Case Report

A Case Report: Remission of Gray Zone Lymphoma on R-CHOP and Adjuvant Radiation Treatment

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Abstract
Gray zone lymphoma (GZL) is a rare hematological malignancy known to usually occur in young men. GZL has features intermediate between diffuse large B-cell lymphoma and classical Hodgkin’s lymphoma. This case report describes a 55-years old woman with GZL. Remission was achieved through R-CHOP chemotherapy and adjuvant radiation treatment over 22 months. This case is exemplary for successful management of GZL with R-CHOP chemotherapy.

Keywords: Gray zone lymphoma; B-cell lymphoma; R-CHOP chemotherapy; Adult granulosa cell tumor

1. Introduction
Gray zone lymphoma (GZL) is a distinct type of B-cell lymphoma with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin’s lymphoma (HL) [1]. GZL is extremely rare and occur mostly in young men [2]. Herein, we present a case of a middle-aged woman with GZL to add to the scant body of knowledge for this rare disease.

2. Case Presentation
A 55-years old woman presented with 6 weeks’ history of dull aching abdominal and back pain. She also has been experiencing tingling and numbness from her feet all the way up to her navel. She reported multiple episodes of fall due to sudden loss of coordination. Her medical history was significant for rheumatoid arthritis and atrial fibrillation. A computerized tomography (CT) with contrast demonstrated filling defects in the liver and spleen, consistent with lymphoma. Multiple small lymph nodes (LN).
The largest LN measured about 2.9 cm in the right axilla. The LNs varied in size between 4.6 to 9.6 mm at the periaortic and aortopulmonary window. The LNs at the axillary regions were palpable and felt firm and rubbery in the physical examination. Excisional biopsy performed for a LN (1.5 cm) in the left axilla to further explore the abnormal findings.

The H&E stained section showed a LN in which the normal nodal architecture has been diffusely effaced by a proliferation of small lymphocytes and histiocytes in a highly vascular background. Scattered throughout the lymphoid infiltrates are large atypical cells with convoluted nuclear contours and prominent nucleoli; some of these cells resembled Reed-Sternberg cells. Immunochemical study showed that the diffusely scattered large atypical cells strongly express CD 45 and CD 20. An anti CD-3 stain showed that greater than 90% of the lymphocytes are small T-cells. These immunomorphologic findings were consistent with Diffuse Large B-Cell Lymphoma (DLBCL). Her bone marrow (BM) biopsy was taken from her hip on both sides. The left BM had no hematopoietic cells.

The right BM was hyperplastic and showed diffuse infiltrates of lymphoid cells mixed with small numbers of eosinophil and plasma cells. The number of lymphoid cells accounted for 24% of the hematopoietic cells. Nonetheless, other hematopoietic cells were moderately reduced in numbers. Iron store was also reduced in amount. These characteristics are consistent with nodular sclerosis type of Hodgkin’s disease.

Combining the LN and BM findings, this neoplasm was classified as gray zone lymphoma. The patient was treated with a regimen known as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). Following 22 months of systemic chemotherapy with adjuvant radiation treatment, the gray zone lymphoma eventually went into remission.

3. Discussion
Our case is exemplary for successful management of gray zone lymphoma (GZL). Our patient had excellent therapeutic outcome to R-CHOP chemotherapy and adjuvant radiation treatment. By reporting this case, we hope to help expanding the knowledge on therapeutic options for GZL. Since the formal identification of GZL by World Health Organization (WHO) in 2008, definition of this disease is still rapidly evolving [2]. The pathophysiology underlying this disease remains poorly understood due to its recent recognition in the medical community and rarity. For the same reason, there is no well-established treatment for this malignancy.

However, like our case, some oncologists had good outcome by adding rituximab to standard chemotherapy regimens, such as DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) and CHOP, for GZL positive for CD20 [3]. Another chemotherapeutic regimen reported to be effective in GZL is doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) with rituximab [4].
Hematopoietic stem cell transplantation (HSCT) is reserved for patients with GZL refractory to chemoradiotherapy. Brentuximab vedotin is a monoclonal anti-CD30 antibody that can be used to treat relapsing GZL [5]. There is no sufficient evidence to support the efficacy of adjuvant radiotherapy for GZL.

However, the use of radiotherapy is generally recommended for GZL localized to mediastinum or bulky mass of GZL with diameter greater than 10 cm [4, 5]. Autologous peripheral blood stem cell transplantation is an alternative option available for adjunctive treatment [6]. At the time of diagnosis, majority of GZL mass is larger than 10 cm in diameter and confined to mediastinum. Early detection and intervention is critical as the mass can cause superior vena cava syndrome and progress to involve distant sites, such as kidneys, liver, adrenal glands, brain, and spinal cord [7]. In our patient, GZL was found after it spread to multiple organs. However, she could achieve remission with R-CHOP chemotherapy and adjuvant radiation treatment.

References
