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TITLE

AUTHOR

Abstract
A 53 year old gentleman presented with progressive breathlessness and abdominal pain for 2 weeks. Examination revealed pallor, increased respiratory rate and left supraclavicular lymphadenopathy. There was decreased air entry in bilateral lower zones and it was stony dull on percussion. Routine blood investigations were within normal limits. CXR revealed bilateral pleural effusion following which thoracentesis was done. Pleural fluid was milky white in color with triglyceride >500mg/dl. Pleural fluid analysis suggested a possible malignant etiology in the absence of significant trauma. CT chest and abdomen were suggested for further evaluation, which showed bulky mediastinal nodes, multiple para aortic, celiac and mesenteric group of lymph nodes. PET CT revealed multifocal lymphadenopathy with splenic lesion. Biopsy of left supraclavicular node confirmed follicular lymphoma. A final diagnosis of bilateral chylothorax with follicular lymphoma was made.

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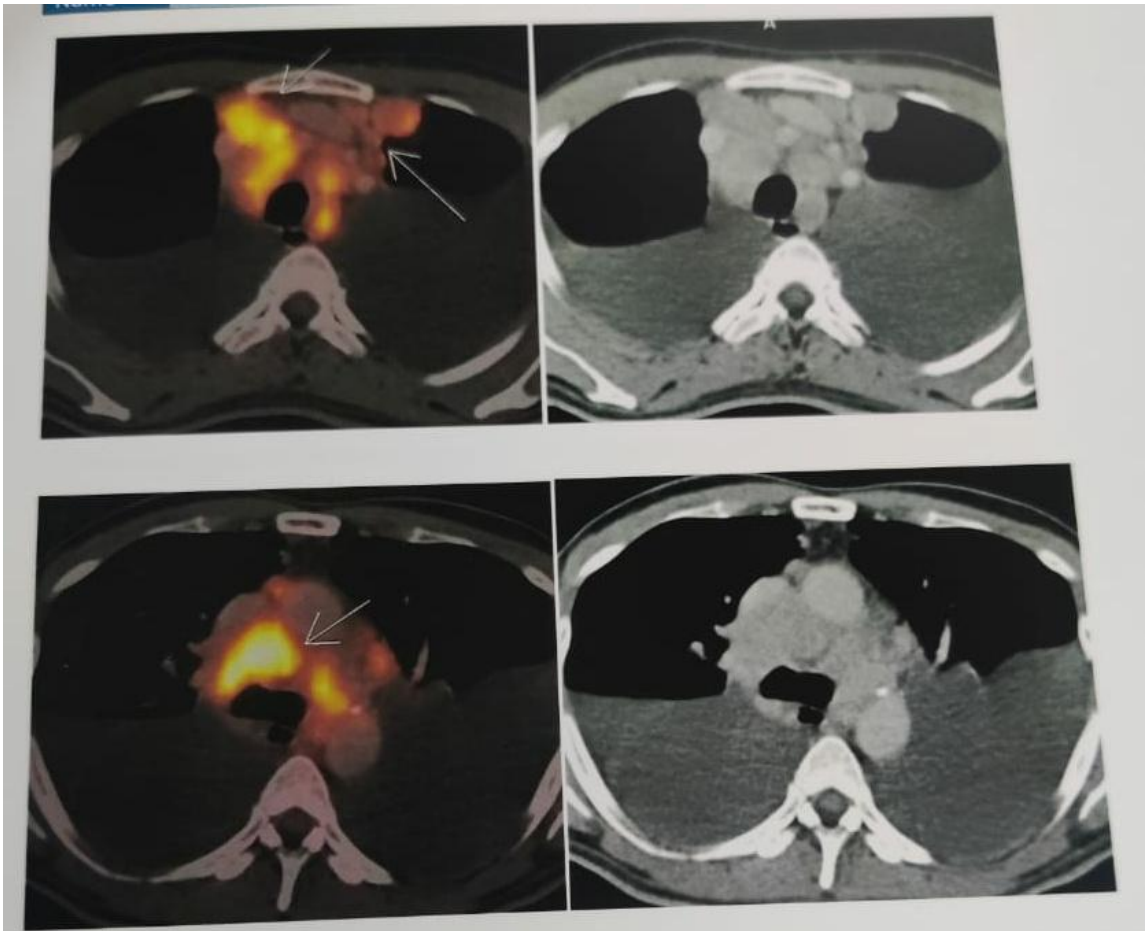
I. Introduction

Chylothorax is the accumulation of chyle in the pleural cavity characterized by a pleural fluid triglyceride >110 mg/dl, due to obstruction and disruption of the lymphatic channels. Etiologies can be either traumatic or non-traumatic. Neoplastic chylothorax is the most common cause of non-traumatic chylothorax. Cancers like lymphoma and metastatic carcinoma have been implicated in chylothorax with lymphomas contributing to 10% of neoplastic chylothorax[i]. Follicular lymphoma is the second most common type of non-Hodgkin lymphoma accounting for almost 30% of all lymphomas and 20% of non-Hodgkin lymphomas[ii]. It is the neoplastic proliferation of small B cells that form follicle like nodules, driven by t(14,18) resulting in an over expression of Bcl2, an anti- apoptotic protein.

II. Case Report

A 53 year old man presented to the outpatient clinic with the complaints of progressive breathlessness and abdominal pain for the past 2 weeks without any significant past, family or social history. His pulse rate was 110/min with the other vitals within the normal range. On general examination, his respiratory rate was 20/min and he had pallor and left supraclavicular lymphadenopathy. On examination of the respiratory system, air entry was decreased in bilateral lower zones and stony dull on percussion. Abdominal examination was insignificant.

CBC, LFT and RFT values were within the normal range. CXR revealed bilateral pleural effusion following which thoracentesis was done and the pleural fluid was milky white in color with analysis revealing a triglyceride level >500 mg/dl. Pleural fluid ADA was negative. CT chest and abdomen showed bulky mediastinal lymph nodes with bilateral pleural effusion, multiple para aortic, celiac and mesenteric group of lymph nodes. PET CT showed multifocal lymphadenopathy with splenic lesion. Biopsy of left supraclavicular node confirmed follicular lymphoma. Patient was shifted to medical oncology department where chemotherapy was initiated after 2 cycles of which he improved.



III. Discussion

Clinical features of chylothorax are typical of any pleural effusion with dyspnea, cough and chest discomfort being the main symptoms. Pleuritic chest pain and fever are uncommon because chyle is not irritating to the pleural space.The course of the thoracic duct explains why injury to the duct above the level of the fifth thoracic vertebra usually produces left sided chylothorax and injury to the duct below that level produces right sided chylothorax. Half of the chylothroraces are right sided, one third left sided and the remainder bilateral. Initial presentation of chylothorax is more likely in patients with occult lymphoma or malignancy involving the thoracic lymph nodes. Enlarged lymph nodes in the mediastinum compresses the lymphatic channels and the thoracic duct and impede centripetal drainage of lymphatic flow from the periphery of lung parenchyma and the pleural surfaces resulting in diffuse extravasation or oozing of chyle and lymph into the pleural space.[iii]

Gross inspection of the color, odor viscosity of pleural fluid may suggest a specific diagnosis. Milky pleural fluid limits the diagnosis to chylothorax, cholesterol effusion, erosion of central venous catheter through thoracic veins when lipid nutrients are being infused or intrathecal misplacement of enteral tubes with dissection of feeding solution into the pleural space. A pleural fluid triglyceride level >110 mg/dl, cholesterol level <200 mg/dl and the presence of chylomicrons strongly supports the diagnosis of chylothorax.[iv]

Total lymphocyte count is usually <5000 cells/µL with neutrophil predominance occurring in post-surgical chylothoraces and B cell predominance suggesting lymphoma. Wide variation exists in the reported sensitivity of pleural fluid cytology (22%-94%). The combination of immunohistochemistry, morphometry, flow cytometry and cytogenetics/molecular genetics (polymerase chain reaction, in situ hybridization and southern blotting) results in 100% sensitivity and specificity of pleural fluid cytologic evaluation. When lymphoma is a clinical consideration in patients with lymphocyte predominant exudative pleural effusion, flow cytometry is indicated to define the clonality of the lymphocytes[iv].

Follicular lymphoma is the most common cause of clinically indolent non-Hodgkin lymphoma. It is slow growing lymphoproliferative disorder with survival calculated in years. Follicular lymphoma typically presents with generalized painless lymphadenopathy that is waxing and waning in nature. It commonly involves

the cervical, axillary, femoral and inguinal lymph nodes. Rarely it may present with an asymptomatic large mediastinal mass. Only 20% of the patients experience B symptoms. Serum LDH is also increased in only about 20% of the patients. Usually follicular lymphoma only involves bone marrow and lymphoid organs[ii].

Histopathology of the lymph node will show variable sized closely packed follicles containing small cleaved cells without nucleoli (centrocytes) and larger non cleaved cells with moderate cytoplasm, open chromatin multiple nucleoli (centroblasts), minimal apoptotic cells and tangible body macrophages. The mantle zones are typically absent and necrosis is rare. Usually there is interfollicular involvement or capsular infiltration. It typically involves the paratrabecular areas of the bone marrow. Positive stains supporting FL include CD10, CD19, CD20 (strong), CD79a, BCL2 within follicles, and BCL6. Variable stains include CD30, CD11c, CD23, CD25, CD43 and surface immunoglobulin[ii].

Malignancy associated with chylothorax is not uncommon, but chylothorax as a presentation of malignancy is rare. Among malignancy associated conditions, malignant lymphoma and bronchogenic carcinoma are the most common. While hilar and mediastinal nodes are usually involved large mediastinal masses are rare. Pleural fluid cytology is usually negative for malignant cells and diagnosis is made by available lymph node biopsy. Bilateral chylothorax is a rare presentation of follicular lymphoma. Pleural fluid flow cytometry is an important diagnostic tool in the absence of significant lymphadenopathy. Primary effusion lymphoma is diagnosed by a null lymphocyte panel in flow cytometry[v].

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