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Intravascular Large B–cell Lymphoma Diagnosed Incidentally after a Renal Biopsy: A Case Report of a Rare and Elusive Malignancy

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Abstract Intravascular large B-cell lymphoma (IVLBCL) is a form of diffuse large B-cell lymphoma (DLBCL) characterized by the proliferation of malignant B-cells within the lumen of small blood vessels. With an incidence rate of one in a million, it is one of the rarest forms of DLBCL. This rarity, combined with the absence of extravascular tumor masses or circulating malignant cells in the peripheral blood and potential involvement of multiple organs, makes the diagnosis of IVLBCL exceptionally difficult. We discuss that case of a 64-year-old female who presented with symptoms of altered mental status, expressive aphasia, and fatigue. She was also found to have normocytic anemia with elevated hemolysis markers. Over a period of months, her neurological symptoms and anemia with elevated hemolysis markers persisted despite repeated hematological, infectious, and neurological workup. Overall, we hope to highlight the unusual clinical manifestations of IVLBCL, as early diagnosis and treatment can be lifesaving.

Keywords*: lymphoma, B-cell, hematological malignancy, oncology, renal malignancy*

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1. Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive form of diffuse large B-cell lymphoma (DLBCL). It is characterized by proliferation of malignant B-cells within the lumen of small blood vessels. The annual incidence of IVLBCL is fewer than 0.5 cases per 1,000,000 [1]. With an average age of diagnosis of 70-years-old, the median survival time is 13 months [1]. The 5-year survival rate is estimated to be 46.3% [2].

IVLBCL is associated with poor prognosis due to its nonspecific symptoms, difficulty in diagnosis, and aggressive nature. We present the case of an elderly female with hematological and neurological dysfunction that eluded clinicians for months before a delayed diagnosis of IVLBCL was made. This led to a fatal delay in treatment. By highlighting key clinical features that the malignancy presents with, we hope to increase awareness and subsequent early diagnosis of IVLBCL among clinicians.

2. Case Report

A 64-year-old Caucasian, Non-Hispanic female with a past medical history of hypertension, hyperlipidemia, type II diabetes mellitus, nephrolithiasis, and carpal tunnel syndrome presented to the hospital with a chief concern of altered mental status, expressive aphasia, and fatigue. These symptoms developed suddenly one month prior and progressively worsened since. She denied any recent trauma, falls, neuropathy, or loss of consciousness. She had no previous history of tobacco, alcohol, or illicit drug use. Magnetic resonance imaging (MRI) showed evidence of an acute lacunar infarct. She was also found to have paroxysmal atrial fibrillation and this was hypothesized to be the cause of the stroke. The hospital course was initially complicated by a tonic myoclonic seizure. Laboratory testing, electroencephalogram (EEG), and lumbar puncture did not reveal any abnormalities; she was started on Levetiracetam 500 mg twice a day intravenously.

During her admission, the patient was found to be anemic with a hemoglobin of 9.1 and a mean corpuscular volume (MCV) of 84. This normocytic anemia, combined with a decreased haptoglobin, elevated LDH, and elevated reticulocyte count, raised concern for active hemolysis. Coomb's testing was negative. Paroxysmal nocturnal hemoglobin, glucose-6-phosphate dehydrogenase deficiency, thrombotic thrombocytopenic purpura, hereditary spherocytosis, and cryoglobulin work-up was unrevealing. A peripheral blood smear and flow cytometry revealed an aberrant/abnormal population of monocytic

cells, raising concern for a myeloid disorder. Further imaging revealed hepatic steatosis and splenomegaly without any history of hepatic disease. A bone marrow biopsy was unrevealing. Given the extensive negative testing, the patient was given oral Prednisone 70 mg once a day while admitted with instructions for outpatient hematology follow-up.

Two months following discharge, the patient presented to the hospital with a chief complaint of bilateral lower extremity weakness, altered mental status, and expressive aphasia. Laboratory testing again revealed normocytic anemia with elevated hemolysis markers. Extensive hematological (including a repeat bone marrow biopsy), gastroenterological, and neurological workup did not reveal any abnormalities, and she was subsequently discharged on oral Prednisone with instructions for outpatient hematology follow-up.

One month later, the patient was readmitted for severe, unexplained dyspnea. There was suspicion for atypical hemolytic uremic syndrome due to persistent normocytic anemia and elevated hemolysis markers. A kidney biopsy was performed to assess for the presence of vascular microthrombi. However, the biopsy revealed numerous intracapillary large cells with high nucleus-cytoplasm ratios, atypical hyperchromatic nuclei with loose chromatin and prominent nucleoli, and CD-20 positive immunohistochemical staining. These findings were consistent with IVLBCL. She was scheduled to begin aggressive inpatient chemotherapy, however her condition progressively worsened and she ultimately succumbed to multi-organ failure/cardiac arrest.

3. Discussion

The pathogenesis of IVLBCL remains poorly understood. Studies have found that neoplastic B-cells may express molecules that promote adhesion to the endothelium of blood vessels–Cxc4 and Cxcx4 [1]. They may also lack molecules that promote lymphocyte extravasation into the periphery–Cxcr5, Ccr6, and Ccr7. Most malignant cells will express the CD20 marker characteristic of mature B-cells [3].

The occlusion of small blood vessels leads to a variety of nonspecific, yet deadly, symptoms in IVLBCL. There are two recognized forms, the Eastern and Western variants, each named after the geographical regions where they are most commonly encountered [2]. However, there may be considerable variation in individual presentation. The Eastern variant presents with cytopenias and hepatic and splenic dysfunction [3]. It is characterized by rapid progression and a median survival time of 2-8 months [3]. The Western variant presents with skin lesions, dementia, cerebral vascular accidents, and neuropathy [3]. It is often seen in younger patients (median age of 59-years-old) and has a less aggressive course [3] The median survival time in such cases is 3 years.

Laboratory studies most often reveal varying degrees of cytopenias [4]. Anemia is present in nearly 66% of cases, while thrombocytopenia and leukopenia occur in almost 25% of cases [4]. Thrombocytopenia will most often reflect bone marrow and hepatosplenic involvement [3]. Elevated serum lactate dehydrogenase (LDH), beta-2-microglobulin, sedimentation rate (ESR), and C-reactive protein (CRP) are also commonly found.

Due to the absence of extravascular tumor masses or circulating malignant cells in the peripheral blood, the diagnosis of IVLBCL is exceptionally difficult. The gold standard diagnostic test is excisional biopsy of pathological skin lesions [3]. However, such lesions are only present in a minority of cases. Random excisional biopsies of normal-appearing skin or biopsy of organs suspected to be affected by the malignancy can be done, but require a high suspicion for the malignancy. Further immunophenotyping is also required to distinguish IVLBCL from other types of lymphomas.

IVLBCL can involve any organ system. The CNS, bone marrow, spleen, and skin are the most common organs [5]. Previous reports have highlighted the success of suspected-organ biopsy [6,7,8]. However, high suspicion for involvement, combined with some degree of constitutional symptoms, must be present.

Renal involvement in IVLBCL is rare, with only a handful of reported cases [9,10,11,12]. The largest review found only 39 reported cases of kidney-biopsy proven renal involvement of IVLBCL. In nearly all these cases, signs of impaired renal function led to a biopsy, in comparison to our case where the patient had intact kidney function and we suspected atypical HUS. Renal failure (66%), proteinuria (92%), and nephrotic syndrome (33%) were also common [14]. However, none of these findings were present in our patient.

Given its nature, IVLBCL is considered disseminated and requires systemic therapy. The R-CHOP regimen, consisting of rituximab and a combination of cyclophosphamide, doxorubicin, vincristine, and corticosteroids is the most used treatment. Response rates with this regimen are estimated to be >90% [13]. In some cases, especially in younger patients or those with a higher disease burden, more intensive chemotherapy regimens may be considered, such as dose-adjusted Etoposide, Prednisone, Vincristine, Cyclophosphamide, and Doxorubicin (R-DA-EPOCH). Due to the high risk of central nervous system (CNS) involvement, prophylactic intrathecal chemotherapy or high-dose methotrexate is often administered to prevent or treat CNS relapse.

Prognosis for IVLBCL remains poor due to the aggressive nature of the disease and often delayed diagnosis. However, with appropriate treatment, particularly with R-CHOP, the prognosis has improved significantly, with some studies reporting a 2-year overall survival rate of 60-80% [14]. Relapse is common, particularly in patients who do not receive CNS prophylaxis. In such difficult cases, different salvage chemotherapy regimens can be utilized along with autologous stem cell transplants. Regular follow-up with imaging (PET/CT) and CNS evaluation is crucial in patients with IVLBCL due to the high risk of relapse. Long-term follow-up is needed to monitor for late relapses and secondary malignancies, which can occur in patients treated with intensive chemotherapy.

4. Conclusion

Our patient’s symptoms were most consistent with the

Western variant of IVLBCL. Her altered mental status and “strokes" were likely secondary to the malignancy. In this malignant, the aberrant cells are known to cause cerebral occlusive ischemia that mimics embolic strokes [15]. Her normocytic anemia, thrombocytopenia, and elevated hemolysis markers likely reflect renal involvement. However, she lacked cutaneous involvement, which further muddled her diagnosis.

IVLBCL is a rare, aggressive, and elusive malignancy. Given the possible widespread symptoms, and possibility of a normal bone marrow biopsy, the diagnosis requires shrewd suspicion. However, with treatment and early diagnosis, the malignancy can be effectively treated. Clinicians must recognize the two variants of IVLBCL and the possibility of widespread organ involvement. Furthermore, clinicians must be aware that, in the absence of cutaneous lesions, biopsy of normal skin and suspected organs should be performed as soon as possible.

References

[1] Fonkem E, Lok E, Robison D, Gautam S, Wong ET. The natural history of intravascular lymphomatosis. Cancer Med. 2014; 3(4): 1010-1024.

[2] Piccaluga PP, Paolini S, Campidelli C, Vianelli N, Bolondi L. A Western Case of Intravascular Large B-Cell Lymphoma as Unusual Cause of Persistent Fever. Case Rep Hematol. 2019; 2019: 1480710. Published 2019 Nov 16.

[3] Ponzoni M, Campo E, Nakamura S. Intravascular large B-cell lymphoma: a chameleon with multiple faces and many masks. Blood. 2018; 132(15): 1561-1567.

[4] Ponzoni M, Ferreri AJ. Intravascular lymphoma: a neoplasm of 'homeless' lymphocytes?. Hematol Oncol. 2006; 24(3): 105-112.

[5] Fonkem E, Lok E, Robison D, Gautam S, Wong ET. The natural history of intravascular lymphomatosis. Cancer Med. 2014; 3(4): 1010-1024.

[6] Mukherjee A, Ibrahim IF. Intravascular large B-cell lymphoma: an elusive diagnosis with challenging management. J Community Support Oncol. 2018; 16(6):e280-e282.

[7] Roy AM, Pandey Y, Middleton D, Broadfoot B, Sasapu A, Veeraputhiran M. Intravascular Large B-Cell Lymphoma: A Diagnostic Dilemma. Cureus. 2021; 13(7): e16459. Published 2021 Jul 18.

[8] Li Q, Li J, Yang K, et al. EBV-positive intravascular large B-cell lymphoma of the liver: a case report and literature review. Diagn Pathol. 2020; 15(1): 72. Published 2020 Jun 8.

[9] Sawa N, Ubara Y, Katori H, et al. Renal intravascular large B-cell lymphoma localized only within peritubular capillaries. Report of a case. Intern Med. 2007; 46(10): 657-662.

[10] Bai X, Li X, Wan L, Wang G, Jia N, Geng J. Intravascular large B-cell lymphoma of the kidney: a case report. Diagn Pathol. 2011; 6: 86. Published 2011 Sep 23.

[11] Kado H, Hatta T, Ueno R, et al. Nihon Jinzo Gakkai Shi. 2011; 53(7): 1046-1052.

[12] Desclaux A, Lazaro E, Pinaquy JB, Yacoub M, Viallard JF. Renal Intravascular Large B-cell Lymphoma: A Case Report and Review of the Literature. Intern Med. 2017; 56(7): 827-833.

[13] Ferreri AJ, Dognini GP, Bairey O, et al. The addition of rituximab to anthracycline-based chemotherapy significantly improves outcome in 'Western' patients with intravascular large B-cell lymphoma. Br J Haematol. 2008; 143(2): 253-257.

[14] Rajyaguru DJ, Bhaskar C, Borgert AJ, Smith A, Parsons B. Intravascular large B-cell lymphoma in the United States (US): a population-based study using Surveillance, Epidemiology, and End Results program and National Cancer Database. Leuk Lymphoma. 2017; 58(9): 1-9.

[15] Woo KA, Yoo D, Jung KH. Intravascular lymphoma as a Potential Cause of Recurrent Embolic Stroke of Undetermined Source. J Clin Neurol. 2019; 15(3):415-417.