

A unique cause of lower back pain: Lymphoma transformation presenting as IVC tumor thrombus

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Abstract

We present a case of a 54-year-old male with a past medical history of follicular lymphoma, who presented with back pain and bilateral leg swelling. The patient's symptoms were found to be due to an inferior vena cava tumor thrombus secondary to transformed follicular lymphoma to diffuse large B-cell lymphoma. In addition, the management decisions in this case balanced the need to aggressively treat the patient's lymphoma with the risk of inferior vena cava perforation. This case demonstrates the importance of the recognition of unique presentations of transformed lymphoma as delays in diagnosis can impact outcomes.

Keywords

lymphoma transformation; back pain; tumor thrombus

Abbreviations

DLBCL: diffuse large B cell lymphoma; CT: computed tomography; PET: positron emission tomography; IVC: inferior vena cava; ACCP: American College of Chest Physicians

Introduction

The transformation of low-grade B-cell neoplasms, such as follicular lymphoma, to more aggressive, higher-grade lymphoid neoplasms is a well-recognized phenomenon. Most commonly, follicular lymphoma transforms to diffuse large B-cell lymphoma (DLBCL) at a rate of 3% per year [1,2]. Biopsy demonstrating histologic transformation is the gold-standard for diagnosis in a patient with follicular lymphoma [3]. Specifically, for DLBCL, a germinal cell pattern is most common in which large B-cells infiltrate lymph nodes and obliterate the follicular architecture [4]. Histologic transformation is typically marked by the clinical features of aggressive lymphoma, such as, "B symptoms," evidence of rapid cell turnover (elevated lactate dehydrogenase, hypercalcemia, hyperuricemia), enlargement of lymph nodes, and involvement of extranodal sites; however, pain at the site of transformation is the most common presenting symptom [2,3]. At the time of detection of transformation, most patients have advanced stage of disease and a poor prognosis [3]. The median post-transformation survival is 1.7 years; although, Rituximab in addition with novel chemotherapy combinations have improved survival rates [2,5]. We present a case of a 54-year-old male with a history of follicular lymphoma who presented with

lower back pain and bilateral lower leg swelling. Computed Tomography (CT) Angiogram demonstrated an inferior vena cava tumor thrombosis secondary to transformed lymphoma.

Case Presentation

This is a case of a 54-year-old male with a past medical history of hypertension, obesity, type 2 diabetes mellitus, and follicular lymphoma (stage 3B, grade 1-2) which had been diagnosed 5 months prior to presentation. The patient had completed 5 of 6 cycles of bendamustine-rituximab, and repeat scans after 3 cycles of treatment showed complete remission.

Our patient presented to the emergency department with a 1-week history of low back pain and bilateral leg swelling. His back pain localized to the mid-lumbar region and was exacerbated by walking and lying supine. It had progressed in intensity over the week prior to presentation despite trials of non-steroidal anti-inflammatory drugs and steroids. The patient reported that his leg swelling had been most noticeable the few days prior to presentation and had been refractory to leg elevation and diuretics. In addition, the patient noted associated testicular swelling. Review of symptoms was negative, except for a subcutaneous abdominal mass that was biopsied the day prior to presentation.

On presentation to the emergency department, our patient was well-appearing and in no acute distress. Physical exam revealed bilateral edema of the lower extremities, a 3x3cm subcutaneous mass on the right anterior abdominal wall, and generalized edema of the testes. He had normal range of motion, strength, and sensation in all extremities, along with absence of palpable lymphadenopathy. There was no costovertebral angle tenderness. Laboratory evaluation demonstrated anemia (hemoglobin 10.4 g/L; reference range 13.2-17.3 g/dL), elevated lactate dehydrogenase (232 U/L; reference range 100-190 U/L) and uric acid (7.1 mg/dL; reference range 3.5-7.0 mg/dL), and a normal brain natriuretic peptide. A lumbosacral radiograph was negative for acute compression and fracture of the lumbar spine which was confirmed by a complete spine magnetic resonance image that also showed no evidence of metastatic disease. The patient was admitted to the inpatient hematology service for further management.

After initial imaging studies were negative, a positron emission tomography (PET) scan was ordered due to suspicion for transformed lymphoma given the patient's subcutaneous abdominal mass. The patient's PET scan revealed interval enlargement of intra-abdominal lymph nodes and subcutaneous soft tissue lesions in the anterior abdominal wall (Figure 1). This further increased suspicion for transformed lymphoma since the patient's PET scan 2 months prior showed no evidence of lymphoma. The patient also underwent vascular duplex ultrasound due to his lower extremity swelling that showed decreased venous flow at the bilateral common femoral veins and a nearly occlusive thrombus in the mid/distal inferior vena cava (IVC).

Pathologic examination of the biopsied abdominal wall lesion confirmed transformation of preexisting follicular lymphoma to DLBCL, germinal center cell architecture and follicular structure. While the diagnosis of DLBCL was established, the question of the patient's IVC thrombus remained. Due to concern for tumor thrombus in the setting of transformed lymphoma, the patient underwent a CT Angiogram (Figure 2). The CT Angiogram verified a large thrombus in the IVC extending into the renal veins bilaterally which correlated with the hypermetabolic activity seen on PET. The imaging could not confirm if the lymphoma had invaded the IVC wall, or if the neoplasm was only compressing the IVC

causing turbulent blood flow and clotting. Regardless, the diagnosis of IVC tumor thrombus was confirmed by the CT Angiogram.

With the diagnosis of IVC tumor thrombus secondary to transformed DLBCL, urgent combination chemotherapy and intravenous anticoagulation with heparin was initiated. The patient was discharged after completion of cycle 1 of chemotherapy with significant improvement in his clinical signs and symptoms. Subcutaneous low molecular weight heparin was initiated for chronic anticoagulation.

After completing five cycles of combination chemotherapy, interval PET scan showed progression of disease, and the patient was switched to a different chemotherapy regimen for his refractory DLBCL. The patient has not experienced any adverse events from his IVC thrombus and remains on subcutaneous low molecular weight heparin.

Discussion

In this case, the patient's presenting symptoms of lower back pain and bilateral leg swelling were found to be due to an IVC tumor thrombus secondary to transformed follicular lymphoma to DLBCL. Transformation to higher grade neoplasms occurs in 10-70% of low-grade lymphomas, with this variation in reported frequency due to the method of diagnosis (biopsy v. autopsy), length of follow-up, and number of patients in the study [3]. While transformation of lymphoma is not rare, transformation presenting as IVC tumor thrombus is extremely uncommon. IVC tumor thrombus has been associated with renal cell carcinoma and transitional cell carcinoma in the literature, but has not been linked to transformed lymphoma [6,7]. As the patient's presenting symptoms were non-specific and the initial work-up non-revealing, clinical suspicion was vital in making this diagnosis.

As seen in our patient, back pain is exceedingly common in the United States. There is a lifetime prevalence of over 60%, and non-traumatic back pain accounts for 2-3% of emergency department visits [8,9]. Yet, only 5% of patients presenting with back pain have serious pathology that requires immediate treatment to prevent long-term negative sequelae [10]. The vast majority back pain is due to mechanical causes, such as lumbar strain (also characterized as nonspecific), degenerative joint disease, and disc herniation [8]. Nonmechanical etiologies of lower back pain are rare and encompass a wide array of clinical pathology: neoplasia, infection, inflammatory arthritis, and visceral disease, including aortoiliac disease [8]. IVC tumor thrombus falls into the atypical subset "aortoiliac disease." This case reveals both an aberrant non mechanical etiology of back pain that also requires urgent intervention.

While IVC tumor thrombus is a rare presentation of transformed lymphoma, and back pain a rare presentation of IVC thrombus, the patient's presenting symptoms were fairly typical for IVC thrombus. Bilateral lower extremity swelling and back pain is present in about one half of patients with IVC thrombus. Abdominal pain with dilation of superficial abdominal vessels is also common but was not seen in our patient [11,12]. Furthermore, malignancy is a stand-alone risk factor for IVC thrombosis due to the resulting hypercoagulable state [11]. It can be deduced that our patient's hypercoagulable state was not the primary driving factor for his IVC thrombus. Rather, as seen in the CT Angiogram, our patient's IVC thrombus was secondary to the rapid enlargement of abdominal lymph nodes which compressed, and possibly even invaded, the IVC, resulting in turbulent flow and the formation of a thrombus.

Given the aggressive nature of transformed lymphoma, our patient required urgent chemotherapy and had rapid and significant clinical improvement. The American College of Chest Physicians (ACCP) guidelines for the treatment of venous thromboembolism, while based on deep venous thrombosis, have also been accepted for the treatment of IVC thrombosis [12]. For the initial treatment of acute venous thromboembolism, the ACCP recommends parenteral anticoagulant therapy; low molecular weight heparin is recommended over intravenous unfractionated heparin and subcutaneous low-molecular weight heparin [13]. Our initial treatment strategy departed from these guidelines due to the tenuous nature of the patient's IVC thrombus. As it could not be confirmed through imaging if the lymphoma had invaded the IVC, we had to consider the risk of possible IVC perforation that could result with tumor shrinkage after chemotherapy versus the risk of holding anticoagulation. Therefore, the patient was anticoagulated with intravenous heparin as it could be immediately ceased if there was concern for IVC perforation.

Conclusion

Our case demonstrates a unique presentation of a well-recognized clinical situation – transformed follicular lymphoma to DLBCL presenting as IVC tumor thrombus. While the patient's presenting symptoms of back pain and bilateral lower extremity swelling are common for IVC thrombosis, these symptoms are non-specific and more typically indicate alternative pathology. Our management decisions in this case were influenced by the need for treatment of the DLBCL with that of a possibly penetrating IVC tumor thrombus. It also highlights the need for early detection and appropriate treatment of this potentially catastrophic presentation of transformation.

Figures

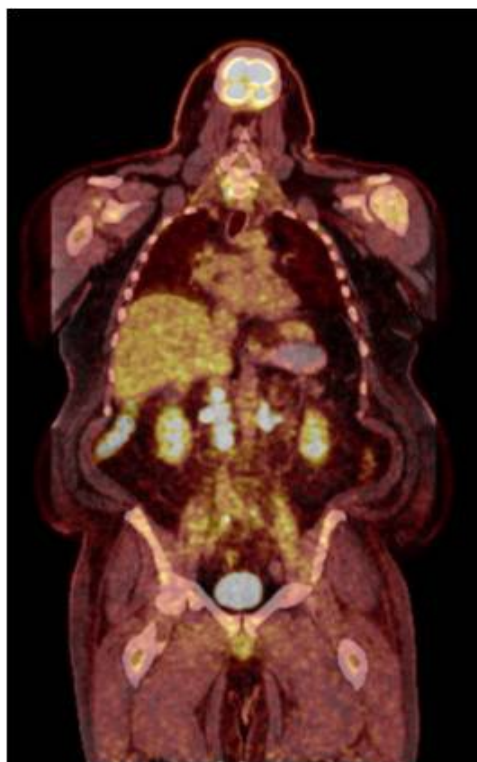


Figure 1: PET Scan showing interval enlargement of intra-abdominal lymph nodes.



Figure 2: CT Angiogram confirming IVC tumor thrombus. It was unable to be determined if the lymphoma had invaded the IVC.

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