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Sclerotic marginal zone lymphoma: A case report

Moureiden Z et al. Sclerotic MZL
Abstract

BACKGROUND
Marginal zone lymphoma (MZL) is an indolent non-Hodgkin B cell lymphoma with various architectural pattern including perifollicular, follicular colonization, nodular, micronodular, and diffuse patterns. A sclerotic variant has not been previously reported and represents a diagnostic pitfall.

CASE SUMMARY
A 66-year-old male developed left upper extremity swelling. Chest computed tomography (CT) 9/2020 showed 14 cm mass in left axilla. Needle core biopsy of axillary lymph node showed sclerotic tissue with atypical B lymphoid infiltrate but was non-diagnostic. Excisional biopsy was performed for diagnosis and showed extensive fibrosis and minor component of infiltrating B cells. Flow cytometry showed a small population of CD5-, CD10-, kappa restricted B cells. Monoclonal immunoglobulin heavy chain and light chain gene rearrangement were identified. Upon being diagnosed with MZL, patient was treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone and achieved complete remission by positron emission tomography/CT.

CONCLUSION
This is an important case report because by morphology this case could have easily been overlooked as non-specific fibrosis with chronic inflammation representing a significant diagnostic pitfall. Moreover, this constitutes a new architectural pattern. While sclerotic lymphomas have rarely been described (often misdiagnosed as retroperitoneal fibrosis), we do not know of any cases describing this architectural presentation of MZL.

Key Words: Sclerotic; Marginal zone lymphoma; Architecture; Pitfall; Diagnosis; Fibrosis; Case report

**Core Tip:** In the clinical context of suspicious lymphadenopathy, the presence of an extensive sclerosis on biopsy should not deter the clinician from a diagnosis of lymphoma and careful evaluation and work up is needed to exclude covert lymphoma.

**INTRODUCTION**

Marginal zone lymphoma (MZL) is an indolent B-cell non-Hodgkin lymphoma derived from marginal zone B cells within the lymphatic system[1]. The incidence of MZL, based on data from the United States SEER-18 program, is 19.6 per 1000000 person-years[2]. MZL is typically classified into extranodal MZL (EMZL) of mucosa-associated lymphoid tissue (61%), nodal MZL (NMZL) (30%), and splenic MZL (SMZL) (9%). Other subtypes include pediatric MZL and immunoproliferative small intestinal disease[3]. 5-year relative survival rate for EMZL, NMZL, and SMZL are 88.7%, 76.5% and 79.7%, respectively with EMZL being most likely to transform to diffuse large B cell lymphoma[4,8].

Marginal zone B cells typically display a morphology of small to medium sized lymphocytes with somewhat irregular nuclei containing mature chromatin and relatively abundant pale cytoplasm. They may classically assume a monocytoid morphology[6]. In SMZL, villous lymphocytes can be seen in the periphery. MZL typically expresses an immunohistochemistry profile positive for B cell-associated antigens (CD19, CD20, CD22, CD79a) and complement receptors (CD21 and CD35). MZLs are usually negative for CD5, CD10, CD23, BCL6, and cyclin D1. Furthermore, SMZL has a high concentration of immunoglobulin D (IgD) cell surface antigens; whereas, EMZL and NMZL show expression of IgM and IgD[3]. MZL can assume various architectural patterns including perifollicular, follicular colonization, nodular,
micronodular, and even diffuse patterns[6]. In the bone marrow, an intrasinusoidal pattern is often seen in SMZL[8].

We present a remarkable case of MZL masquerading in a sclerotic background as fibrosis with chronic inflammation. This constitutes the first report of this architectural pattern in MZL and represents a serious and important diagnostic pitfall in lymphoma diagnosis.

CASE PRESENTATION

Chief complaints
The patient is a 66-year-old male who developed left upper extremity swelling.

History of present illness
The patient had an episode of syncope of unclear etiology in January 2020. He started to have pain under his left arm in February that waxed and waned, then over the course of a few weeks, he started having left upper extremity swelling, and this was followed by an ultrasound and mammogram that were reportedly negative, incomplete records. This was followed by a computed tomography (CT) of the chest without contrast on April 9, 2020 that showed a large, irregularly margined mass arising in the left axilla.

History of past illness
Past medical history is notable for benign prostatic hyperplasia, chronic kidney disease stage III, type 2 diabetes, hypertension, hyperlipidemia, and pulmonary hypertension.

Personal and family history
The patient had a mother with history of breast cancer and colon cancer.

Physical examination
Temperature: 36.78 °C, heart rate: 93/min, RR: 16/min, BP: 125/73 mmHg, SpO2: 100%, Weight: 104.5 kg, body mass index: 31.20. General: Alert and oriented, no acute distress.

Laboratory examinations
The specific examinations were in Table 1.

Imaging examinations
Chest CT 9/2020 showed a 14 cm irregularly, margined mass arising in left axilla. There was questionable invasion of the left subscapularis muscle and thickening the right pectoralis minor muscle. Positron emission tomography (PET) scan showed standardized uptake value (SUV) of 26.

FINAL DIAGNOSIS
MZL.

TREATMENT
Upon being diagnosed with lymphoma, patient was treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). More specifically, he received 6 cycles of R-CHOP, and doxo/cyclophosphamide 50% dose reduction starting cycle 4 due to severe cytopenias.
OUTCOME AND FOLLOW-UP
The patient achieved complete remission by PET/CT (July 20, 2021). He is under surveillance post treatment and 1-year post-treatment scans show no evidence of disease.

DISCUSSION
MZL can demonstrate a wide spectrum of clinical manifestations due organ-specific variability. Genomically, there is also heterogeneity although dysregulation of B-cell receptor, nuclear factor κB, and NOTCH signalling pathways is typical\(^5\). Significant variation is also seen in the architectural patterns manifested by MZL\(^7\). This is complicated by the fact that there is no single universal biomarker for MZL, and the diagnosis is often only arrived at after integrating phenotypic, cytogenetic, and molecular features\(^9\).

There are a few studies that have cataloged the architectural patterns in MZL. Salama et al\(^{10}\) evaluated 51 NMZL and found four major patterns, namely: Diffuse (75%), well-formed nodular/follicular (10%), interfollicular (14%) and perifollicular (2%). Interestingly, they noted compartmentalizing interstitial sclerosis in 28% of cases most commonly in the diffuse variant (12/15 cases). However, this was illustrated as relatively inconspicuous comprising of delicate tendrils of sclerosis which in no way resembles our case. Others have documented variable architectural patterns depending on the site of involvement: Spleen (nodular to diffuse), bone marrow (intrasinusoidal, interstitial, nodular, and even paratrabecular), lymph node (nodular to diffuse, liver (intrasinusoidal and portal tract lymphoid nodules), etc\(^9\).

Rarely, lymphomas can present in a markedly fibrotic background or be clinically misdiagnosed as retroperitoneal fibrosis\(^\text{11,12}\). Sclerosing lymphomas are rare and typically of follicle center origin\(^\text{13}\). We do not know of any cases describing this architectural presentation of MZL. As such, this case could have easily been overlooked as non-specific fibrosis with chronic inflammation representing a significant diagnostic pitfall. Clues with regard to the diagnosis as the radiologic findings of a large (14 cm)
mass with high SUV. Furthermore, the B cell predominance by immunohistochemistry was atypical. Flow cytometry and immunoglobulin heavy and light chain gene rearrangement studies were vital in order to arrive at the correct diagnosis. Response to R-CHOP further confirms the diagnosis clinically.

CONCLUSION
In summary, we present the first case report of sclerotic MZL which should be recognized as a rare architectural pattern in MZL and poses a diagnostic challenge, especially on limited fine-needle aspiration or needle core biopsy specimens. Integration of all clinical and pathological data is essential to arrive at the correct diagnosis.
### ORIGINALITY REPORT

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