Development of Gray Zone Lymphoma During Remission of Classical Hodgkin Lymphoma

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Introduction :

Hodgkin lymphoma (HL) is the most common occurring lymphoma of adolescents and young adults with approximately 8,500 new cases annually. Although HL is largely curable with frontline treatment, many patients will not have a complete response or will later relapse. Recurrence of HL often occurs within the first two years in remission. However, recurrence rates vary widely and are largely dependent on lymphoma type, stage, patient age, and other variables.

In this case, we discuss an individual with HL in remission for over a decade, who was found to have gray zone lymphoma (GZL). GZL is a rare lymphoma with features intermediate between classical Hodgkin lymphoma (cHL) and diffuse large B-cell lymphoma (DLBCL), but cannot be classified as one or the other. We report this case to discuss the recurrence of HL that progressed and transformed into GZL.

Case Description:

A 75-year-old male with a significant history of HL in remission, presented with sudden onset bilateral lower extremity weakness. The patient had associated back pain, three weeks of fatigue, decreased appetite, and decreased urine output for the last two days. He denied nausea, vomiting, fever, chest pain, cough, and bowel or bladder incontinence.

Vital signs were significant for blood pressure of a 97/56 mm Hg and fever of 102.5 °F. Pertinent physical examination findings include hepatomegaly and diffuse cervical, axillary, and inguinal lymphadenopathies. Initial pertinent labs were leukocytosis of 37,600 u/L, lactic acid of 6.4 (0-1.99 mmol/L), hyponatremia of 133 u/L, and bicarbonate of 18 (22-30 mEq/L) with a normal anion gap.

The patient was admitted for sepsis of unknown origin and was started on vancomycin and meropenem. Ultrasound of the right leg was consistent with deep venous thrombosis. CT of chest and abdomen with and without contrast revealed pulmonary embolism of the left lung and lymphadenopathy in the chest and abdomen, in addition to numerous retroperitoneal soft tissue masses suspicious for enlarged lymph nodes. The patient was started on therapeutic enoxaparin.

Cervical lymph node biopsy (Figure 1) revealed CD30+ large cell hematolymphoid neoplasm with features intermediate between DLBCL and HL - otherwise classified as GZL. Since there is no standard treatment for GZL, the patient was given cHL chemotherapy regimen of ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine). The patient received 1 dose of ABVD during the hospital stay. Although the patient was initially admitted for sepsis, pan cultures were unremarkable, suggesting that his symptoms were attributable to malignancy.

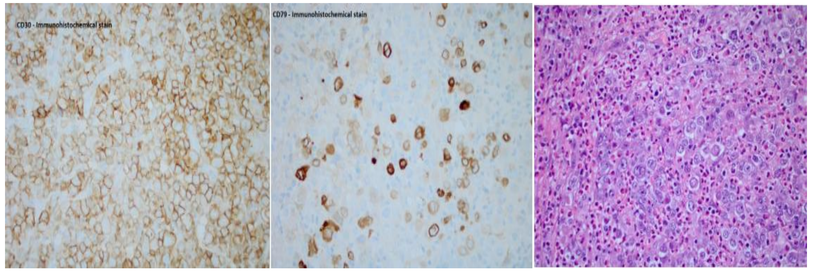

Figure 1: Cervical lymph node biopsy with **(A)** immunohistochemical stain showing strong expression of CD30, **(B)** immunohistochemical stain showing strong expression of CD79, and **(C)** H&E stain showing diffuse infiltrate of large, highly atypical cells with prominent areas of necrosis, prominent nucleoli, and multilobulated nuclei (Reed-Steinberg cytomorphology). Confluent sheets of mononuclear tumor cells are predominant.

Discussion:

We discuss this case to describe the recurrence and progression of HL to GZL. Very few cases of GZL have been described in the literature. The diagnosis of GZL has not been established, as there is no consensus on the clinical characteristics, treatment regimen, and prognosis.

To date, a treatment regimen for GZL remains to be elucidated due to the sparsity of this phenomenon. Because GZL shows intermediate characteristics between cHL and DLBCL, it is currently treated as cHL, as presented in this case.

There have been several reports that have shown response to PD-1 inhibitors such as pembrolizumab and nivolumab, however, due to the low incidence of this malignancy, a clear treatment plan has yet to be established.

References:

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