of non-traumatic cases [8]. However, the current case was different as it presented a biochemically confirmed chylothorax of a transudative nature; such a finding is quite rare and difficult to diagnose.

Transudative chylothorax has been reported now and then in connection with systemic disorders that impact the balance of hydrostatic or oncotic pressures but not through the injury of lymphatic vessels. Hillerdal has mentioned the likelihood of transudative chylous pleural effusions, particularly in patients with cirrhosis, heart failure, and nephrotic syndrome [9]. The supposed mechanism of action adds more lymphatic flow and at the same time lowers plasma oncotic pressure, thus resulting in the chyle being passively leaked through the intact lymphatic walls. Transudative chylothorax is still a rare complication of nephrotic syndrome, although it has been noted. The calmed side of Valdés et al. when serum albumin level is very low, the oncotic pressure of the plasma is greatly reduced and this acts as a facilitator for chylous fluid to migrate from the pleura into the peritoneal cavity where the fluid still retains the characteristics of a transudate [10]. In our case, the hypoproteinaemia was very pronounced it was indeed nephrotic-range proteinuria and so these were the reasons for the peculiar characteristics of the pleural fluid. Membranous nephropathy (MN) is regarded as the number one cause of nephrotic syndrome in older patients and it is now recognized as an autoimmune disease which is usually caused by the production of anti-phospholipase A2 receptor (anti-PLA2R) antibodies. The study of Beck et al. was pivotal in showing the involvement of anti-PLA2R antibodies in primary MN, which has now become one of the mainstays of diagnosis and treatment monitoring [11]. In the patient of ours, the raised levels of anti-PLA2R antibodies and the confirming renal biopsy together with

the linkage of MN to the patient were very strong.

One more crucial aspect in this case was the occurrence of venous thromboembolism. The hypercoagulable condition resulting from nephrotic syndrome has been well-explained in the literature. Lionaki et al., in their large cohort study of patients with MN, found a notable increase in the incidence of thromboembolic events, particularly pulmonary embolism, in patients with severe hypoalbuminaemia (<2.8 g/dL) [12]. The pulmonary artery thrombus detected in our patient corroborates these findings and most probably led to heightened venous and lymphatic pressures, thus creating a more favorable environment for chylous leakage.

The concurrence of transudative chylothorax and pulmonary embolism in MN is very rare but possible from the point of view of pathogenesis. Doerr et al. suggested that venous thrombosis could block lymphatic drainage by raising venous pressure at lymphovenous junctions, thus causing chyle to leak without any ductal damage [13]. This theory might account for the chylothorax in our patient despite the fact that the imaging revealed neither malignancy nor thoracic duct injury. The medical handling of transudative chylothorax is entirely different from that of exudative chylothorax. It is common for surgical or interventional methods to be required in the case of trauma or tumor, while nephrotic syndrome treatment should be focused on the correction of the underlying renal pathology. In the past described cases, including those by Bhatnagar et al., chylothorax was resolved after immunosuppressive therapy and higher serum albumin levels, without pleural intervention [14]. In the same way, our patient experienced the gradual reduction of pleural effusion after the therapy of corticosteroids and immunosuppressive drugs, in addition to anticoagulation and supportive care.

This instance shows the need of not ruling out chylothorax just because of the biochemical nature of transudate pleural fluid. Light's point is that pleural fluid appearance and triglyceride analysis are still the main diagnostic methods particularly in strange clinical situations. The lack of recognition of transudative chylothorax can result in misdiagnosis, delayed treatment and conducting tests that are not needed. To summarize, this case presents a rare but clinically significant connection between membranous nephropathy, venous thromboembolism, and transudative chylothorax. The combination of recognizing this unusual presentation, performing a detailed analysis of the pleural fluid, and conducting a proper renal evaluation will result in rapid diagnosis and effective treatment.

CONCLUSION

Transudative chylothorax is a very rare complication of membranous nephrotic and nephropathy syndrome but it still has significant clinical implications. This case shows that a very suspicious attitude towards chylothorax is necessary to distinguish it from nephrotic patients with pleural effusion presentation, even if the biochemical profile corresponds to transudative criteria. Factors like low albumin levels, changed lymphatic flow, or thromboembolic complications might be responsible for this rare presentation. It is important to quickly identify and properly assess the condition in order to obtain the correct diagnosis and direct management. This is particularly true for patients with underlying glomerular disease who are already difficult to treat. Furthermore, this case points to a more significant problem, that is, the need to increase awareness and carry on research into the rare pleural fluid abnormalities in nephrotic syndrome which could ultimately lead to the improvement of diagnostic accuracy and the optimization of therapeutic outcomes.

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All authors have reviewed the final version of the manuscript, approved it for submission, and agreed to be accountable for all aspects of the work.

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No writing assistance was utilized in the production of this manuscript.

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