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A case of triple hit lymphoma and rapid deterioration

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ABSTRACT

Triple hit lymphomas (THL) comprise a rare, heterogenous group of lymphomas and like many B-cell lymphomas, chromosomal translocations are biologic and diagnostic hallmarks of disease. Traditionally referred to as a subset of double hit lymphomas (DHL) in literature, THLs characteristically involve chromosomal rearrangements of c-MYC, BCL-2, and BCL-6 oncogenes. Many case series of high-grade B-cell lymphoma, especially MYC/BCL2 double hit lymphoma, have been described in the literature, but relatively few cases of triple hit lymphoma have been reported. Additionally, without chemotherapy, triple hit lymphomas are known to have a rapid clinical course and poor prognosis compared to double hit lymphomas. Here we present a case of MYC/BCL2/BCL6 triple hit lymphoma in a patient previously diagnosed with marginal B-cell lymphoma at stage IIA after biopsy of intra-abdominal lymph nodes status post one treatment with rituximab and bendamustine. Unfortunately, this patient had a rapid decline and presumed central nervous system (CNS) infiltration and passed away within 30 days of diagnosis.

Keywords: B-cell lymphoma, Lymphoma, Oncogenes

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INTRODUCTION

Triple hit lymphomas (THL) comprise a rare, heterogenous group of lymphomas and like many B-cell lymphomas, chromosomal translocations are biologic and diagnostic hallmarks of disease [1]. Classical diffuse large B-cell lymphoma (DLBCL) shows a rearrangement that involves the immunoglobulin heavy chain (IGH) locus (14q32) with different genes such as BCL2 (18q21). On the contrary, classical Burkitt lymphoma (BL) presents translocations joining MYC (8q24) and immunoglobulin genes, usually IGH [2]. Traditionally referred to as a subset of double hit lymphomas (DHL) in literature, THLs characteristically involve chromosomal rearrangements of c-MYC, BCL-2, and BCL-6 genes. However, unlike other B-cell lymphomas, THLs do not have uniquely specific morphological features but instead manifest as various non-Hodgkin lymphomas [3]. Specifically, THLs have morphologic, phenotypic, and genetic features intermediate between DLBCL, BL, and *follicular lymphoma* (FL) [1]. The overlapping morphology and complex cytogenetic findings in double and triple hit lymphomas thus led to a revision to a single entity of lymphomas in the 2016 World Health Organization (WHO) classification: "High grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements."

Generally, triple hit lymphomas are associated with worse clinical outcomes and have a high incidence of bone marrow and central nervous system involvement [1, 4]. However, despite their aggressive clinical behavior and

often, poor prognosis, rare confounding nonaggressive cases of THL have been documented with reported long-term survival [4].

Many case series of high-grade B-cell lymphoma, especially MYC/BCL2 double hit lymphoma, have been described in the literature, but relatively few cases of triple hit lymphoma have been reported. Here we present a case of MYC/BCL2/BCL6 triple hit lymphoma.

CASE REPORT

The patient was a 71-year-old male with a past medical history of hypertension, hyperlipidemia, and deep vein thrombosis (DVT) of the right lower extremity on apixaban. The patient originally presented with flank pain and constitutional B symptoms and was found to have intra-abdominal lymph nodes with mass compression of the right ureter resulting in right hydronephrosis. He underwent stent and nephrostomy tube placement and was discharged with a Foley catheter. Subsequent biopsy of the intra-abdominal lymph node was remarkable for stage IIA marginal B-cell lymphoma. One week following diagnosis, the patient began chemotherapy and received 1 treatment cycle with rituximab and bendamustine. However, the patient presented to the hospital 3 days later for concerns of hematuria from both his Foley catheter as well as nephrostomy bag. Apixaban was held at the time of this admission. The patient underwent a transurethral resection of the prostate (TURP) which revealed no overt bladder tumors; however, preliminary pathology results showed high grade lymphoma. He required 1 unit of packed red blood cells due to acute blood loss. The Foley catheter was discontinued on day 2 of hospital admission, but there was a recurrence of hematuria again on day 7 and day 10 after Apixaban was resumed. Apixaban was then held again. A coude catheter was placed at that time due to difficulty navigating the patient's anatomy post TURP.

The patient's hospital course was made complicated by an episode of sudden onset confusion and word-finding difficulties. Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain were both negative for any acute intracranial abnormalities. A video electroencephalography (vEEG) revealed left temporal delta activity suggesting an underlying area of neuronal dysfunction. The patient was started on Lacosamide and Levetiracetam at that time.

Overnight, on day 12 of hospital admission, the patient became febrile with a maximum temperature of 103.9F. Procalcitonin and lactic acid levels were normal. A chest X-ray revealed possible right lower lobe consolidation. A CT of the chest, abdomen, pelvis revealed right retroperitoneal and pelvic hematoma, mild to moderate right hydroureteronephrosis, omental infiltration concerning for metastatic disease, left iliac chain adenopathy and possible DVT in the right common femoral vein (Figures 1 and 2). No inferior vena cava (IVC) filter was placed because of external compression from a tumor preventing propagation of the clot. He was started on broad-spectrum antibiotics with vancomycin and piperacillin-tazobactam per infectious disease (ID) in the setting of unknown etiology of the patient's fevers at that time. Transthoracic echocardiogram (TTE) showed moderate to severe mitral regurgitation. Medical oncology was consulted and recommended pursuing a lumbar puncture with cytology to investigate for CNS infiltration but was ultimately inconclusive. At that time, ID and oncology were concerned for acute deterioration due to rapid progression of the patient's lymphoma as a peripheral smear revealed rare blasts and immature myeloid cells in addition to the radiographic evidence of rapid progression of metastatic disease. Prior to pursuing a bone marrow biopsy, the following day, the patient's TURP pathology results were finalized and was positive for triple hit lymphoma with MYC, BCL2, and BCL6 mutations. The patient's family decided to transition to comfort care at that time. He passed away shortly after, within three weeks of hospital admission.

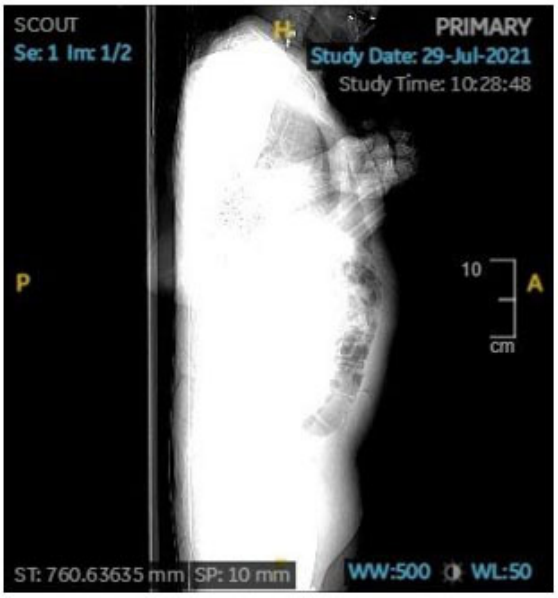

Figure 1: CT of the chest, abdomen, pelvis without contrast demonstrating omental infiltration concerning for peritoneal metastases, new from prior study.

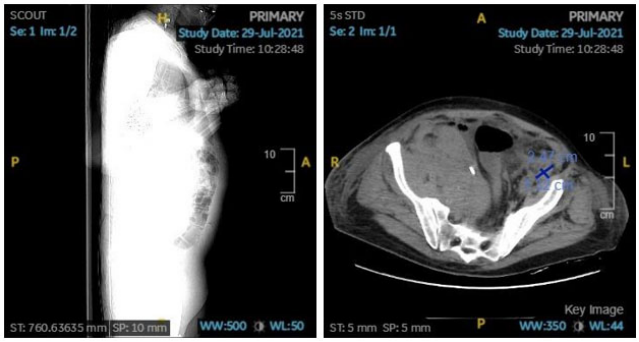

Figure 2: CT of the chest, abdomen, pelvis without contrast highlighting left iliac chain adenopathy (right).

DISCUSSION

It is well known that chromosomal translocations occur frequently in various types of B-cell non-Hodgkin lymphoma. Translocation of the BCL2 gene on chromosome 18q21 or BCL6 gene on chromosome 3q2 results in constant inactivation of apoptosis. Translocation of the c-MYG gene on chromosome 8q24 results in constant cell proliferation [1]. The presence of two gene rearrangements, commonly c-MYC and BCL2, defines a double hit lymphoma and more infrequently, the presence of all three gene rearrangements is distinctive of triple hit lymphomas. The exact prevalence of these lymphomas is unknown but both DHLs and THLs have an incidence of 8–10% among diagnoses of de novo DLBCL [5].

By definition, the diagnosis of THL requires cytogenetic studies that demonstrate rearrangements involving all three of the aforementioned genes. Initially, immunohistochemistry can be used to screen for and visualize positivity of MYC, BCL2, and BCL6 markers [6]. The most common diagnostic modality utilized to confirm the presence of these translocations is fluorescence in situ hybridization (FISH) [6, 7]. However, there is no specific guideline that outlines which select patients require FISH testing. Some believe that all patients with DLCBL should undergo genetic studies for detection of gene rearrangements, while others recommend a more conservative approach and suggest limiting testing to high-grade morphology cases or those which have >50% positivity on immunohistochemical staining [6]. Conversely, once the diagnosis of THL or DHL is established, it is recommended that all patients have diagnostic lumbar puncture as part of their initial staging, due to the high incidence of CNS involvement [7].

Unfortunately, despite early recognition and diagnosis of THL, prognosis is poor and overall survival without treatment is 0.2 to 1.5 years [4]. The biological aggressiveness of this malignancy is exemplified by the high likelihood of bone marrow and CNS infiltration [6]. In addition to CNS and bone marrow disease, P53 overexpression and older age (> 60 years) are associated with a worse prognosis [4]. Controversies persistent over the choice of first-line treatment for THL and include R-CHOP (rituximab plus cyclo-phosphamide, doxorubicin, vincristine, and prednisone) DA-R-EPOCH (dose adjusted, rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), R-ACVBP (rituximab, doxorubicin, cyclophosphamide, vincristine, bleomycin, and prednisone), and R-COPADEM (rituximab, cyclophosphamide, vincristine, prednisone, doxorubicin, and methotrexate) [5]. However, even with treatment, studies have demonstrated a median overall survival of 18 months and there are high rates of early treatment failure and relapse of death [8].

CONCLUSION

Overall, our case highlights a rare disease causing a rapid deterioration. The patient unfortunately only survived one month after his diagnosis. Despite initial chemotherapy treatment, his malignancy progressed at such a pace that could not facilitate any intervention.

REFERENCES

1. Pemmaraju N, Gill J, Gupta S, Krause JR. Triple-hit lymphoma. Proc (Bayl Univ Med Cent) 2014;27(2):125–7.
2. Motlló C, Grau J, Juncà J, et al. Translocation (3;8)(q27;q24) in two cases of triple hit lymphoma. Cancer Genet Cytogenet 2010;203(2):328–32.
3. Aukema SM, Siebert R, Schuuring E, et al. Double-hit B-cell lymphomas. Blood 2011;117(8):2319–31.
4. Kallen ME, Alexanian S, Said J, Quintero-Rivera F. Triple hit lymphoma: Rare cases with less dire than usual prognosis. Int J Surg Pathol 2016;24(8):709–14.
5. Laude MC, Lebras L, Sesques P. First-line treatment of double-hit and triple-hit lymphomas: Survival and tolerance data from a retrospective multicenter French study. Am J Hematol 2021;96(3):302–11.
6. Oliveira CC, Maciel-Guerra H, Kucko L, et al. Double-hit lymphomas: Clinical, morphological, immunohistochemical and cytogenetic study in a series of Brazilian patients with high-grade non-Hodgkin lymphoma. Diagn Pathol 2017;12(1):3.
7. Rosenthal A, Younes A. High grade B-cell lymphoma with rearrangements of Myc and BCL2 and/or BCL6: Double hit and triple hit lymphomas and double expressing lymphoma. Blood Rev 2017;31(2):37–42.
8. Huang W, Medeiros LJ, Lin P, et al. Myc/BCL2/BCL6 triple hit lymphoma: A study of 40 patients with a comparison to Myc/BCL2 and MYC/BCL6 double hit lymphomas. Mod Pathol 2018;31(9):1470–8.

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Author Contributions

Jasmit Walia – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Timothy Daly – Acquisition of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Kunal Bhagatwala – Conception of the work, Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.