SPLENIC MARGINAL ZONE LYMPHOMA – A Case Report

ABSTRACT:

BACKGROUND: Out of the various malignant tumours originating from the lymphatic hematopoietic system, lymphoma is one such important entity. It is divided into Non-Hodgkin's Lymphoma (NHL) and Hodgkin Lymphoma (HL) depending on its cell source. A very rare type of malignant variant of lymphoma is the primary splenic lymphoma, involving exclusively the spleen and splenic hilar lymph nodes. Moreover, splenic marginal zone lymphoma (SMZL) is even more infrequent. SMZL is an uncommon chronic B lymphocyte proliferative disease, which only accounts for about 1–2% of all non-Hodgkin's lymphoma. The mean age of SMZL incidence is about 65 years. There is no known significant gender predominance. A quarter of patients with early diagnosed SMZL have known to have vague symptoms like abdominal pain and distention; and other patients may be accompanied by loss of weight, malaise, cachexia, splenomegaly, or other manifestations.

CONCLUSION: Although, a good prognostic outcome is what is usually expected from most patients of Splenic Marginal Zone Lymphoma who undergo splenectomise, an aggressive transformation leading to a worse direction cannot be ruled out. SMZL is very challenging to be diagnosed pre-operatively due to the lack of specificity in clinical presentation.

KEYWORDS: lymphoma, primary splenic lymphoma and loss of weight

UNDER PEER REVIEW

INTRODUCTION

A very rare type of malignant variant of lymphoma is the primary splenic lymphoma, involving exclusively the spleen and splenic hilar lymph nodes. Moreover, splenic marginal zone lymphoma (SMZL) is even more infrequent[1]. SMZL is an uncommon chronic B lymphocyte proliferative disease, which only accounts for about 1–2% of all non-Hodgkin's lymphoma. The mean age of SMZL incidence is about 65 years[2]. There is no known significant gender predominance. A quarter of patients with early diagnosed SMZL have known to have vague symptoms like abdominal pain and distention; and other patients may be accompanied by loss of weight, malaise, cachexia, splenomegaly, or other manifestations[3]. The origin of the cells of SMZL is believed to originate from memory B lymphocytes in the marginal zone of the secondary lymphoid follicles, yet more research is undertaken to prove its certainty[4].

Researchers are still exploring the pathogenesis and progression of the disease but there has been some evidence that it is related to changes in the short arm of chromosome 7. Even though SMZL is a slow-growing lymphoma, one-tenth of the affected individuals can progress to diffuse large B cell lymphoma, deteriorating the condition of the patient and developing symptoms[5]. SMZL progresses with a relatively better prognosis than other types of lymphomas. The median survival time of the disease is known to be 10 years provided the disease doesn't progress or there is no obvious hypersplenism[6]. Considering how less the

incidence of this tumor is, very little is known about the diagnostic and therapeutic approach of the patient and thus the treatment modalities are constrained to long-term follow-up, keeping in mind the absence of hypersplenism or disease progression. Generally, surgical excision for both diagnostic and therapeutic purposed, along with postoperative adjuvant chemotherapy and/or radiotherapy is recommended to improve the prognosis[7]. To date, SMZL clinically falls under Non-Hodgkin's Lymphoma and therefore, it is classified as Stage III Non-Hodgkin's Lymphoma as the spleen is involved. Though NHL is known to have an aggressive nature, SMZL is relatively indolent with a favorable prognosis[8]. Given this background, we herein reported a case of SMZL of a 49-year-old male with gross hepatosplenomegaly.

Case Report

A 49-year-old male was admitted with complaints of generalized weakness, cough, and abdominal pain off and on for 1-2 months. On examination general condition was moderate, afebrile, pulse was 80 beats/min, blood pressure - 130/90 mmHg, respiratory rate - 22/min, pallor was present, while the cardiovascular, nervous and respiratory system examination revealed no abnormal findings. The abdomen was soft and non-tender. CT abdomen was advised which shows gross hepatosplenomegaly and a few mildly enlarged pedophiliac and paraaortic lymph nodes. To make a definite diagnosis, a splenectomy was planned after 7 days.

Splenectomy with lymph node biopsy with liver wedge biopsy was performed and the specimen was sent for histopathology. The Department of Pathology received a specimen of spleen measuring 26 x 17 x 7 cm in size. On the cut section, it was colored reddish-brown. On microscopy, the spleen shows congestion of sinuses and effacement of architecture by centrocytes-like cells. These cells are having cleaved nuclei and eosinophilic cytoplasm. Follicle formation was seen, so reported as suggestive of primary splenic lymphoma with infiltration in liver and lymph nodes. Immunohistochemistry was advised for confirmation which was reported as Splenic Marginal Zone Lymphoma (SMZL) with lymph node involvement and liver infiltration. It was positive for ki-67, CD20, and BCL-2 and negative for CD3, CD5, cyclin D1, and CD23. The oncologist decided to go with 6 cycles of chemotherapy. After 2 years of follow-up, the patient showed no signs of recurrence and spread.

Discussion

SMZL forms less than 2 % of all cases of Non-Hodgkin's Lymphoma and thus is known to be a rare form of torpid B-cell neoplasm, affecting the bone marrow, spleen, and also the peripheral blood[7]. The definitive diagnosis of this condition pre-operatively has been demanding in the early stages of the disease due to the lack of specific clinical features, imaging, or laboratory findings and by the time patients present with symptomatic splenomegaly and cytopenia, the disease has already advanced in course. This fact makes histopathology the only modality to give a definitive diagnosis. Splenectomy alone has been enough for patients with SMZL to have a maintained remission for several years[8].

UNDER PEER REVIEW

Splenomegaly, sometimes very massive that the spleen weighs more than 2 kilograms is also seen. On microscopy, there is a proliferation of the lymphoma cells thereby replacing the white pulp and also infiltrating into the marginal zone. At times, there is infiltration in the splenic sinuses of red pulp which can be in a patchy or diffuse fashion[9]. The peripheral blood smear shows characteristic villous lymphocytes having basophilic cytoplasm with short polar villi, round nuclei with condensed chromatin. This feature is needed to differentiate SMZL from hairy cell leukemia. SMZL is immunophenotypically positive for CD79a, CD20, BCL-2 and IgM. It is negative for BCL-6, CD5, CD10, CD43, and CD103. Immunohistochemistry and flow cytometry is considered the gold standard to rule out other lymphomas[10].

Though SMZL is known to have a gradual disease progression, it is mandatory to maintain a patient follow-up to avoid the development of an aggressive type of lymphoma, like diffuse large cell lymphoma which has a common occurrence in a SMZL leading to a worse prognosis. Involvement of the spleen, lymph nodes, bone marrow, liver, and central nervous system is evidence of high-grade lymphoma[8-11].

Recent guidelines suggest the intervention of only those cases who present with symptomatic splenomegaly, or other systemic presentations, cytopenia, or aggressive form of the nodal disease. Splenectomy has zero downed as the choice for the management for the definitive diagnosis and treatment of SMZL. Parallelly, the administration of anti-CD20 monoclonal antibody-like rituximab, alone or in combination with chemotherapy, has also been recognized as a treatment option. Recently, infection with Hepatitis C virus has also been reported to have a relation with the etiology of SMZL, thereby, prompting ways for novel treatment options that include antiviral agents[12-15].

CONCLUSION

Although, a good prognostic outcome is what is usually expected from most patients of Splenic Marginal Zone Lymphoma who undergo splenectomise, an aggressive transformation leading to a worse direction cannot be ruled out. SMZL is very challenging to be diagnosed pre-operatively due to the lack of specificity in clinical presentation. With this case report, we want to encourage further study on this lesion to understand the disease progression and thus channelize the treatment accordingly.

Ethical clearance: Taken from institutional ethics committee

REFERENCES

1. Vallisa D, Bernuzzi P, Arcaini L, Sacchi S, Callea V, Marasca R, Lazzaro A, Trabacchi E, Anselmi E, Arcari AL, et al. Role of anti-hepatitis C virus (HCV) treatment in HCV-related, low-grade, B-cell, non-Hodgkin's lymphoma: a multicenter Italian experience. J Clin Oncol. 2005;23:468–73.

UNDER PEER REVIEW

2. Algara P, Mateo MS, Sanchez-Beato M, Mollejo M, Navas IC, Romero L, Solé F, Salido M, Florensa L, Martínez P, et al. Analysis of the IgV(H) somatic mutations in splenic marginal zone lymphoma defines a group of unmutated cases with frequent 7q deletion and adverse clinical course. Blood. 2002;99:1299–304.
3. Ozawa MG, Bhaduri A, Chisholm KM, et al. A study of the mutational landscape of pediatric-type follicular lymphoma and pediatric nodal marginal zone lymphoma. Mod Pathol. 2016;29(10):1212-1220. doi:10.1038/modpathol.2016.102
4. Mateo M, Mollejo M, Villuendas R, Algara P, Sanchez-Beato M, Martínez P, Piris MA. 7q31-32 allelic loss is a frequent finding in splenic marginal zone lymphoma. Am J Pathol. 1999;154:1583–9.
5. Thieblemont C, Felman P, Berger F, Dumontet C, Arnaud P, Hequet O, Arcache J, Callet-Bauchu E, Salles G, Coiffier B. Treatment of splenic marginal zone B-cell lymphoma: an analysis of 81 patients. Clin Lymphoma. 2002;3:41–47.
6. Daniel, V. ., & Daniel, K. (2020). Diabetic neuropathy: new perspectives on early diagnosis and treatments. *Journal of Current Diabetes Reports*, *1*(1), 12–14. https://doi.org/10.52845/JCDR/2020v1i1a3
7. Thieblemont C, Felman P, Callet-Bauchu E, Traverse-Glehen A, Salles G, Berger F, Coiffier B. Splenic marginal-zone lymphoma: a distinct clinical and pathological entity. Lancet Oncol. 2003;4:95–103.
8. Daniel, V., & Daniel, K. (2020). Perception of Nurses' Work in Psychiatric Clinic. *Clinical Medicine Insights*, *1*(1), 27-33. https://doi.org/10.52845/CMI/2020v1i1a5
9. Chacón JI, Mollejo M, Muñoz E, Algara P, Mateo M, Lopez L, Andrade J,Carbonero IG, Martínez B, Piris MA, Cruz MA. Splenic marginal zone lymphoma: clinical characteristics and prognostic factors in a series of 60 patients. Blood. 2002;100:1648–54.
10. Camacho F et al. Progression to large B-cell lymphoma in splenic marginal zone lymphoma: a description of a series of 12 cases, Am. J. Surg. Pathol. 2001 (25): 1268–1276.
11. Conconi, S et al., Histologic transformation inmarginal zone lymphomas, Ann. Oncol. 2015(26): 2329–2335.
12. Dierlamm J, Pittaluga S, Wlodarska I et al. Marginal zone B-cell lymphomas of different sites share similar cytogenetic and morphologic features. Blood 1996;87:299–307.
13. Arcaini L. Splenic marginal zone lymphoma: from geneticsto management, Blood. 2016 (127): 2072–2081.
14. Isaacson P et al. The histopathology of spleniclymphoma with villous lymphocytes, Blood. 1994; 84: 3828–3834.
15. Mollejo M et al. Splenic marginal zone lymphoma: a distinctive type of low-grade B-cell lymphoma. A clinicopathological study of 13 cases, Am. J. Surg. Pathol. 1995; 19: 1146–1157.

UNDER PEER REVIEW