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Grey Zone Lymphoma, Diagnostic and Therapeutic Challenges: A Rare Case Report

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Abstract Grey zone lymphoma (GZL) remains a challenging diagnosis because it has mixed features of diffuse large B cell lymphoma (DLBCL) and classic Hodgkin lymphoma (cHL). In this case report, we present a 69-year-old man who was diagnosed with GZL after an incidental finding of right axillary lymphadenopathy on Computed tomography (CT) scan during a recent hospitalization for an ischemic stroke. Excisional biopsy of the axillary node pathology was consistent with classic Hodgkin lymphoma (Nodular Sclerosing type). Subsequent Positron Emission Tomography (PET)/CT scan showed adenopathy above and below the diaphragm, as well as possible liver, bone, and colon disease. Liver biopsy revealed pathology consistent with DLBCL contrary to the Hodgkin disease seen on axillary biopsy resulting in an eventual diagnosis of GZL on further pathology review.

Keywords: *Grey zone lymphoma, B cell Lymphoma, classic Hodgkin Lymphoma*

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1. Introduction

GZL is an extremely rare hematologic malignancy that was initially described in 2005 and classified as a distinct entity by the World health organization (WHO) in 2008 [1,2,3]. It occurs mostly in young men [4] and requires extensive sampling for correct diagnosis. Although It has shared features of both DLBCL and cHL, it has a more aggressive course and inferior survival compared to each of them. It typically involves the mediastinum in young males (mediastinal grey zone lymphoma, MGZL). However, non-mediastinal presentation of GZL (NMGZL) is recognized more frequently in older patients [1]. We present our case as an example of the diagnostic challenge GZL poses, as well as the importance of making the diagnosis, as it has treatment implications.

2. Case Presentation

This is a case of a sixty-nine-year-old man with a past medical history of Type II diabetes mellitus and hyperlipidemia who presented to our emergency department for stroke symptoms including facial droop and dysarthria. During his hospitalization, he was incidentally found to have right axillary lymphadenopathy on a CT scan of the neck. He underwent an excisional lymph node biopsy. Pathology showed Classic Hodgkin lymphoma (Nodular Sclerosing type) (Figure 1). Five weeks following this admission, he had a PET scan for further staging. It showed lymphadenopathy above and below the diaphragm as well as a disease within the Liver, colon, and bone.

PET scan was concerning for possible second colon malignancy with liver metastasis, given that the patient did not have a colonoscopy in at least 5 years. The patient was slated to undergo Liver biopsy and colonoscopy, however, he developed right upper extremity deep vein thrombosis as a complication related to mass effect from his axillary lymphadenopathy that required thrombectomy and stent placement. Due to the inability to interrupt anticoagulation and antiplatelet therapy for at least 4 weeks, colonoscopy and liver biopsy were delayed. The patient had a liver biopsy performed two and a half months following his initial presentation. Biopsy of the liver showed Non-Hodgkin lymphoma with morphology consistent with a CD30 positive non-germinal center DLBCL (Figure 2). This was a different read from the classic Hodgkin Lymphoma read on previous axillary biopsy. Due to the discrepancy between the axillary and the liver biopsy, the case was presented at a malignant hematology tumor board at a tertiary care center. The consensus was that this is most likely a Grey-Zone lymphoma as it combines features of Hodgkin disease and DLBCL. It was determined that patient should be treated with six cycles of R-CHOP a traditionally used therapy for non-Hodgkin Lymphoma.

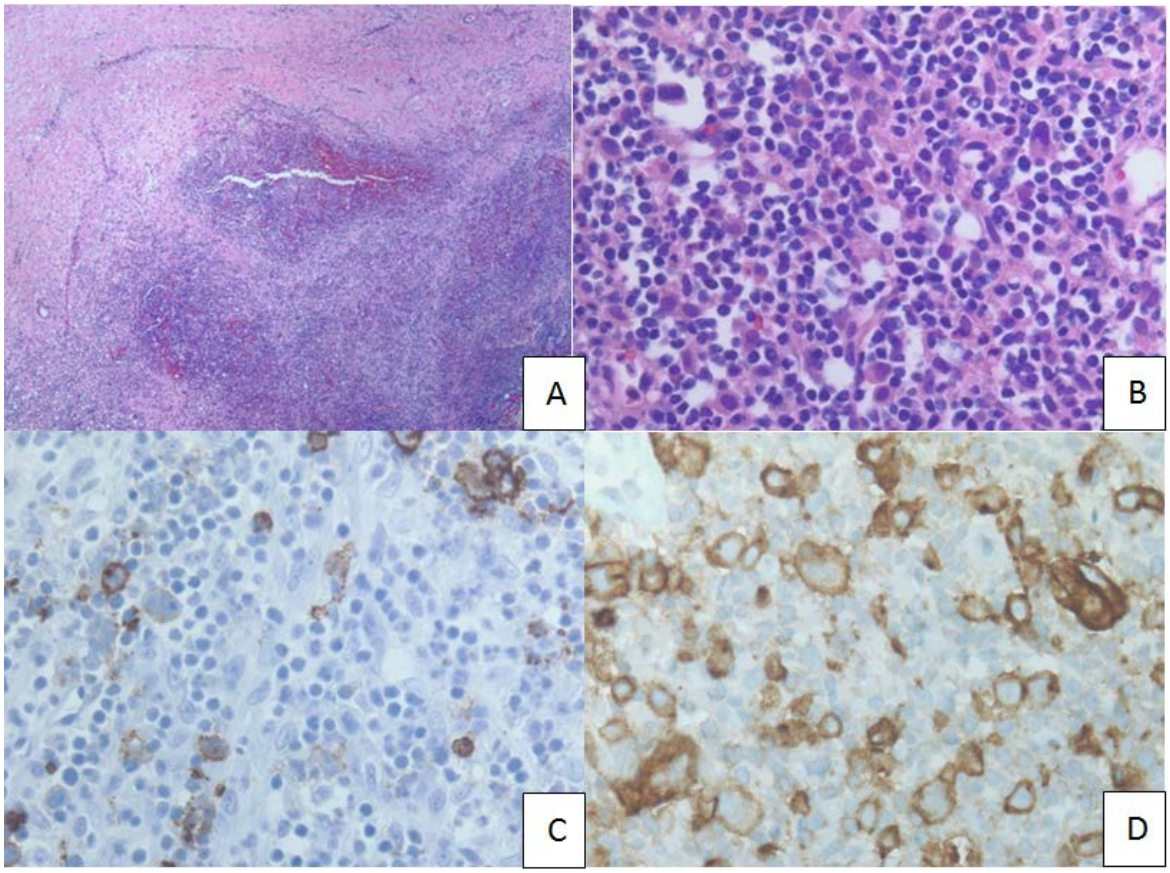

Figure 1. Axillary Lymph node biopsy showing: [A] Architectural effacement by collagenous Bands forming nodules. [B] A polymorphous infiltrate with scattered large atypical Cells.[C] Large cells are highlighted by CD30.[d] Large cells are variably Positive for CD20

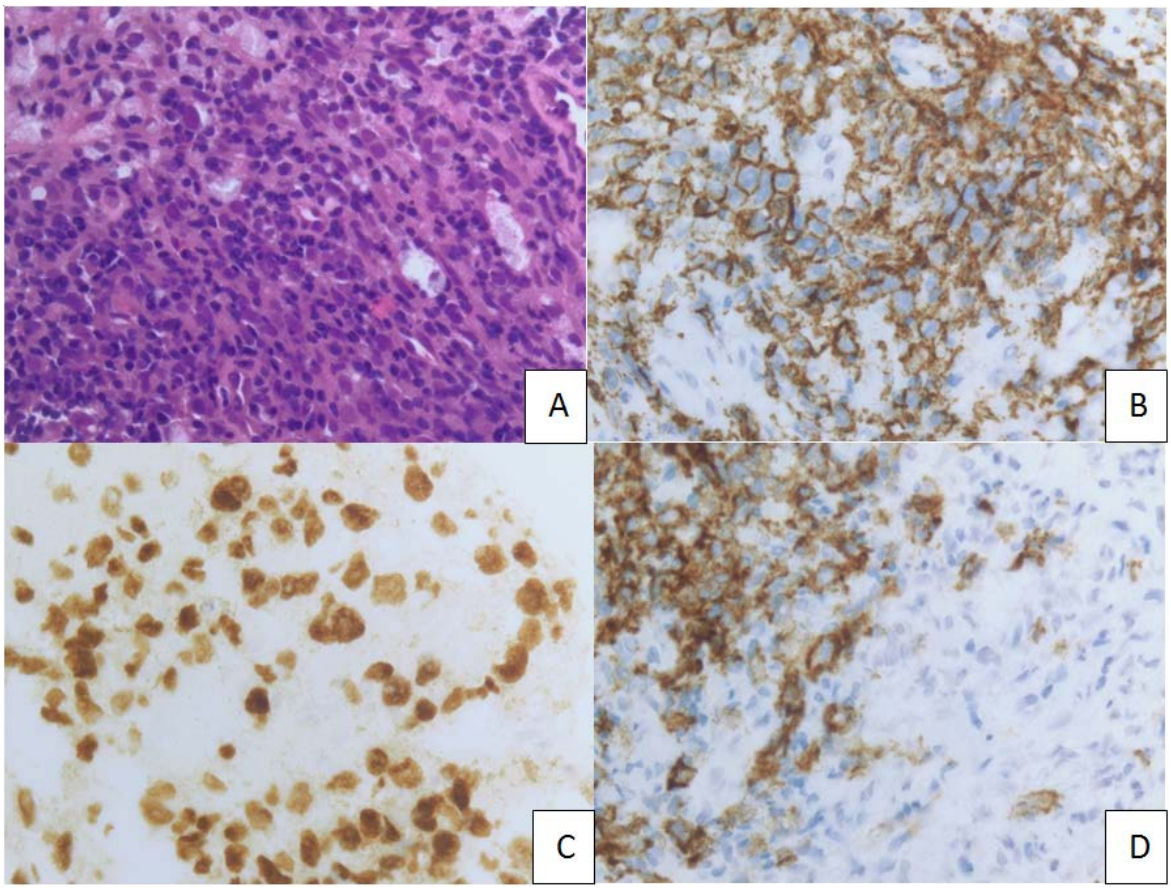

Figure 2. Liver biopsy showing: [A] Scattered atypical large cells with oval nucleus and prominent nucleolus in a polymorphous background of histocytes, lymphocytes, eosinophils and neutrophils. [B] Large cells show membranous staining with CD30.[C] Large cells show membranous staining with CD20.[D] large cells show variable intensity of nuclear staining with PAX5

3. Discussion

Grey zone lymphoma is a distinct type of B cell lymphoma with mixed features of diffuse large B cell lymphoma and classic Hodgkin lymphoma. It is more common in men and can occur at any age {3-4}. Clinicians are usually guided by the initial biopsy result. GZL should also be suspected when there is failed response to initial treatment. Repeating biopsy with extensive sampling using either invasive excisional or incisional biopsy rather than needle core biopsy is required to make a correct diagnosis [4]. Immunophenotypically, GZL has mixed features of cHL and DLBCL. Most GZL has a strong expression of CD20, CD30, MUM1, and PAX5. A small subgroup may show loss of CD20 [1,2,4].

In our patient, axillary lymph node biopsy immunostains were positive for CD 20, CD 30, CD 15, and PAX5 which was consistent with a diagnosis of nodular sclerosing Hodgkin lymphoma. On the other hand, liver biopsy immunostains were positive for CD30, CD20, PAX5, MUM1, BCL2, BCL6, and N-MYC positive, consistent with diffuse large B cell lymphoma. Because of the overlapping morphological and immunophenotypical features in our patient, the diagnosis of GZL was made.

Due to the rarity of the disease, management is very challenging. Patients were primarily treated with either Hodgkin lymphoma regimens like ABVD (doxorubicin, bleomycin, vincristine, and dacarbazine) or DLBCL regimens like R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) or DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin). Some data has shown that progression free survival (PFS) was best for patients with GZL treated according to a DLBCL regimen [2]. Our case was presented at a hematology malignancy tumor board. Consensus with the group to start treatment with R-CHOP (Non-Hodgkin Lymphoma) regimen based on the pathology discrepancy and the available data supporting the use of DLBCL regimens.

Other treatment options such as hematopoietic stem cell transplantation and Brentuximab Vedotin (BV) (a monoclonal anti-CD30 antibody) can be used in relapsing and refractory cases of GZL {1-4}. Radiotherapy can be used for adenopathy or bulky mass, however, there is no sufficient evidence to support the efficacy of adjuvant radiotherapy for GZL [3].

4. Conclusion

GZL is a rare hematologic malignancy that requires extensive sampling for correct diagnosis. Currently, morphologic and immunophenotypic evaluation by an expert in conjunction with knowledge of the disease entity itself are required to reach the final diagnosis. Further studies are needed to determine the optimal treatment strategy, but the first step is to make practitioners aware of the disease itself.

Conflict of Interest

None of the authors have any conflicts of interest to declare.

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