Navigating Diagnostic Challenges: A Case Study of DLBCL Relapse as Cutaneous IVLBCL

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Introduction: Intravascular large B cell lymphoma (IVLBCL) is a rare and aggressive non-Hodgkin's lymphoma that predominantly grows in the lumen of blood vessels. We present a diagnostically challenging case of IVLBCL involving dermal and subdermal blood vessels diagnosed on skin biopsy. This case was particularly challenging as the patient presented with persistent signs and symptoms of lymphoma with no radiographic or pathologic evidence of disease.

Case Report: 78 year old Caucasian female with prior oncologic history significant for breast and bladder cancers, of which she was cured. She presented with B symptoms, normocytic anemia, elevated LDH in 1000's and diffuse lymphadenopathy. Lymph node biopsy revealed Diffuse Large B cell Lymphoma (DLBCL) in October 2021. Pathology revealed high Ki-67 > 90%, positive for CD20, BCL-2, BCL-6, negative for CD5, CD10 and cyclin D1. FISH was negative for rearrangements of MYC, BCL-2 or BCL-6 with expression of c-MYC. Her initial staging PET/CT also showed cutaneous lesions. She received 6 cycles of R-CHOP along with IT methotrexate. PET scan in December 2021 was consistent with complete response.

In follow up, she was noted to have recurrence of B symptoms, rising LDH and worsening anemia concerning for relapsed disease. Interestingly, she also had developed subcutaneous nodules on her shin which, in conjunction with her presentation, was concerning for cutaneous lymphoma though further imaging with ultrasound and MRI failed to reveal a biopsy amenable lesion. Further evaluation with bone marrow biopsy and PET/CT were also negative. She continued to have persistent anemia, elevated LDH and disabling fatigue necessitating hospitalization and further work up including peripheral blood flow cytometry, repeat bone marrow biopsy and liver biopsies. All of these tests were unrevealing. We also considered and ruled out alternate etiologies of her anemia and elevated LDH including nutritional deficiencies, hemolysis, paroxysmal nocturnal hemoglobinuria, hemophagocytic lymphohistiocytosis, pulmonary embolism and GI bleeding.

After approximately 6 months of presumed relapse as described above, the patient's skin nodules became painful and erythematous though non-palpable. She was referred to general surgery for skin biopsy but was noted to only have small blotchy red spots with skin thickening without any subcutaneous mass. Elliptical skin biopsy revealed dilated dermal and subdermal vessels with numerous large lymphoid cells which were positive for CD20, PAX5, CD79a, negative for CD43 and myeloperoxidase along with a high Ki-67 of > 90% consistent with IVLBCL. This was considered relapse of her original DLBCL and she was started on second line therapy with Tafasitamab and Lenalidomide. She has had excellent response to this therapy with resolution of her skin nodules, anemia and performance status to prior baseline.

Discussion: This is a challenging case of DLBCL relapsed as IVLBCL manifesting as insidious skin lesions. Clinical suspicion for lymphoma remained high despite negative extensive radiologic and pathologic evaluations. IVLBCL is often diagnosed in the post-mortem setting and this case highlights the often surreptitious presentation of IVLBCL and the need to maintain a high degree of suspicion. Eventual pathologic diagnosis was made and treatment initiated after relentless and thorough investigations.