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CASE REPORT

Sclerotic marginal zone lymphoma: A case report

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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) in September 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.

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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[4,5].

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[7]. 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 complaint

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. The patient had an ultrasound and mammogram that were reportedly negative. This was followed by a computed tomography (CT) of the chest without contrast on April 9, 2020 that showed a large, irregularly marginated 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, respiratory rate: 16/min, blood pressure: 125/73 mmHg, SpO_2: 100%, weight: 104.5 kg, body mass index: 31.20 kg/m^2. General: Alert and oriented, no acute distress. Eye: Normal conjunctivae, anicteric. Head/ears/nose/mouth/throat: Normocephalic, no trauma, normal hearing. Neck: Supple, non-tender. Cardiovascular: Regular rate and rhythm, normal peripheral perfusion. Lung: Lungs were clear to auscultation, respirations were non-labored. Abdomen: Soft, nontender, nondistended, no splenomegaly. Hematological/lymphatics: No lymphadenopathy: Cervical, supraclavicular, axillary, inguinal. Extremities: Normal range of motion, normal strength, no deformity. Integumentary: Warm, dry, intact. Neurologic: Alert, oriented, no focal defects. Cognition and speech: Oriented, speech clear and coherent, functional cognition intact. Psychiatric: Cooperative, appropriate mood and affect.

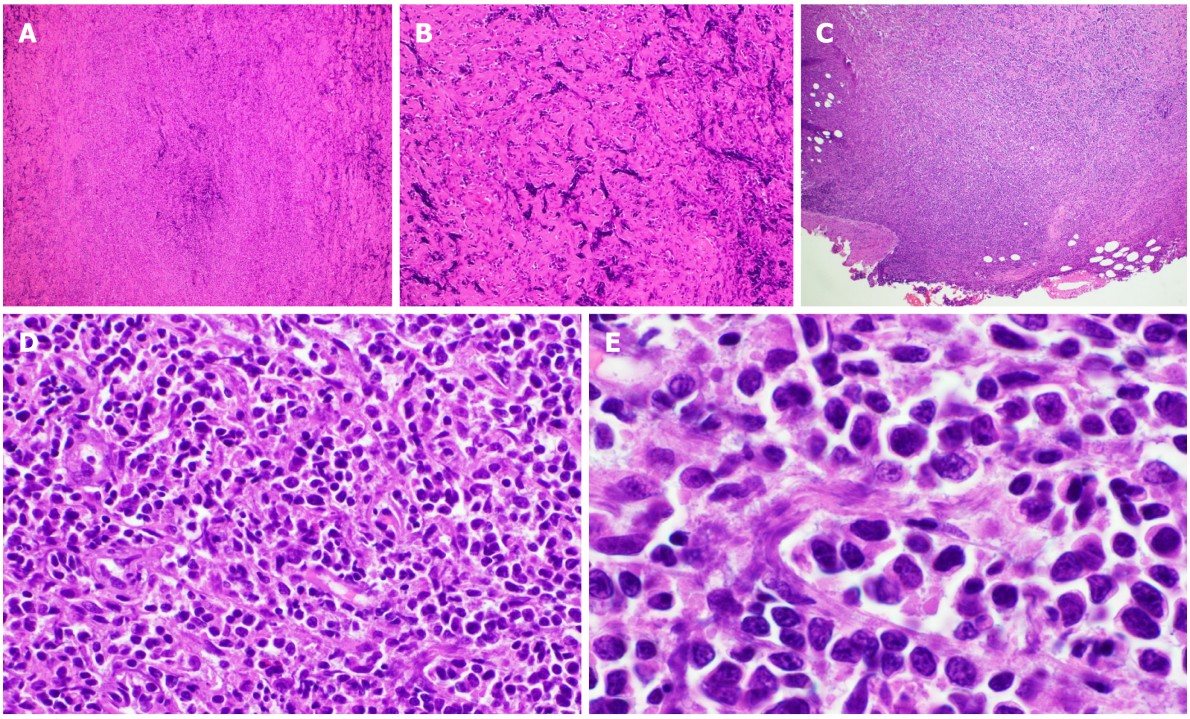

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Figure 1 Histology of sclerotic marginal zone lymphoma. A: Low power hematoxylin and eosin (H&E) section showing extensive fibrosis and crush artifact, 40 × (Olympus BX43); B: Low power H&E section showing extensive fibrosis and crush artifact, 40 × (Olympus BX43); C: More cellular area with small lymphocytes is seen focally (lower-left hand) compared with more sclerotic pattern (upper-right), 40 ×; D: High power H&E showing morphology of cells in cellular area (non-crushed), some have monocytoid features (400 ×); E: High power H&E showing morphology of cells in cellular area (non-crushed), some have monocytoid features (1000 ×).

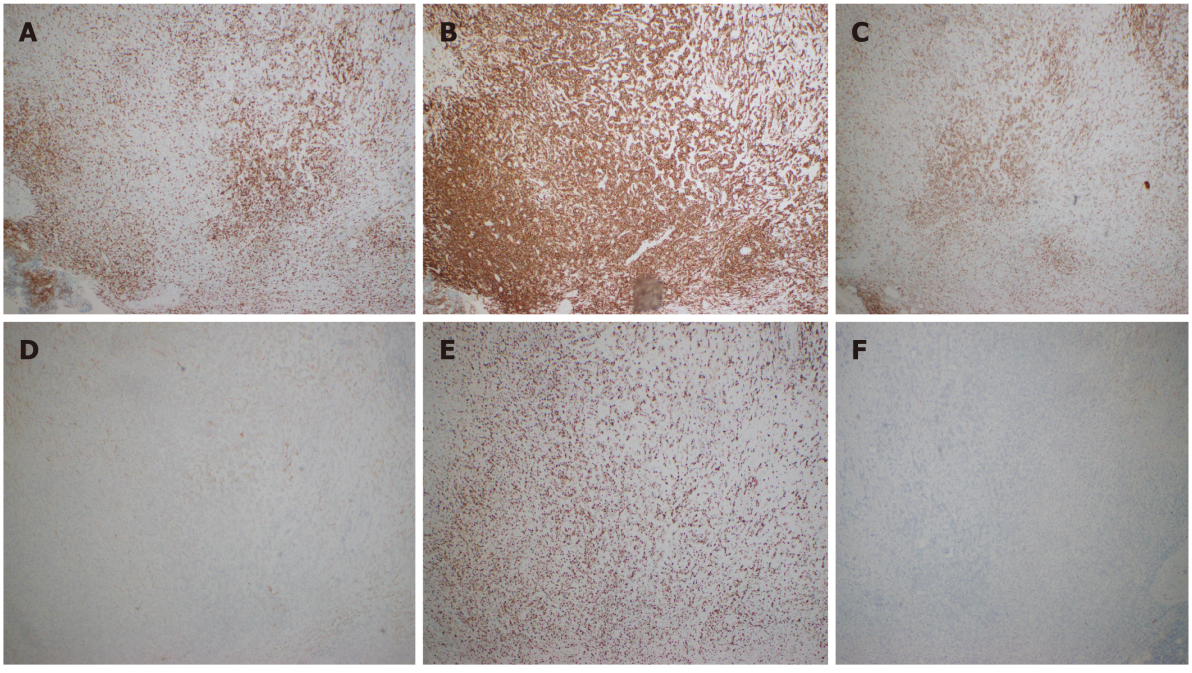

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Figure 2 Immunohistochemical profile of sclerotic marginal zone lymphoma. A: CD3; B: CD20; C and D: CD5; E: Ki67; F: BCL6.

Laboratory examinations

The specific examinations and results are listed in Table 1. Pathology results are provided in Figures 1-3.

Table 1 Laboratory examinations

	Value w/units	Normal range
CBC		
WBC	5.59 k/uL	4.00-10.90
Preliminary ANC	> 1.5 k/uL	
RBC	3.50 mil/uL	4.45-5.73
Hemoglobin	11.1 g/dL	13.4-16.9
Hematocrit	34.1%	40.0-48.0
Mean cell volume	97.4 FL	80.3-94.0
MCH	31.7 pg	27.4-33.4
MCHC	32.6 g/dL	32.0-36.8
RDW	50.6 FL	36.8-46.1
Platelet count	113 k/uL	143-382
MPV	10.1 FL	7.4-11.7
Differential		
Neutro auto	3.57 k/uL	1.80-7.80
Eos auto	0.37 k/uL	0.00-0.45
Basophil auto	0.04 k/uL	0.00-0.20
Immature Gran auto	0.03 k/uL	0.00-0.10
Mono auto	0.71 k/uL	0.30-0.80
Lymph auto	0.87 k/uL	1.10-3.50
Nucleated RBC	0.00 k/uL	0.00-0.10
Differential %		
Neutro auto %	63.9	
Eos auto %	6.6	
Basophil auto %	0.7	
Immature Gran auto %	0.5	
Mono auto %	12.7	
Lymph auto %	15.6	
Nucleated RBC %/100 WBC	0.0/100 WBC	0.0-1.0
Coagulation		
Prothrombin time	11.6 s	10.2-12.9
INR	1.0	0.8-1.1
APTT	27.0 s	25.1-36.5
Reticulocyte percent	1.78%	0.80-1.90
Reticulocyte number	0.0623 mil/uL	0.0360-0.1000
Immature retic fraction (%)	14.5	3.0-13.4
Eryth. sed rate	20 mm/hr	0-15
Metabolic panel		
Sodium	140 mmol/L	134-145
Potassium	4.0 mmol/L	3.4-4.5
Chloride	102 mmol/L	96-107
Total CO_2	26 mmol/L	22-30

Glucose level	111 mg/dL	70-110
BUN	13 mg/dL	6-23
Creatinine	1.5 mg/dL	0.7-1.3
Est. GFR	47 mL/min/1.73 m^2	
Est. GFR (Af-Am)	57 mL/min/1.73 m^2	
Uric acid	6.9 mg/dL	3.5-8.5
Calcium	11.3 mg/dL	8.6-10.2
Calcium corrected	11.2 mg/dL	8.6-10.2
Phosphorus	2.7 mg/dL	2.5-4.5
Total protein	6.8 gm/dL	6.6-8.7
Albumin	4.1 gm/dL	3.5-5.2
Total bilirubin	0.80 mg/dL	0.00-1.20
Alk. phosphatase	65 U/L	40-130
AST	34 U/L	10-50
ALT	25 U/L	0-41
LDH	158 U/L	135-225
Magnesium level	1.4 mg/dL	1.6-2.3

CBC: Complete blood count; WBC: White blood cell; ANC: Absolute neutrophil count; RBC: Red blood cell; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red blood cell distribution width; MPV: Mean platelet volume; INR: International normalized ratio; APTT: Activated partial thromboplastin time; BUN: Blood urea nitrogen; GFR: Glomerular filtration rate; AST: Aspartate aminotransferase; ALT: Alanine transaminase; LDH: Lactate dehydrogenase.

Imaging examinations

Chest CT in September 2020 showed a 14 cm irregularly, marginated 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

The final diagnosis is 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 signaling pathways is typical[3]. 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,

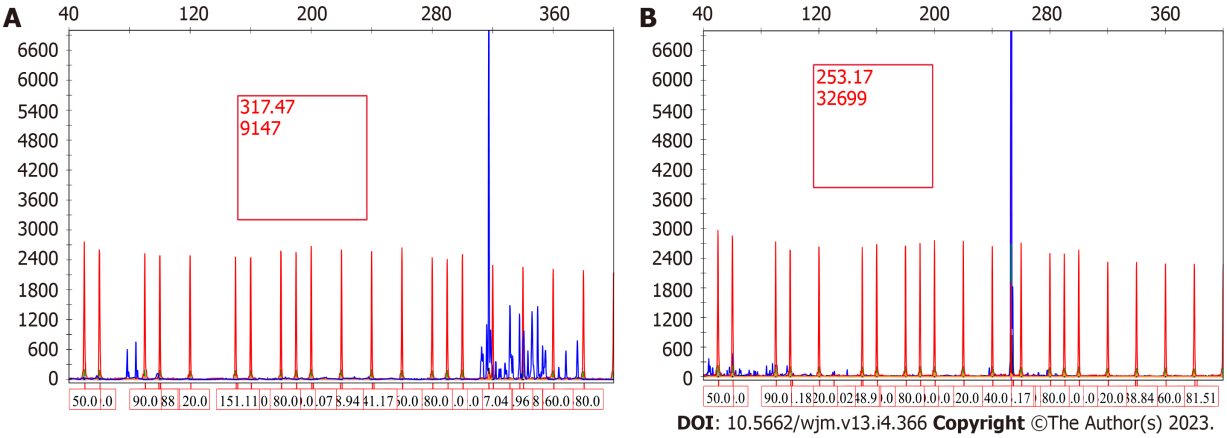

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Figure 3 Clonal peaks detected in immunoglobulin heavy chain. A: Framework 1 region; B: Framework 2 region.

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[11,12]. Sclerosing lymphomas are rare and typically of follicle center origin[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 include 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.

FOOTNOTES

Author contributions: Moureiden Z, Tashkandi H, and Hussaini MO contributed to the conception and design of the study, acquisition and analysis of data; Moureiden Z and Hussaini MO drafted the manuscript or figures.

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