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"*Lien Vasti*"- A Case of Splenic Marginal Zone Lymphoma

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Authors' contributions

This work was carried out in collaboration among all authors. Authors RKP, JM and NE participated in the preoperative and postoperative clinical care of the patient. Authors MSS and RG performed the patient's splenectomy. All authors, participated in the acquisition, analysis, or interpretation of the data, drafting and revising of the manuscript and the final approval of the paper. Furthermore, all authors agreed to be accountable for the integrity of the case report and have read and approved the final manuscript.

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Case Study

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ABSTRACT

Splenic marginal zone lymphoma (SMZL) is a rare and uncommon subtype of B cell Non Hodgkin's lymphoma (NHL) that may present with marked splenomegaly with CD20 rich B-cells in blood and bone marrow and absent generalized lymphadenopathy. Here, we present a case of massive splenomegaly with pancytopenia, normal peripheral blood smear (PBS) and bone marrow picture, with generalized lymphadenopathy.

Case Capsule: A 63-year-old lady, presented with hepatosplenomegaly, loss of appetite & weight for 4 years, with generalized lymphadenopathy for 2 months. PBS and bone marrow aspiration revealed simple pancytopenia and normal picture. Intra operatively, the spleen measured 43 centimetres (cms) in (length) and weighed 7.2 kilograms (kgs), making it the longest as well as

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the largest spleen ever surgically removed, in Asia and second largest in the world. The immuno-histochemistry (IHC) was quite consistent, with splenic marginal zone lymphoma.
Conclusions: SMZL is a rare condition, with an unexpected course that leads to progressive splenomegaly. In a case of SMZL, without blood and bone marrow involvement with symptoms secondary to massive splenomegaly and hypersplenism, upfront splenectomy rapidly alleviates symptoms of hypersplenism and further, aids in histological diagnosis for systemic chemotherapy. Management of SMZL requires a multidisciplinary approach with chemotherapy +/- splenectomy to achieve optimal outcomes.

Keywords: Splenectomy; longest; non hodgkin's lymphoma; splenic marginal zone lymphoma; multi disciplinary team; immuno histochemistry.

1. INTRODUCTION

Splenic marginal zone lymphoma (SMZL), is a rare and uncommon subtype of NHL that may present with asymptomatic splenomegaly with or without cytopenias and lymphadenopathy. It ~~r~~equires a multidisciplinary management with chemotherapy, monoclonal antibodies and splenectomy based on the symptoms of the patient. Here, we present a case of a very slowly progressive and symptomatic massive splenomegaly with pancytopenia, generalized lymphadenopathy and which, underwent successful surgical removal, of the largest known spleen in Asis.

2. PRESENTATION OF CASE

A 63-year-old lady with history of weight loss presented with slowly enlarging hepato splenomegaly Fig. 1.

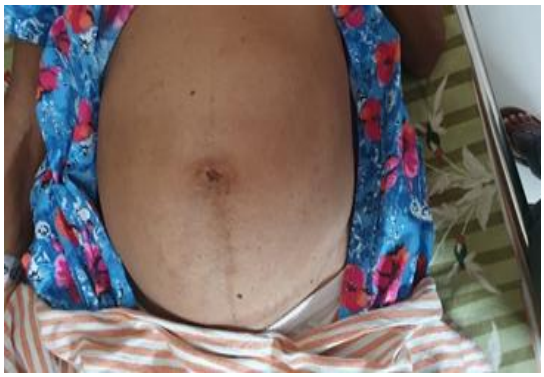

Fig. 1. Image demonstrating massive splenomegaly reaching well into right iliac fossa

She also–complained of worsening nausea and early satiety without fever, chills, night sweats and two month history of weight loss with generalized lymphadenopathy. Laboratory evaluation was significant for anemia (hemoglobin 6.0 g/dl), thrombocytopenia (25,000/mm^3), and ~~l~~eucopenia (1500/mm^3). Peripheral blood picture showed pancytopenia Fig. 2.

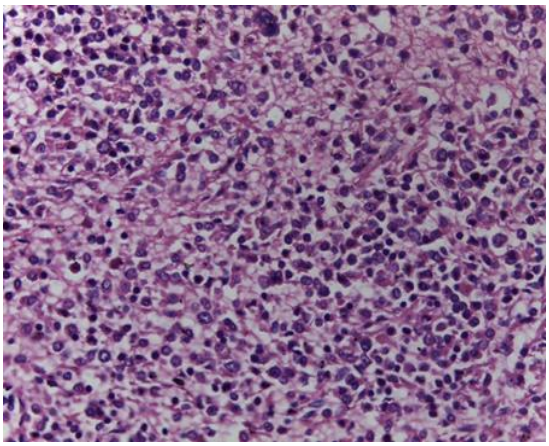

Fig. 2. Sheets of mononuclear cells

Bone marrow aspiration and trephine biopsy revealed tri-lineage hematopoiesis. Axillary lymph node biopsy showed no evidence of lymphoma. After discussion, with the multi - disciplinary team (MDT) and patient, decision was made to proceed with surgery in view of significant pancytopenia. Intra operatively, a standard midline incision revealed a massive spleen Fig. 3 measuring 43 cms (length) and weighing 7.2 kgs Fig. 4.

IHC showed follicular colonisation in ki 67 with cd 20 Fig. 5, kappa, and lamda 'positivity' with a diagnosis of marginal zone subtype of NHL. Postoperatively, she did quite well and was sent home on the fourth day, after the standard pneumococcal vaccine. She is currently, undergoing anti-cd20 based chemotherapy in our institution.

Fig. 3. Length 43 cms

Fig. 4. Weight 7.2 kgs

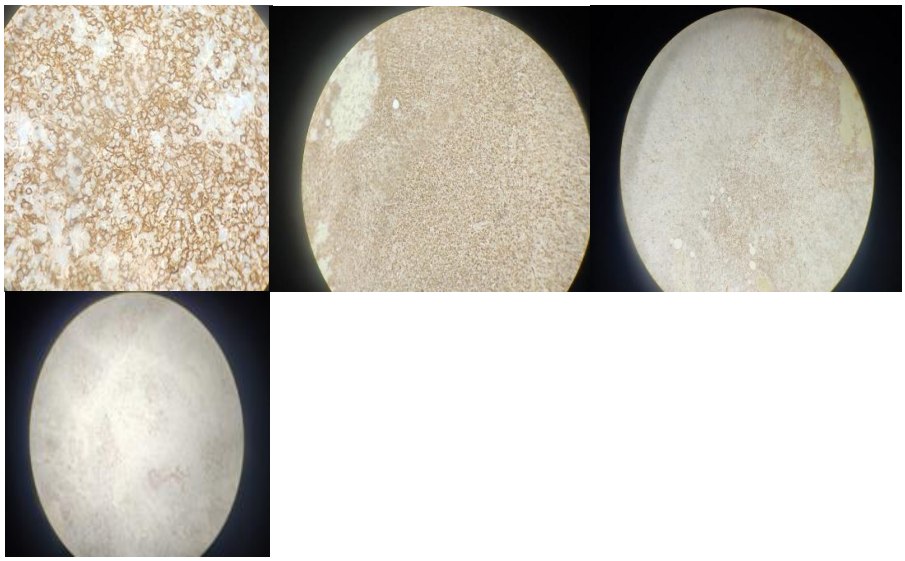

Fig. 5. Immuno histochemistry staining showing cd 20 positive lymphocytes, lambda, kappa, ki 67 (left to right)

3. DISCUSSION

The spleen represents the largest solid immune organ of the body containing numerous lymphocytes and macrophages and serves as the center of cellular and humoral immunity. Located between the white and red pulp of the spleen, the marginal region is approximately 100 μm in width and is regarded the main anatomical channel for peripheral lymphocytes to enter the lymphatic system of spleen. Functionally, this region provides the main platform for the recognising antigens and activation of immune reactions. Splenomegaly is found to be the most typical symptom of SMZL, and some patients present with decreased appetite, fever, night sweats, and sudden weight loss. Ultrasonography (USG) is widely used in clinical

practice as a screening tool, and the performance of SMZL is generally low or anechoic. Computed tomography (CT) mainly shows splenomegaly, decreased lesion density on plain scan, and mild to moderate enhancement on enhanced scan. Positron emission (PET/CT) shows increased splenic uptake of 18 fluorodeoxyglucose (F-FDG), which is considerably higher than the liver. However, because of the high price and radiation involved with PET/CT, it is not routinely recommended as the first choice in clinical practice. Due to unspecific imaging features, diagnostic splenectomy is still the preferred diagnostic method. The splenic histology is characterized by small lymphocyte infiltration with nodular hyperplasia. It is also suggested to use biopsy to preoperatively diagnose SMZL regarding the advantages of reducing the risks of post-splenectomy complications typical of intraperitoneal hemorrhage and infection [1].

The patient, in our report, presented with slow growing asymptomatic abdominal fullness clinically identified to be the result of massive splenomegaly. This case is quite unusual and novel in several ways.

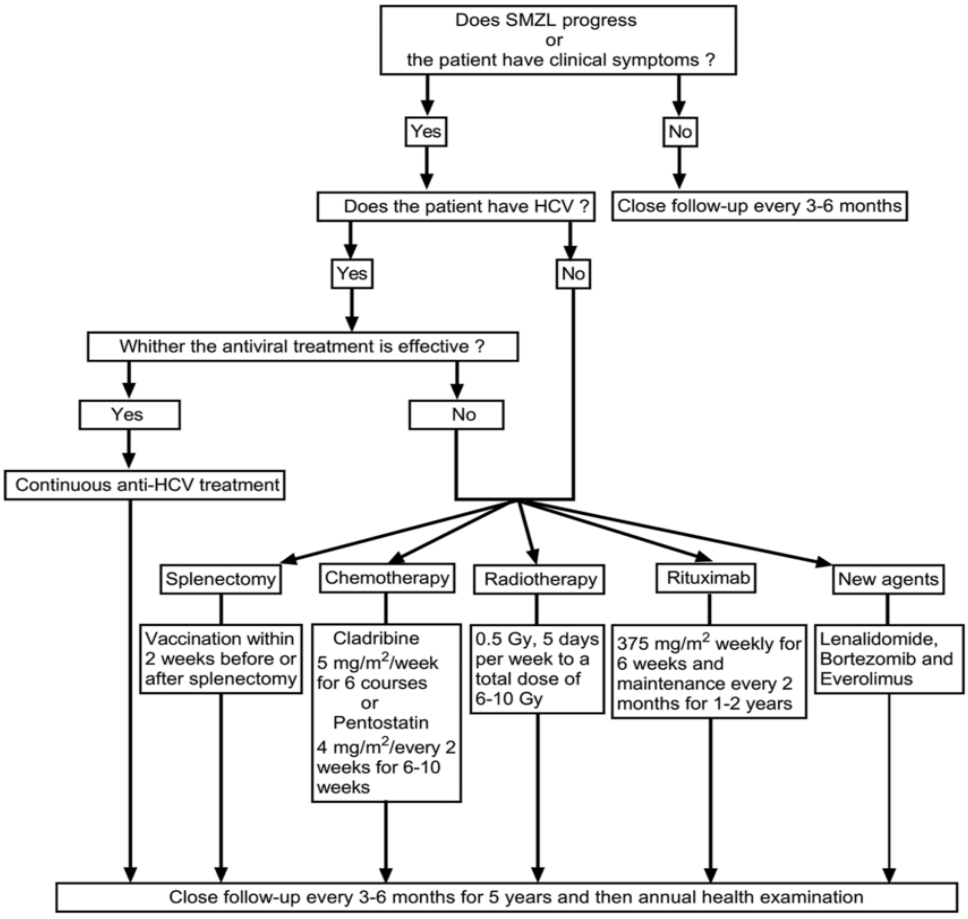

Fig. 6. Flowchart depicting management of SMZL [1]

Table 1. Summary of the size of the surgically resected spleen [1]

For patients with SMZL	Spleen size centimeters
Min	18 × 13 × 5
Max	40 × 20 × 15
Average	24.9 × 15.8 × 8.6

Table 2. Staging criteria for SMZL [1]

Stage	Feature
Stage I	Tumors were confined to the spleen only; no metastatic lesions were found in the splenic lymph nodes and outside the spleen
Stage II	The tumor involved in the splenic lymph nodes but no other parts of the lymph nodes or the external organs of the lymphatic system
Stage III	Lymph node involvement outside the spleen or extra-lymphatic organs and their associated lymph nodes (liver and bone marrow)

Primarily, in cases of slow progressive lymphoma-related splenomegaly, there is mostly a histologic evidence of transformation into probable, large b-cell lymphoma. In this case the final pathologic specimen (after IHC) revealed a SMZL, without large cell transformation.

Secondly, we also, could demonstrate a successful MDT approach in a patient with suspected SMZL involving evaluation by the medical oncology team and, splenectomy with intraoperative hemodynamic monitoring and optimization by the anesthesiology team.

Finally, this case is significant in that, it is the longest and the largest spleen ever surgically removed on record, in Asia and the second largest in the world [2]. Asymptomatic patients, without splenomegaly or cytopenias could initially be managed with chemotherapy. But patients who develop symptomatic splenomegaly and cytopenias require splenectomy, for alleviating their symptoms and adjuvant chemotherapy for the systemic disease. For symptomatic patients, with a variable risk profile, surgery still, continues, to be the mainstay of therapy.

Splenectomy, provides rapid symptomatic improvement as well as the correction of cytopenias related to hypersplenism. In patients with SMZL, who underwent splenectomy, in a large series, the median progression-free survival was found to be 8.25 years with 84% and 67% overall survival at 5 and 10 years, respectively [3]. Additionally, the removal has been shown to be relatively safe.

A 2019 review, by Fallah and Olszewski of 6450 patients with splenic lymphoma in the national cancer data base from 2004 to 2013 found that 58% of patients were treated with splenectomy, with a thirty-day overall mortality of 4% [4]. Splenectomy, while traditionally being the treatment for symptomatic patients, frequently results in only a partial response due to occasional, persistent extra splenic disease with nearly all patients having bone marrow involvement and warranting further therapy. Various chemotherapeutic strategies, including Hepatitis C eradication, are frequently utilized for the treatment of SMZL and have been reviewed elsewhere, too [5]. Immunotherapy has shown promise in offering potential effective treatment. Rituximab shows, promise as a first-line treatment for SMZL, improving complete response and disease-free survival rates, alone or in combination with chemotherapy compared, to chemotherapy alone in few series and can be proposed as a replacement for splenectomy as first-line therapy [6,7,1]. In patients who are refractory to or unsuitable for surgery or chemotherapy, splenic irradiation can be used as an option, and also has the potential to amplify response rates to immune chemotherapy with Rituximab, if the patient requires further treatments [8]. Splenic irradiation, has been shown in several small case series to be effective in the palliation of pain and abdominal discomfort in splenomegaly with success rates between 50 and 91% and minimal side effects [9–11]. Due to its low overall incidence, the optimal therapy for SMZL remains controversial and is still, a topic of ongoing study. In an enviable attempt, to provide guidance for stratification and selection of risk-tailored treatment approaches, an international group reviewed 593 SMZL patients and developed criteria for the diagnosis, treatment initiation, response assessment, management, and prognostic stratification of SMZL patients [12,1]. However, it must be noted that severe infection after splenectomy, also known as overwhelming post-splenectomy infection (OPSI), is highly lethal, with an estimated mortality rate of 5%. The majority of OPSI is caused by encapsulated bacteria, typically of the pneumococcus, Meningococcal C pathogens and Hemophilus influenza B. To prevent the development of

OPSI, vaccination against encapsulated bacteria is mandatory within 2 weeks before or after splenectomy and then once a year for 5 consecutive years. While for patients who cannot tolerate surgery or experience tumor recurrence after surgery, chemotherapy should be considered [1].

4. CONCLUSION

A wide awareness of SMZL, among primary care physicians can promote prompt referral for appropriate therapy and tailoring of a MDT approach. In cases of SMZL without blood and bone marrow involvement, but with symptoms secondary to massive splenomegaly and cytopenias, an upfront splenectomy rapidly alleviates symptoms of hyper splenism and, can further aid in histological diagnosis for systemic chemotherapy. Here, we have, demonstrated that even cases of massive splenomegaly can be managed surgically providing equally rapid symptomatic improvement and an overall satisfactory oncologic outcome. A MDT approach to complex cases of SMZL splenomegaly is absolutely imperative to achieving optimal outcomes.

CONSENT

All authors declare that 'written informed' consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office/chief editor/editorial board members of this journal.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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