CASE REPORT

Massive splenomegaly and lymphopenia: a unique case of obstructive shock

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SUMMARY

We present a patient with intravascular large B-cell lymphoma (IVLBCL)-induced obstructive shock. This case represents a unique presentation of the disease, while highlighting the difficulty of establishing the diagnosis. Although there was a high clinical suspicion for a lymphomatous process, the obstructive shock component of the patient's presentation was perplexing. It was not until the autopsy reports demonstrated lymphocytes within the pulmonary vasculature that the clinical picture of altered mental status, weight loss and obstructive shock were unified to the diagnosis of intravascular large B-cell lymphoma.

BACKGROUND

Obstructive shock is typically attributed to extracardiac aetiologies such as cardiac tamponade, tension pneumothorax, constrictive pericarditis and mechanical ventilation due to an obstructive physiology that leaves the heart with an impaired diastolic filling.¹ Massive pulmonary embolism, acute pulmonary hypertension, aortic dissection and systemic embolisation cause obstructive shock by increasing the afterload state and ultimately resulting in dysfunctional cardiac contractility.¹ Rarely is malignancy considered in the differential diagnosis of obstructive shock, except when a large intrathoracic obstructive tumour is identified as having direct occlusion of the vena caval system or a malignant pericardial effusion results in tamponade.¹ Lymphoma, especially when systemic vasculature is involved, has been rarely associated with obstructive shock.^{1–3} We present a case obstructive shock without a clear aetiology, where autopsy demonstrated intravascular large B-cell lymphoma (IVLBCL).

CASE PRESENTATION

A 63-year-old woman with limited medical history presented to the emergency department with an altered mental status. She had been admitted to our hospital twice previously for polyarticular gout and urosepsis over the past 4 months. At this presentation, her family reported of intermittent word finding difficulties, a 50 pound unintentional weight loss over the previous 3 months and recurrent low blood pressure measurements despite self-discontinuing antihypertensive medication.

INVESTIGATIONS

Physical examination findings: On presentation, blood pressure was 107/58 mm Hg, heart rate 95 bpm, respiratory rate 22 breaths/min and temperature was 100.6°F. Her oxygen saturation was

86% on room air. Oropharyngeal examination was notable for thrush. Slight crackles were observed in the lung bases bilaterally. The abdominal examination demonstrated diffuse tenderness, large splenomegaly and caput medusa. Lower extremities revealed pretibial, pitting oedema extending to the knees bilaterally.

Diagnostic studies: Significant laboratory and radiographic findings included creatine 1.54 mg/dL, sodium 127 mmol/L, white blood cell 12 200 cells/ μ L (79.5% neutrophils, 14% bands, 4% lymphocytes), lactate 3.5 mmol/L and serum uric acid 15.3 mg/dL (normal 2.0–7.5). Arterial blood gas demonstrated pH 7.47, pO₂ 70 mm Hg and pCO₂ 29 mm Hg. Cardiac biomarker levels, brain natriuretic peptide and ammonia levels were unremarkable. A CT scan of the abdomen with oral and intravenous contrast demonstrated a large heterogeneous mass-like appearance of the spleen with gastrohepatic lymphadenopathy (figure 1).

TREATMENT

The patient was admitted to the medical floor and resuscitated with normal saline. Oncology was consulted due to lymphopenia, lymphadenopathy, splenomegaly and weight loss. Over the next 72 h, she received empiric broad spectrum antibiotics and 6 L normal saline with no improvement in her mental status. Owing to labile blood pressures, worsening mental status, increasing lactate levels (4.2 mmol/L) and increasing oxygen requirement, the patient was transferred to the ICU for unresolved shock.

Upon arrival at the ICU, she was intubated and placed on pressor support to maintain mean arterial

Figure 1 Large heterogeneous, mass-like appearance of the spleen.

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pressures greater than 65 mm Hg. A transthoracic echocardiogram to evaluate undifferentiated shock revealed a preserved ejection fraction, grade 1 diastolic dysfunction, a severely dilated right ventricle, a flattened septum consistent with RV pressure/volume overload and a right ventricular systolic pressure of 40 mm Hg. A CT pulmonary angiogram was performed with no evidence of pulmonary embolus, pneumothorax or pericardial effusion. Insertion of a pulmonary artery catheter demonstrated a pulmonary artery pressure of 55/30 mm Hg with a cardiac output of 4.05 L/min, cardiac index of 8.4 L/min/m², pulmonary capillary wedge pressure of 24 mm Hg and a systemic vascular resistance index of 1304 dynes/(s/cm⁵/m²). Central venous pressures were 18 mm Hg.

Over the next week, the patient required intensive support for worsened cardiovascular and pulmonary functions. A bedside inhaled nitric oxide challenge demonstrated no changes in pulmonary haemodynamics. On ICU day 8, a splenectomy was performed for evaluation of the lymphoma—enlarged peripheral lymph nodes were not readily accessible. It was also hypothesised that a splenectomy may improve her haemodynamics, as splenic girth may have been contributing to her obstructive presentation. Gross evaluation demonstrated marked splenomegaly. Low-power microscopic assessment showed areas of extensive necrosis and vaguely nodular foci of neoplastic cells. High-powered magnification showed red pulp displaying diffuse involvement with medium-to-large atypical lymphoid cells with numerous mitotic figures.

Despite transient improvement in hemodynamics following splenectomy, the patient remained in refractory shock. Over the next four days, she progressed to oliguric renal failure and suffered two cardiac arrests. With a continued multifactorial, depressed mental status and worsening of multiorgan failure, her family elected to compassionately extubate on ICU day 12 and she died several hours later.

OUTCOME AND FOLLOW-UP

Autopsy demonstrated diffuse IVLBCL, multiorgan involvement including the lungs, brain, spleen and liver and additional extravascular involvement. Immunohistochemical staining of the pulmonary vasculature demonstrated intravascular lymphocytes with strong staining for a B-cell-associated antigen, CD20 (figure 2). B-cell receptor gene rearrangement studies on sections of the right lung and spleen showed a clonal pattern with the same monoclonal peaks, suggesting that intravascular cells in pulmonary vasculature and extravascular lymphoma populations were genetically related.

DISCUSSION

We described a case of a refractory, obstructive shock from IVLBCL. On initial presentation at the ICU, echocardiographic assessment and pulmonary artery catheter data supported a diagnosis of obstructive shock with common causes excluded. While elevated uric acid, lymphopenia and massive splenomegaly were suggestive of an infiltrative lymphomatous process, splenic histopathology alone did not establish a clear diagnosis. It was not until diffuse lymphocytic infiltration of the vasculature was discovered on pulmonary autopsy that the diagnosis was confirmed.

IVLBCL is a rare subtype of diffuse large B-cell lymphoma, notable for preferential growth of lymphocytes within the lumens of medium-to-small blood vessels, sparing lymphatics and larger vessels.^{4 5} The specific pathological mechanism for preferential growth in blood vessels is not completely understood; however, a defect in adhesion molecules CD29, CD54 and CD11a has been suggested.^{6–8}

A

B

Figure 2 (A) Neoplastic cells filling a vessel in a postmortem lung artery section on H&E stain. (B) The atypical intravascular lymphocytes within a lung artery showing strong staining for a B-cell associated antigen, CD20.

IVLBCL typically presents at a median age of 67 years.⁹ Occurring equally among men and women, it has been diagnosed in less than one in one million people.⁹ Common clinical manifestations include fatigue, deterioration in performance status, mental status changes and fever of unknown origin.⁸ IVLBCL is differentiated into two major variants based on clinical manifestation: Western and Asian.⁵ Western variant symptoms include fever, skin rashes and neurological symptoms (altered mental status, dementia and gait disturbances). The Asian variant often presents with hemophagocytic syndrome, fever, hepatosplenomegaly and thrombocytopenia.¹⁰ Isolated cutaneous manifestations can be seen in younger women with minimal systemic symptoms. Multiorgan involvement is common at the time of diagnosis.^{4 8} Pulmonary abnormalities are cited in approximately 60% of cases, often with acute and subacute findings of elevated pulmonary pressures.^{2 3 11–13}

Accurate diagnosis of IVLBCL is based on a combination of high clinical suspicion and organ biopsies. Laboratory findings are non-specific but may raise suspicion for IVLBCL. IVLBCL tumours are often associated with increases in lactic acid production, serum lactate dehydrogenase and β_2 microglobulin.^{5 11} Peripheral blood involvement is only present in 5–9% of patients.⁵ While biopsies of affected organs may provide a good diagnostic yield, reports have also demonstrated high yield from random skin biopsies regardless of cutaneous involvement.¹⁴ The utility of imaging modalities for diagnostic purposes remains controversial and incompletely assessed.¹¹

Case reports have suggested improved survival with early chemotherapy, although many patients do not survive their presenting organ dysfunction. Most treatment algorithms utilise CHOP, CHOP-like and anthracycline-based therapies.¹⁵ Unfortunately, mortality rates have remained high, with a 22% survival rate at 3 years and median survival of 13 months.^{9 16} Current literature does not suggest specific regimens targeted towards particular organ dysfunction such as pulmonary infiltration. Instead, current research is studying the utility of rituximab combined with anthracycline or stem-cell therapies.¹⁷ Although these studies have had some promising improvements in mortality, the broad application of these regimens is still undergoing further investigation.

This case of IVLBCL-induced obstructive shock represents a unique presentation of the disease, while highlighting the difficulty of establishing the diagnosis. Although there was a high clinical suspicion for a lymphomatous process, the obstructive shock component of her presentation was perplexing. It was not until autopsy demonstrated lymphocytes within the pulmonary vasculature that the clinical picture of altered mental status, lymphoma and obstructive shock were unified to the diagnosis of intravascular large B-cell lymphoma.

Learning points

- Typical causes of obstructive shock include pulmonary embolus, cardiac tamponade and tension pneumothorax. Intravascular large B-cell lymphoma (IVLBCL) should be considered as a possible cause in patients with risk factors for lymphoma.
- IVLBCL is a rare lymphoma affecting medium and small vessels throughout the body. Presenting signs and symptoms are often broad and non-specific.
- High clinical suspicion is paramount in the diagnosis of the disease. While current therapies offer guarded outcomes, new regimens based on rituximab in conjunction with anthracycline may provide better long-term prognosis.

Contributors NAH is the corresponding author and principle author. MTK provided vital components to both the formulation of the manuscript as well as the

manuscript contents. CAM was the staff advisor, providing necessary input for the creation of both the clinical course as well as the discussion, while also providing extensive editorial aid.

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