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Case Report Open Access

Chylothorax in a Patient with Pulmonary Aspergillosis and Chronic Renal Disease in Hemodialysis

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Abstract

Chylothorax is the accumulation of lymphatic fluid (chyle) in the pleural space, as a result of obstruction, injury or leakage of the thoracic duct or one of its tributaries. The frequency of causes of chylothorax depends on the type of hospital and the population served but there are few reports of this complication in people with end- stage renal disease and the outcomes with different interventions. We report the case of a 35-years-old man from a low-altitude agricultural community in northwest Nicaragua, diagnosed with end-stage chronic kidney disease (CKD) of non-traditional etiology three months before admission who developed chylothorax after dysfunction of central venous catheter (CVC) at the right internal jugular vein for hemodialysis. After multidisciplinary approach, we found no cause of the chylothorax other than pulmonary Aspergillosis with mediastinal adenopathy and possible external pressure to the thoracic duct as a mechanism similar described in pulmonary tuberculosis, sarcoidosis and histoplasmosis. Chylothorax resolved with the treatment for aspergillosis and performance of lymphangiography with lipiodol after conservative treatment for chylothorax failed and before we continued to embolization of the thoracic duct, which allowed us to performance pleurodesis with iodine without complications. We reviewed the etiologies of chylothorax in patients with end-stage renal disease in hemodialysis reported so far and found no reports of aspergillosis as a cause of chylothorax.

Keywords: Chylothorax; Chylous effusion; Cholesterol effusion; End stage renal disease; Hemodialysis; Adults; CVC complication; Pulmonary aspergillosis; Lymphangiography

Introduction

Chylothorax is a life-threatening clinical entity and is defined as the accumulation of lymphatic fluid (chyle) in the pleural space due to obstruction, injury or leakage of the thoracic duct or one of its tributaries [1].

Chyle is a milk, white opalescent, odorless liquid that forms when the long chain triglycerides in the diet are transformed into chylomicrons and low molecular weight lipoproteins secreted in the intestine and transported in the lymphatic channels which coalesce in the lymphatic cistern and form the thoracic duct (TD) at the level of the L2 vertebra, which enters the thoracic cavity through the oesophageal hiatus, ascends extrapleurally through the posterior mediastinum along the right surface of the spine, crosses the left side at the level of the main carina, leaves the mediastinum forming an arch above the clavicle and descends to drain at the junction of the left internal jugular and subclavian vein; however, only 50% of the subjects present this route, because considerable anatomic variation has been described and the thoracic duct may also drain in to the left internal jugular vein [2,3].

Accumulation of lymphatic fluid in the pleural cavity can occur through three mechanisms: 1) Traumatic rupture of the duct or its tributaries, 2) Obstruction of the thoracic duct that causes increased intraluminal pressure with escape of lymph out the lymphatics and 3) Transdiaphragmatic flow from a chylous peritoneal fluid [4].

Since up to 13% of chylothorax can have a non-milky macroscopic appearance and milky pleural fluid may be due to other etiologies (pseudochylothorax, empyema) it is important to maintain a high index of suspicion and look for the diagnostic criteria: 1) Triglycerides ≥ 110 mg/dl in pleural fluid, usually on a lymphocytic exudate. 2) Presence of chylomicrons in pleural fluid (lipid electrophoresis) and 3) Lymphangiography (LAG) showing chyle leakage into the pleural cavity [4].

The frequency of the causes of chylothorax depends on the type of hospital and the population served, but are generally classified as traumatic and non-traumatic causes (Figure 1).

Case Report

A 35-years-old man from a low-altitude agricultural community in northwest Nicaragua diagnosed with end stage chronic kidney disease (CKD) of non-traditional etiology three months before admission who was admitted for a hypertensive emergency that resolved quickly in emergency department with nitroglycerine infusion, but developed dyspnea during the hospitalization.

He was stable and adherent to hemodialysis for three months *via*

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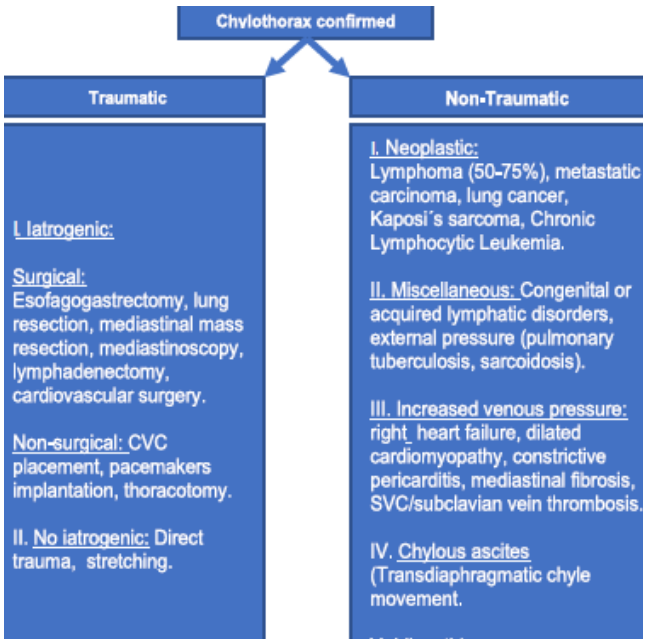

Figure 1: Etiopathogenic classification of chylothorax.

right internal jugular catheter, however by the time the patient arrived our hospital presented catheter dysfunction because a clot of two centimeters long. He recently had arteriovenous fistula created in his right upper extremity and required venous access on contralateral side for hemodialysis until the fistula matured, so the catheter was replaced with a left internal jugular vein CVC under ultrasound guide. He denied recent trauma, fever, chills or cough. Medications at the time of presentation were amlodipine, pantoprazole and carvedilol.

On clinical examination patient was afebrile, showed oxygen saturation of 89% on room air, respiratory rate 24 breaths per minute, blood pressure of 124/73 mmHg and heart rate of 100 beats per minute. No evidence of thyroid or lymph node swelling at neck was observed, neither supraclavicular nor inguinal adenopathy.

There was reduced expansion on the right side of the chest, absence of breath sounds and dull percussion noted over medial and basal right lung fields, and crackles detected above this zone.

A chest radiography showed a large right pleural effusion (Figure 2), associated with multiple alveolar opacities more evident after the removal of fluid. He had a normal white cell count of 7,940 per mm^3, mild anemia, controlled uremia and slightly elevated inflammation markers (Table 1).

A thoracocentesis was performed draining yellow creamy, cloudy, odorless effusion fluid (Figure 3). Intravenous meropenem was given for a presumed empyema, dyspnea and hypoxemia improved after drainage but infectious disease department sought a respiratory opinion and because the results of pleural fluid analysis (Table 2) a diagnosis of typical chylothorax was made. Gram stain and cultures showed no organism, acid-fast bacilli smear and Xpert for tuberculosis were negatives.

Pulmonary department insert a chest drain tube that produced over 500 mL of fluid daily in the first week despite conservative management with diet and use of subcutaneous octreotide, meanwhile completed the

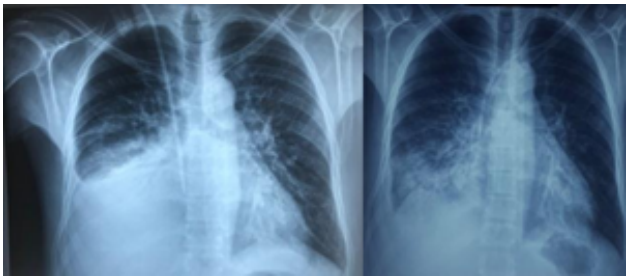

Figure 2: Chest radiography on admission. Before and after thoracocentesis and replaced catheter.

evaluation of the cause with a thoracic CT scan (Figure 4) that confirm the unilateral right-sided large pleural fluid, presence of enlarged mediastinal lymph and coalescent-nodular opacities at ipsilateral upper and middle lobes.

A bronchoscopy reveals a high tittle positive enzyme immunoassay for galactomannan antigen in bronchioloalveolar lavage (BAL) which was negative for other organism in cultures, acid-fast bacilli smear and Xpert for tuberculosis. Cytology and bronchial biopsy were negative for malignancy.

Bronchoscopy also found extrinsic compression at level of the upper lobe Inter-lobar carina, presumably caused by enlarged mediastinal lymph nodes (Figure 5).

Since pulmonary aspergillosis is not recognized as a cause of chylothorax, we searched for common causes described in this population, at the same time started anti-fungal therapy with endovenous voriconazole.

A venous phased Angio-Tomography ruled out obstruction/thrombosis of neck and central veins (Figure 6), thus we proposed the performance of LAG for interventional-radiology department with the aim to rule out direct TD injury during previous replacement of CVC, identify the site of leakage and eventually to embolize TD.

The Intranodal lymphangiography was performed in a standard fashion: In brief, ultrasound of the inguinal and medial upper thigh was performed using a linear transducer to identify a lymph node, which was directly accessed under real-time ultrasound guidance with a 25-gauge spinal needle preassembled and attached to a short segment of intravenous tubing and a 3-mL polycarbonate syringe containing an oil-based contrast agent (Lipiodol). Once the initial injection was observed under fluoroscopy to confirm proper positioning of the needle, contrast was injected by hand at a rate of approximately 1 mL per 5 minutes (median, 12 mL; range, 8-40 mL), and progression of the contrast was followed by intermittent fluoroscopy, not reporting any leakage, obstruction or mass in TD after two sessions on consecutive days (Figure 7).

Twenty-four hours after the second LAG was performed the rate of fluid production diminished to 150 mL per day and in the following 5 days; pleural fluid was clarifying until it was serous. At this time, patient completed two weeks of intravenous anti-fungal therapy. A decision was made to perform a pleurodesis with iodine that was successful and without complications.

Patient was discharged after completed 4 weeks of intravenous anti-fungal treatment. He did not need additional pleural aspirations

Variable	Reference Range, Adults*	On initial Evaluation
Hemoglobin (g/dl)	12.0-15.0	9.8
Hematocrit (%)	36.0-44.0	30
White-cell count (per mm^3)	4,500-10,000	7,940
Differential (%)		
Neutrophils	35.0-66.0	70.3
Lymphocytes	24.0-44.0	17.9
Monocytes	2.0-10.0	7.6
Eosinophils	0.0-0.5	2.8
Basophils	0.0-2.0	0.4
Platelet count (per mm^3)	15,000-450,000	298,000
Sodium (mmolniters)	135-145	137.89
Potassium (mmolniters)	3.4-4.8	4.52
Chloride (mmol/liters)	100-108	95.83
Magnesium (mg/di)	1.6-2.41	1.9
Calcium (mg/di)	8.5-10.5	8 .71
Urea nitrogen (mg/di)	8-23	43.33
Creatinine(mg/di)	0.6-1.2	4.73
Glucose (mg/di)	70-110	108.91
Tola prolein (g/dl)	6.4-8.7	5.21
Lactate Dehydrogenase (Uiliters)	85-227	259.9
Reactive C Protein (mg/liters)	0.00-5.0	11.87
Procalcitonin(ng/ml)	0.0-0.009	0.27
*Ranges used at Hospital Vivian Pellas for adults who are not pregnant and not have medical conditions that could affect the results.		

Table 1: Laboratory data.

Figure 3: Thoracocentesis drained a yellow milky, cloudy, odourless pleural fluid.

and a repeated thoracic CT scan shown resolution of parenchymal opacities and mediastinal lymphadenopathy. The patient continued on hemodialysis, completed six months of oral voriconazole without recurrence of chylothorax after one year of follow up.

Discussion and Revision of Literature

Our patient is a young man with end-stage renal disease in hemodialysis of non-traditional cause; which is the leading cause of death among working-age men in lower-altitude agricultural communities in northwest Nicaragua and has an estimated prevalence of 20% being considered an epidemic of multifactorial cause (sugar cane workers, heat stroke, urinary infections) since 2009; [5-7] contributing to the global epidemic of CKD. As result our team attends 928 patients each month for hemodialysis and this is the first case of chylothorax that we found.

Physical and Chemical analysis	
pH	8
Glucose (mg/dl)	102.64
Protein (g)	2.64
Lactate Dehydrogenase (Units)	136.03
Triglycerides (mg/dl)	380
Cholesterol (mg/dl)	43.19
Cell Count and Differential	
Leucocytes (per mm^3)	1,434
PMN (%)	1
Lymphocytes	99
Light Criteria	
Pleural Fluid Protein/Serum Protein Ratio	0.5
Pleural Fluid LDH/Serum LDH Ratio	0.52
Pleural Fluid LDH	<2/3 serum LDH
Microbiology and Pathologic analysis	
Gram Stain and cultures	No detected organism
Acid-Fast Bacilli Smear	Negative
GeneXpert-Mtb-Rif	No detected
Cytology	Negative
PMN: Polymorphonuclear leucocytes, LDH: Lactate Dehydrogenase	

Table 2: Laboratory features of the pleural effusion.

Chylothorax is an infrequent complication of CKD patients in hemodialysis and can become a debilitating problem with metabolic and immunologic wasting if not addressed promptly.

Our literature review found only 11 cases reported (Table 3) [8-20], mainly related to vascular access and CVC placement complications (thrombosis, stenosis, obstruction of neck and central veins, direct injuries of TD); which were important differential diagnosis in our case.

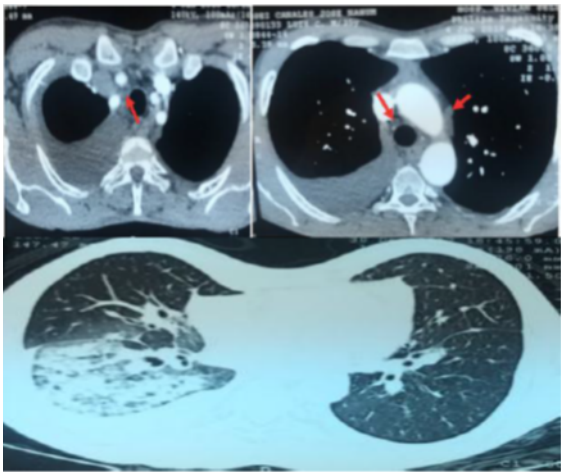

Figure 4: CT scan of thorax showing mediastinal lymph nodes enlargements (red arrows) and coalescent nodular opacities.

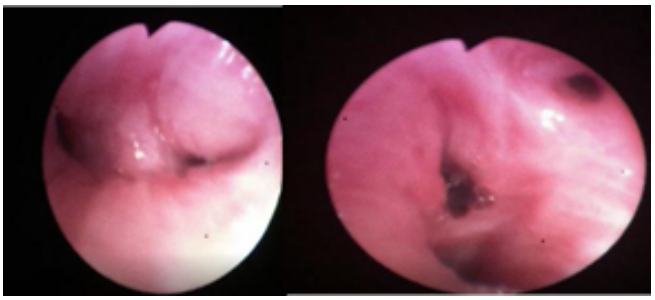

Figure 5: Bronchoscopy showing extrinsic bronchial compression on left upper lobe.

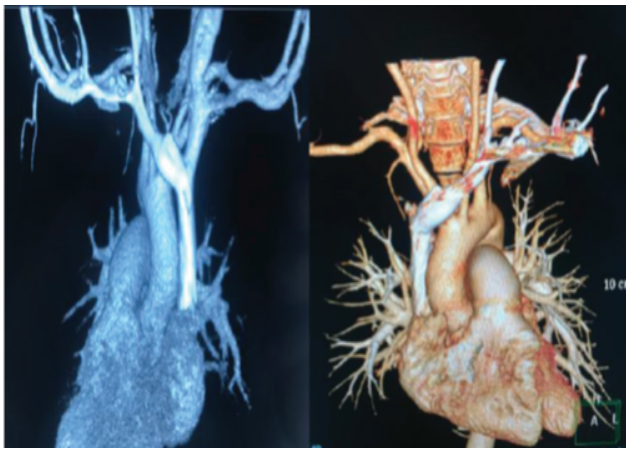

Figure 6: Reconstruction of a Flebo-TC that ruled-out obstruction/thrombosis of neck and central veins as cause of obstruction/compression of thoracic duct.

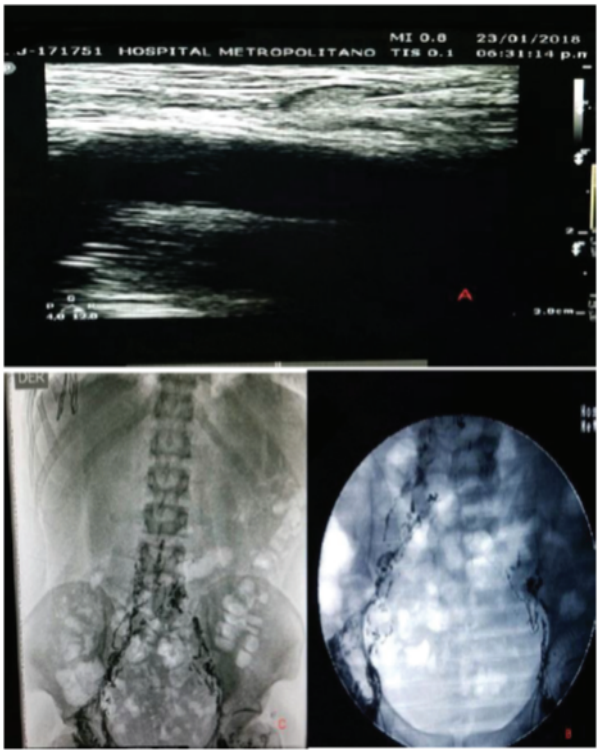

Figure 7: Intranodal Lymphangiography (LAG). (A) Inguinal lymph node access; (B) injection of Lipiodol; (C) Lymphangiography not showing leakage of thoracic duct.

Others uncommon causes of chylothorax reported in this population include infection as tuberculosis [11] and histoplasmosis [12] that cause chylothorax *via* external pressure/obstruction of TD by mediastinal lymphadenopathy or direct erosion, where the immunocompromised state of patients on hemodialysis predisposes them to this type of infections. However, we found no reports of pulmonary aspergillosis as a cause of chylothorax.

To determinate the cause of chylothorax in our patient is difficult, but probably pulmonary aspergillosis played a pathogenic role *via* a mechanism similar to tuberculosis and histoplasmosis. In favor of this theory is the absence of other identifiable etiology, a plausible mechanism of obstruction of TD by mediastinal lymphadenopathy and no recurrence after antifungal therapy.

In this case, the resolution of chylothorax was achieved with the performance of LAG, which served for diagnostic and therapeutic purposes and allowed us to offer our patient a definitive treatment with pleurodesis.

Traditional management for cases of chylothorax (mainly traumatic) refractory to conservative treatment has been the thoracic duct ligation through a right open thoracotomy or closure of the site of duct laceration through an open thoracotomy with a 96% success rate or through video-assisted thoracoscopic surgery (VATS). Surgical pleurodesis is reserved for patients with high operative risk which has an 83% success rate [21-23]. However alternative less invasive techniques has gain acceptance and popularity in last decade including percutaneous embolization of TD (TDE) [24] and lymphatic interventions which includes LAG and TDE with a pooled technical success rate for both of 94.2% and pooled clinical success rate for LAG and TDE of 56.6% and 79.4% respectively according to a recent systematic review and meta-analysis [25].

None of the techniques described above were performed in end-stage renal patients in hemodialysis but as illustrated in our case, it is worthwhile to try less invasive procedures to treat chylothoraces refractory to conservative treatment in patients without identifiable

Authors	Etiology	Main Mechanism	Reference
De Freitas-Gonzalez, et al.	Thrombosis of right jugular CVC	Stenosis/Obstruction of superior vena cava	[10]
Hugh IP, et al.	Tuberculosis with posterior Mediastinal lymphadenopathy	Obstruction/Erosion of thoracic duct	[11]
Shah S, et al.	First case of Histoplasmosls in adults as a cause of chylothorax	External compression/Erosion of thoracic duct.	[12]
Benhamou R, et al.	Licamidipine	Licardnidipine has been associated with chylothorax in Hispanic and Japanese populations during dialysis.	[13]
Torres-Guineas M, et al.	Thrombosis of right jugular CVC/Direct injury to thoracic duct during replacement of left jugular CVC	Superior Vena Cava stenosis/Direct injury to thoracic duct.	[14]
Limesh M, et al.	Left innominate vein stenosis related to eve placement	Obstruction/Compression of thoracic duct	[15]
Adeklle A, et al.	Catheter Induced superior vena cava stenosis	Obstruction/Compression of thoracic duct	[16]
Riza AM, et al.	Constrictive pericarditis	Transdiaphragmatic movement of Chylous ascites of Cardiac caused - elevated right-sided venous pressure	[17]
Un SH, et al.	Nephrotic syndrome	Transdiaphragmatic movement of chylous ascites	[18]
Geilh O, et al.	Catheter induced thrombosis of major Neck veins, superior vena cava and azygos vein	Obstruction/Compression of thoracic duct	[19]
Bonin VM, et al.	Nephrotic syndrome	Transdiaphragmatic movement of chylous ascites	[20]

Table 3: Summary of chylothorax cases reported in patients with end-stage renal disease in hemodialysis.

leakage of TD, including LAG with therapeutic purposes.

Conclusion

Pulmonary aspergillosis is not recognized as a cause of chylothorax, but in our patient with immunocompromised sate of CKD probably played an etiopathogenic role *via* mediastinal lymphadenopathy and should be considered in the differential diagnosis. In the treatments of chylothorax in end-stage renal disease patients in hemodialysis, lymphatic interventions could have a respectable efficacy and are less invasive options. We suggest consider LAG and TDE as first line therapy for this population.

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