Primary Malignant Pleural Effusion with a Profound Type B Lactic Acidosis

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Primary Malignant Pleural Effusion with a Profound Type B Lactic Acidosis

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is a subtype of non-Hodgkin's lymphoma (NHL) that typically presents with a rapidly enlarging nodal mass, most commonly arising in the neck or abdomen with extra-nodal involvement. It is rare for DLBCL to present as a primary malignant effusion. Malignant fluid in the absence of lymphadenopathy is characteristic of primary effusion lymphoma (PEL), a separate subtype of NLH that is almost always associated with Ebstein-Barr Virus (EBV) and human-herpes virus 8 (HHV-8).

Case Presentation

A 61-year-old Caucasian female presented with several weeks of non-productive cough, low-grade fevers, drenching night sweats and worsening confusion. Laboratory evaluation revealed a calcium level of 14.6 mg/dL, lactate of 6.7 mmol/L and anion gap of 23. By hospital day 3, the lactate level peaked at 20.2 mmol/L with an anion gap of 24. Computed tomography (CT) imaging of the chest, abdomen and pelvis revealed a right-sided pleural effusion with no lymphadenopathy or masses (Figure 1). A thoracentesis was performed with cytology from the pleural fluid showing a monoclonal B-cell population, predominantly large cell in nature, accounting for 82% of the total events (Figure 2). Ebstein-Barr Virus (EBV) and human-herpes virus 8 (HHV-8), two viruses often associated with primary effusion lymphoma, were negative. These findings, combined with the cytologic features, confirmed the diagnosis of clinical stage IV Diffuse Large B-cell Lymphoma (DLBCL). Further analysis with fluorescence in-situ hybridization (FISH) showed normal signal patterns. Therefore, the possibility of a double hit lymphoma was unlikely. The revised international prognostic index (R-IPI) was 3, which correlates with a poor prognostic index and an estimated overall survival of only 53%. The R-IPI is a clinically useful prognostic index that identifies 3 distinct groups with poor, good and very good progression free survival and can help guide treatment.

The patient developed respiratory failure and disseminated intravascular coagulation (DIC), was intubated and placed on a ventilator. She was started on continuous renal replacement therapy for worsening renal failure and refractory lactic acidosis. Emergent chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) was initiated with improvement in electrolyte abnormalities. She had a prolonged 40-day hospital course and required admission to an acute rehabilitation facility following discharge. However, she has since completed six cycles of R-CHOP and remains in a sustained, complete remission 17 months from the time of diagnosis. She has functionally returned to baseline.

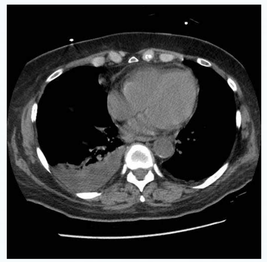

Figure1: Non-contrast computed tomography (CT) scan of the thorax revealed a moderate right lower lobe pleural effusion with associated atelectasis. No masses, hilar, axillary, or mediastianal lymphadenopathy was visualized.

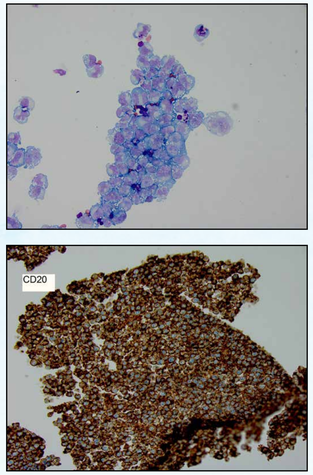

Figure 2: Pleural fluid cytology revealing a monoclonal B-cell population consistent with diffuse large B-cell lymphoma.

Discussion

This case illustrates a unique presentation of DLBCL with an isolated malignant pleural effusion as the only site of disease in the context of a profound lactic acidosis.

DLBCL typically presents with a symptomatic rapidly enlarging nodal mass, most commonly arising in the neck or abdomen with extra-nodal involvement and constitutional "B" symptoms. While our patient presented with classic "B" symptoms, there was no nodal mass and imaging failed to exhibit any lymphadenopathy, with a primary malignant pleural effusion solely present and diagnostic of DLBCL. In this setting, an important differential includes consideration of primary effusion lymphoma (PEL). PEL is a distinct subtype of Non-Hodgkins Lymphoma (NHL) that is almost always associated with HHV-8 and EBV. It tends to affect only patients with longstanding human immune deficiency virus/acquired immune deficiency syndrome (HIV/AIDS) with a tendency to remain localized within serous body cavities such as pleural, peritoneal and pericardial spaces with no solid tumors. EBER (EBV by in-situ Hybridization) and HHV-8 were negative in our patient. This highlights the importance of early pathologic analysis, as it affects both treatment and future outcomes.

Malignancies, particularly hematologic malignancies, are infrequently associated with an elevation in lactate levels. Lactic acidosis occurs when the balance between lactate production and breakdown is disrupted and is divided into two primary categories. Type A lactic acidosis occurs with clinical evidence of tissue hypoperfusion and hypoxia, while Type B lactic acidosis occurs without such evidence and is thought to be secondary to etiologies related to drugs, toxins or malignancy.[1] Acute leukemias and high-grade lymphomas are the most common neoplastic disorders associated with lactic acidosis, though the occurrence is rare.

The cause of lactic acidosis in such malignancies is thought to be multifactorial.[4] It is hypothesized that lactate is produced from local hypoxia in the absence of systemic hypoperfusion due to an increase in glycolytic activity in cancer cells. The excessive lactate is produced from highly aggressive tumors that outgrow their blood supply.[5] Another proposed mechanism concludes that cancer cells have a high rate of glycolysis, even in the presence of oxygen, due to the overexpression of a mitochondrially bound glycotic enzyme, type II hexokinase, which has a high affinity for glucose.[8] This phenomenon is known as the "Warburg effect".[9] Malignancy-associated lactic acidosis is associated with an extremely poor prognosis. A literature review of 31 reported cases between 2000 and 2010 revealed 81% of patients died within 3 months of the onset of lactic acidosis, a majority of which occurred within several days.[6] Chemotherapy is the only effective means of correcting malignancy-associated lactic acidosis,[8] though even with chemotherapy the mortality rate is exceedingly high.

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