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Case Report

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CLL with hemorrhagic pleural effusion

Chronic leukemia is a type of blood and bone marrow malignancy and is the second most common leukemia. It presents more in elderly people and in general has an indolent course, with 5 years survival rate of 83% for those < 65 years old and 68% for those 65 + years old. It represents 22%-30% of all kinds of leukemia worldwide with incidence projected to be between < 1 and 5.5 per 100,000 people.[1] It occurs more commonly in male than female and in whites than black's people.

IN general, the presentation varies from asymptomatic in 20-25% to enlarged lymph nodes in 87%, to an autoimmune hemolytic anemia in 10%.

However, CLL can affect the lung and pleura causing pleura thickened by leukemic infiltration along with extension into interlobular septa and areas of nodular fibrosis, and in rare instances can cause pleural effusion[2].

There are very few reported cases about hemorrhagic pleural effusion in the lung secondary to CLL.[3]

We are reporting two cases of CLL recurrence as pleural effusions. One is a 79 years old male, already diagnosed with CLL 5 years back and the second one is a 72 years old man with CLL diagnosed 1 year before and presented with hemorrhagic effusion.

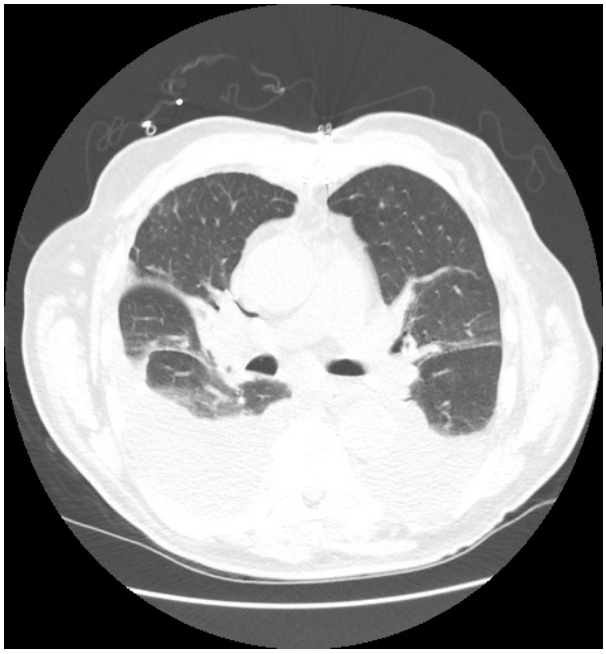
Case 1

79-year-old male, with past medical history of CLL 3 years back not on treatment, aortic valve mechanical replacement currently on warfarin, hypothyroidism, colon cancer currently in remission for the last 2 years, presented with complaint of shortness of breath started one week before presentation and was getting worse. He also admits having dry cough but no fever, chills or hemoptysis. At presentation he was tachypneic with 24 breaths/min, hypoxic required 2 L Nasal cannula.

His labs showed leukocytosis with 136.4, Hgb of 11.3, PLT of 82 with no inflammatory marker indicating infection but D dimer was 0.74mg/L (0.15-0.5) and BNP came with 146 pg/ml (0-100).

Primary chest X ray: There was a moderate right pleural effusion, while CT scan: moderate to large right and moderate left pleural Effusions.

Pulmonology consulted to place bilateral Pig tail chest tubes with immediate drainage of 1.8 L from the right
side and 850 cc from the left side bloody fluid. The fluid sent to the labs and came as exudative fluid and with analysis of WBC



7272 with Lymphocyte of 93%, RBC 11427.

Oncology consulted recommended Leukemia /Lymphoma panel and pleural fluid leukocytes differential.

The culture from the fluid came back negative for growth, while the Leukemia Lymphoma panel showed: An abnormal cell population comprises 64% of CD45-positive leukocytes with the expression of CD5 and CD23, in B-cells (CD19+) is consistent with chronic lymphoproliferative disorder patient chest tube continues draining, oncologist recommended Rituximab.

As the patient had a history of colon cancer and donut mass in the cecum status post resection of the mass 2019 but no further follow up as patient refused, we also checked for CEA to rule out colon cancer and it was negative.

Chest tubes removed and patient will receive 8 weeks of Rituximab.

Case 2

72 years old man with history of HTN, T2DM on insulin, and monoclonal lymphocytosis not enough to diagnose CLL in 2019, presented to the hospital with shortness of breath required 2L Nasal cannula. He mentioned that he has dry cough, but denied fever, chills, rhinorrhea, sore throat.

He was not tachypneic, tachycardic or febrile but had poor air

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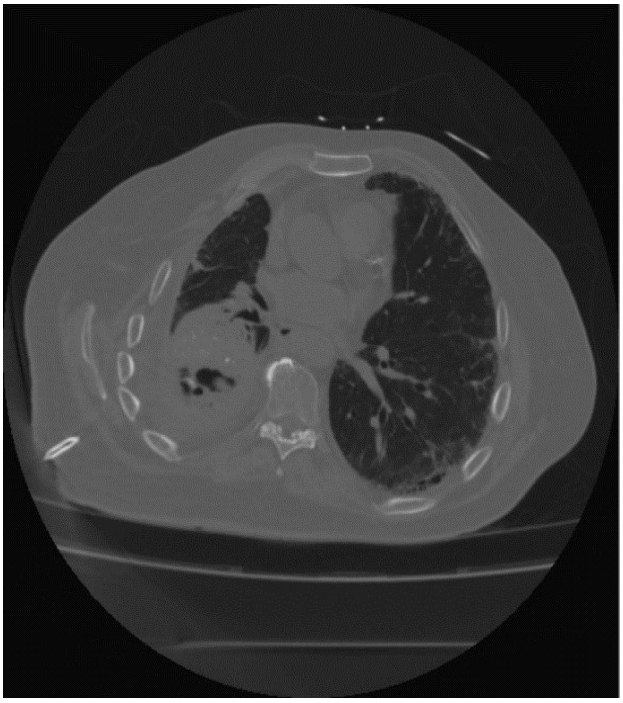

entry to the lower lobes of both lung and crackles in the middle right lobe.

Chest XR Moderate to large left-sided pleural fluid which was new compared to his previous imaging, CT chest confirmed the effusion.

Chest tube placed by Pulmonology and consisted of approximately 160 cc of cloudy, milky, off white serosanguinous fluid and sample sent to the lab. The analysis was WBC 59766 with 30% Lymphocytes, RBC 598503.

Cytology was positive for Lymphocytes: 94.1%, T-cells (86% of lymphoid cells) show a CD4/CD8 ratio of about 3.5 without overt phenotypic abnormality. NK-cells (1% of lymphoid cells) are unremarkable. Mature B-cells (1% of lymphoid cells) are polyclonal (Kappa: lambda 1.2), But CD34+ cells are not detected. So, it was not enough to diagnose CLL, while the flow cytometry: 7% CD5-positive CD23-positive monoclonal B cells.

Bone marrow biopsy recommended: chronic lymphocytic leukemia/small lymphocytic Lymphoma.

Leukemia Lymphoma panel showed an abnormal cell population comprises 7% of CD45-positive leukocytes. The expression of CD5 and CD23 in B-cells (CD19+) consistent with chronic lymphocytic leukemia/small lymphocytic lymphoma.

Patient remain asymptomatic and has no leukocytosis though he had recurrent pleural effusion. There was no reachable lymph node to do biopsy

Decision made to start the patient on Rituximab.

Discussion

Chronic Lymphocytic Leukemia (CLL) is characterized by the progressive accumulation of functionally incompetent monoclonal lymphocytes. It is considered identical to the mature (peripheral) B-cell neoplasm small lymphocytic lymphoma.

While Malignant pleural effusion is characterized by the presence of malignant cells in the pleural fluid.[4] most common sources of primary cancer are lung cancer which is the most common cause of a malignant pleural effusion (40%), followed by breast cancer (25%), ovarian and gastric cancer (5% each), and lymphoma (10%) [5]

The Non-Hodgkin Lymphoma in general represent 16-20% among all other Lymphomas [6]

The expected pathophysiology of pleural effusion is that CLL causes diffuse lymphadenopathy including pulmonary and mediastinal lymph nodes, large amounts of abnormal lymphocytes in the lymph node might lead to infiltration of the Leukemic cell to the pleural space, collection of fluid in the pleural space, usually resulting from excess fluid production and/or decreased lymphatic absorption [7]. as a consequence led to formation of serous or hemorrhagic effusion.

As even CLL might not be the only reason and another cancer coincident leading to the pleural effusion, pleural fluid aspiration and biopsy required to reach the diagnosis and ruling out developing other Lymphoma or developing Richter's transformation.

Flow cytometry is useful in the evaluation of lymphoid cells in pleural fluid because it can detect cell surface antigens in cytological material. immune phenotyping was performed by flow cytometry and the lymphocytes were positive for CD19, CD5 (43%), CD20, CD22, CD23, and CD45, and were negative for CD10 and FCM7. A clonal lambda light chain was also detected [8].

Pleural effusion is regarded as one of the adverse prognostic factors of CLL and considers as advance stage that requires management by thoracentesis though the recurrence risk is quiet high that requires treatment.

Rituximab is anti-CD20 antibody that has shown efficacy in chronic lymphocytic leukemia (CLL), both as a single agent and in combination with traditional chemotherapies [9].

Conclusion

CLL is well known blood cancer, has wide range of presentation including rare presentation including malignant pleural effusion and should be in consideration thinking about pleural effusion causes especially in elderly patient.

The effusion accumulates in the lung quickly and affect the breathing and can re accumulate really quick after draining it with chest tube. though still carries a good response to the treatment including Rituximab.

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