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Diffuse Large B-Cell Lymphoma of the Breast: Diagnostic Challenges and Case Insights

Hammadi Jawaher[1], Hammami Sabra[1], Ben Ali Yasmine[1], Ounissi Amira[1], Ben Jaballah Soukeina[1], Boukadida Rania[1], Ghades Sana[1], Fatnassi Ridha[1]

[1]Department of Obstetrics and Gynecology, Ibn Jazzar Hospital, Kairouan, University of Sousse, Tunisia

Corresponding Author : Hammadi Jawaher , jjawaher284@gmail.com

ABSTRACT

Background: Primary breast lymphoma (PBL) is a rare extranodal non-Hodgkin lymphoma, accounting for less than 1% of breast cancers and 2–3% of all extranodal lymphomas, and may occur at various physiological stages, often mimicking breast carcinoma clinically and radiologically.

Cases: We report two cases of diffuse large B-cell Primary breast lymphoma diagnosed in 2018 and 2023 . The first involved a 72-year-old postmenopausal woman with a mass in the upper outer quadrant of the right breast and two axillary lymph nodes, evolving over a few months. She received initial R-CHOP chemotherapy, but developed a local recurrence 24 months later, which was managed with salvage chemotherapy combined with localized radiotherapy,resulting in complete remission on follow-up. The second case concerned a 41-year-old diabetic woman with a rapidly enlarging mass in the lower outer quadrant of the left breast and a single axillary lymph node. She achieved complete remission after six cycles of R-CHOP chemotherapy without recurrence.

Discussion: These cases highlight the broad spectrum of Primary breast lymphoma presentations and the diagnostic challenges in distinguishing it from breast carcinoma. Imaging features are often nonspecific; histopathology and immunohistochemistry are essential. Management relies on systemic chemotherapy, with or without radiotherapy, contrasting with the surgical-centered approach of breast carcinoma.

Conclusion: Rapidly growing or atypical breast masses should raise suspicion for primary breast lymphoma. Early biopsy and immunophenotyping are essential to ensure correct diagnosis and avoid unnecessary surgery.

KEYWORDS: *Primary breast lymphoma; Diffuse large B-cell lymphoma; Breast mass; Immunohistochemistry; Chemotherapy; Postmenopause.*

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1. INTRODUCTION

Primary breast lymphoma is an uncommon extranodal non-Hodgkin lymphoma, representing less than 1% of breast cancers and approximately 2–3% of all extranodal lymphomas (1). Although most frequently reported in women aged 50–70, cases have also been described from young adults to those beyond menopause (1).

In clinical practice, primary breast lymphoma often manifests as a swiftly growing, painless breast lump that may be mistaken for other types of breast cancer(2) (3).

Radiological features are variable and often nonspecific: mammography may reveal well-defined or polylobulated opacities, sometimes without microcalcifications, while ultrasonography typically demonstrates hypoechoic, heterogeneous lesions (1)–(4). Histologically, most Primary breast lymphomas are diffuse large B-cell lymphomas (DLBCL), expressing CD20 and common leukocyte antigen (CLA) (4) (5).

Unlike breast carcinoma, the management of PBL relies primarily on systemic chemotherapy, with or without localized radiotherapy, while surgery is usually limited to diagnostic biopsy (1)(2)(5).

This report presents two cases with contrasting clinical presentations - one in a younger woman and another postmenopausal woman highlighting the diagnostic challenges and the importance of distinguishing primary breast lymphoma from conventional breast carcinoma.

2. CASE REPORTS

Case 1
A 72-year-old postmenopausal woman, with a history of hypertension and cardiopathy, consulted for mastodynia in the right breast evolving over a few months.

The right breast was bulky with skin edema and ecchymosis. Physical examination revealed a 6 cm nodule in the upper outer quadrant with irregular borders, fixed to the overlying skin. These features are consistent with a suspicious malignant breast mass (Figure 1). Two mobile axillary lymph nodes, each measuring 2 cm, were palpable in the right axilla. The contralateral breast was normal.

Mammography showed a radio-opaque, heterogeneous lesion measuring 6 cm with irregular margins and numerous vermicular microcalcifications (Figure 2). Ultrasound confirmed a heterogeneous lesion with polylobulated borders, classified ACR 5 (Figure 3).

Core needle biopsy revealed a diffuse proliferation of large lymphoid cells, immunoblastic or centroblastic in appearance (Figure 4).

Immunohistochemistry showed tumor cells expressing CD20 but not CD3 nor cytokeratin (Figure 5). Staging workup, including thoracoabdominal CT scan, abdominal ultrasound, and bone marrow biopsy, showed no systemic involvement. The patient received initial R-CHOP chemotherapy, achieving complete remission.

A local recurrence occurred 24 months later, which was managed with salvage chemotherapy combined with localized radiotherapy, leading to good outcome at follow-up.

Case 2
A 41-year-old woman with a history of type 2 diabetes presented with a progressively enlarging mass in the lower outer quadrant of the left breast, evolving over one month. The lesion was painless. On clinical examination, a 4 cm, well-circumscribed, mobile nodule was found without skin changes or nipple retraction. lymph node measuring 1 cm in diameter was palpable.

Breast ultrasound showed a homogeneous, hypoechoic lesion without microcalcifications, initially suggestive of a fibroadenoma.

A core needle biopsy was performed, revealing a diffuse proliferation of large lymphoid cells, often immunoblastic or centroblastic in appearance (Figure 6). Immunohistochemistry demonstrated strong positivity for CD20 and CLA, and negativity for CD3 and cytokeratin (Figure 7).

Staging investigations, including thoracoabdominal CT scan and bone marrow biopsy, excluded systemic disease.
The patient was treated with six cycles of R-CHOP chemotherapy and achieved complete remission without any recurrence. At the last follow-up, she remained in remission.

3. DISCUSSION

Primary breast lymphoma (PBL) is a rare entity, representing less than 1% of breast malignancies and 2–3% of extranodal lymphomas(1) (4) Our two cases illustrate the wide spectrum of clinical presentations, demonstrating that Primary breast lymphoma can occur at any age from young adults to postmenopause, and often mimics breast carcinoma (1) (2).

The first patient, a 72-year-old postmenopausal woman, presented with a firm, fixed mass in the upper outer quadrant of the right breast and two mobile axillary lymph nodes. She initially achieved remission with R-CHOP chemotherapy, but developed a local recurrence 24 months later, which was successfully managed with salvage chemotherapy and localized radiotherapy.

The second patient, a 41-year-old diabetic woman, presented with a rapidly enlarging, mobile, well-circumscribed mass in the lower outer quadrant of the left breast with a single mobile axillary lymph. She achieved complete remission after six cycles of R-CHOP chemotherapy without recurrence.

Previous reports, including Sakhri et al. and Teng et al., emphasize that age and physiological status can influence clinical presentation (1) (4). Case reports by Santiago-Sanabria et al. and Hammood et al. describe similar variability, highlighting

that Primary breast lymphoma may be misinterpreted as benign lesions in younger patients or as carcinoma in older patients (7,8).

This heterogeneity can delay diagnosis, particularly when imaging suggests carcinoma. Radiologic features of Primary breast lymphoma are often nonspecific; lesions may appear well-circumscribed and homogeneous or irregular with microcalcifications (2) (3) (5). Therefore, early histopathological evaluation with comprehensive immunohistochemistry (IHC) is essential to avoid misdiagnosis (3) (5).

In our cases, the younger patient's lesion initially resembled a fibroadenoma, whereas the postmenopausal lesion suggested carcinoma. This radiologic variability has been noted by Surov et al. James et al., and Maccio et al., reinforcing that imaging alone cannot reliably differentiate Primary breast lymphoma from carcinoma (2) (3) (5). Clinicians should maintain a high index of suspicion for Primary breast lymphoma in atypical masses, especially if growth is rapid or imaging findings are discordant with clinical context.

Definitive diagnosis relies on tissue evaluation. Both cases were diffuse large B-cell lymphoma (DLBCL), CD20+ and CLA+, CD3– and cytokeratin–, consistent with prior studies (4) (5) (6) These findings distinguish Primary breast lymphoma from invasive breast carcinoma, which typically expresses cytokeratins and may be ER/PR/HER2 positive. Case reports by Santiago-Sanabria et al. and Hammood et al. further confirm that this immunophenotypic profile is highly reliable for differentiating PBL from invasive breast carcinoma (7) (8).

Table 1 summarizes the key differences between primary breast lymphoma (PBL) and invasive breast carcinoma, highlighting clinical, radiological, histopathological, and therapeutic distinctions to guide diagnosis and management.

Table 1 – Key differences between PBL and invasive breast carcinoma

Aspect	Primary Breast Lymphoma (PBL)	Invasive Breast Carcinoma
Frequency	Very rare (<1% of breast cancers; 2–3% of extranodal lymphomas)	Most common breast malignancy
Typical Age / Condition	Any age, including pregnancy and postmenopause	Usually postmenopausal, occasionally younger women
Presentation	Rapidly enlarging, painless, or atypical mass; can mimic benign lesion	Firm, fixed mass; may cause nipple or skin changes; generally slower growth
Imaging Features	Often nonspecific; mammography: well-defined/polylobulated mass; ultrasound: hypoechoic, heterogeneous; microcalcifications rarely	Mammography: irregular/spiculated mass ± microcalcifications; ultrasound heterogeneous
Histology / IHC	DLBCL; CD20+, CLA+, CD3–, cytokeratin–	Epithelial origin; cytokeratin+, may be ER/PR/HER2 positive
Treatment Approach	Primarily systemic chemotherapy (R-CHOP) ± radiotherapy; surgery usually diagnostic	Surgery-centered (lumpectomy/mastectomy) ± chemotherapy, radiotherapy, or targeted therapy
Prognostic Factors	Age, LDH, performance status, nodal involvement	TNM stage, tumor grade, receptor status, lymph nodes Status
Follow-up	Close clinical and imaging monitoring; risk of local recurrence	Standard breast cancer follow-up; recurrence risk depends on stage/type

The management of Primary breast lymphoma differs fundamentally from breast carcinoma. Curative surgery is not indicated; treatment relies on systemic chemotherapy (R-CHOP) ± localized radiotherapy (4) (9). The standard R-CHOP regimen includes rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, typically administered every 21 days for 6 to 8 cycles, with adjustments based on disease severity and patient tolerance (4). Localized radiotherapy is recommended for patients with bulky tumors, residual disease, or limited nodal involvement, as it has been shown to enhance local control and decrease the risk of recurrence (1) (4).

Unlike Primary breast lymphoma, breast cancer treatment is primarily surgical, often supplemented with chemotherapy, radiotherapy, or targeted therapy. Prognosis depends on lymphoma-specific factors, including age, LDH, performance

status, and nodal involvement, rather than TNM staging (10) (11). Notably, epidemiologic data suggest a small but measurable increased risk of non-Hodgkin lymphoma in breast cancer survivors, emphasizing the need for vigilance in patients with prior breast malignancy (10).

These cases reinforce that Primary breast lymphoma should be considered in any rapidly enlarging or atypical breast mass, irrespective of age or physiological status. Misleading imaging and distinct immunophenotype highlight potential diagnostic pitfalls, and early biopsy with IHC is essential to prevent unnecessary surgery. By providing a direct comparison between PBL and invasive breast carcinoma and incorporating epidemiological insights, this report offers a novel and clinically relevant perspective for physicians managing atypical breast lesions (1)–(11).

4. CONCLUSION

Primary breast lymphoma is uncommon but clinically important, often resembling invasive breast cancer. Presentation varies with age and physiological status. As illustrated by the young adult patient with a lower outer quadrant lesion and the postmenopausal patient with an upper outer quadrant mass, diagnosis requires accurate histopathology with immunohistochemistry. Treatment is primarily systemic chemotherapy, with or without radiotherapy, unlike the surgery-focused approach for carcinoma. Clinicians should suspect Primary breast lymphoma in any atypical or rapidly growing breast mass to ensure prompt diagnosis and appropriate management, avoiding unnecessary surgery.

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Figure 1: Lymphomatous proliferation with large lymphoid cells (magnification ×40).

Figure 2: A diffuse immunolabelling of the tumor cells with anti-CLA (common leukocyte antigen) antibodies and CD20 positivity (original magnification ×40).

Figure 3: Right breast with a bulky 6 cm nodule in the upper outer quadrant, associated with skin edema and ecchymosis.

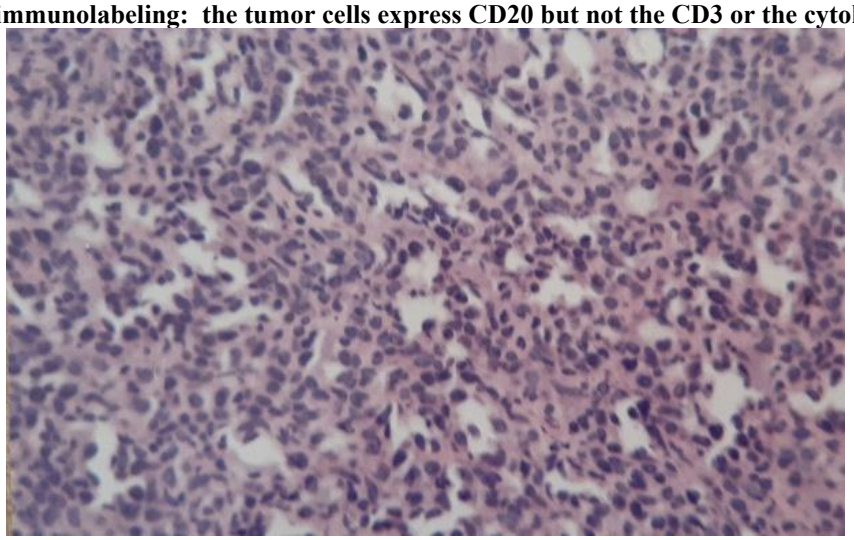
Figure 4: Nodular, opaque formation of 6 cm in the upper outer quadrant, with high density, irregular margins, and associated vermicular microcalcifications.

Figure 5: Breast ultrasound: Polylobed, heterogeneous tumor formation of 6 cm associated with multiple axillary

lymph nodes.

Figure 6: A lymphomatous proliferation of large immunoblastic and centroblastic cells with numerous mitoses (original magnification ×40).

Figure 7: The immunolabeling: the tumor cells express CD20 but not the CD3 or the cytokeratin. (x40)



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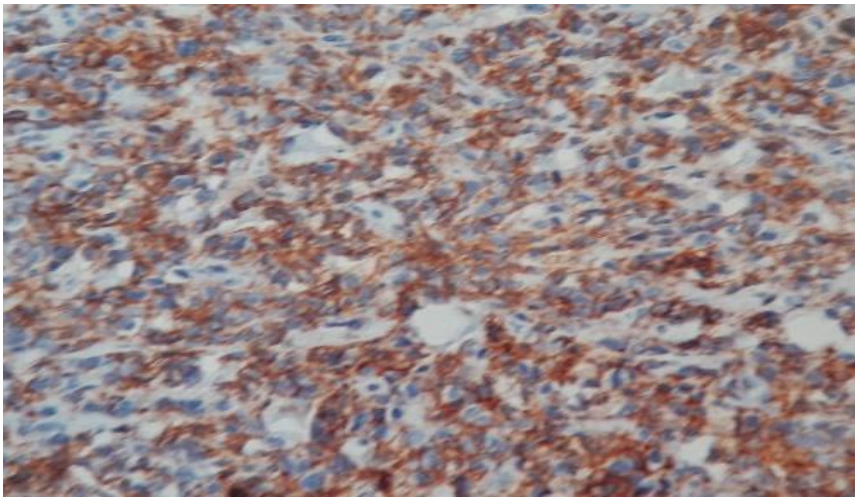

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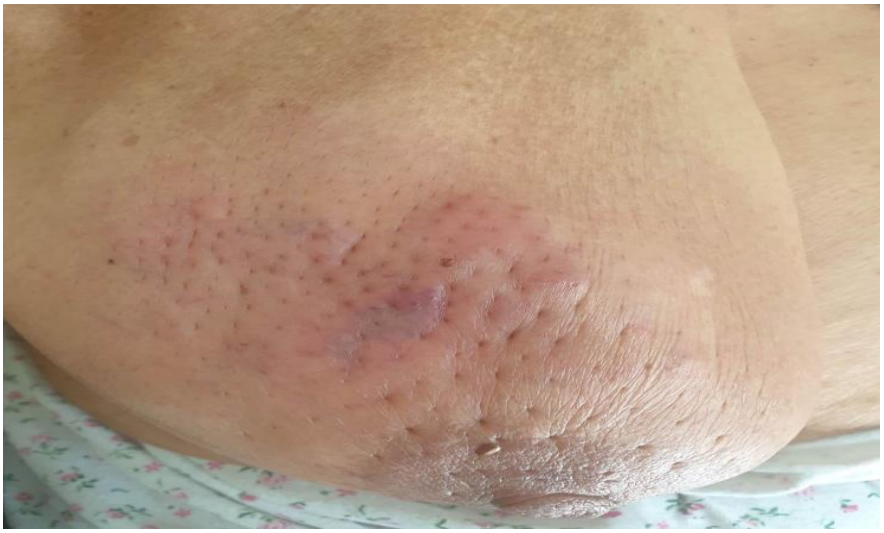

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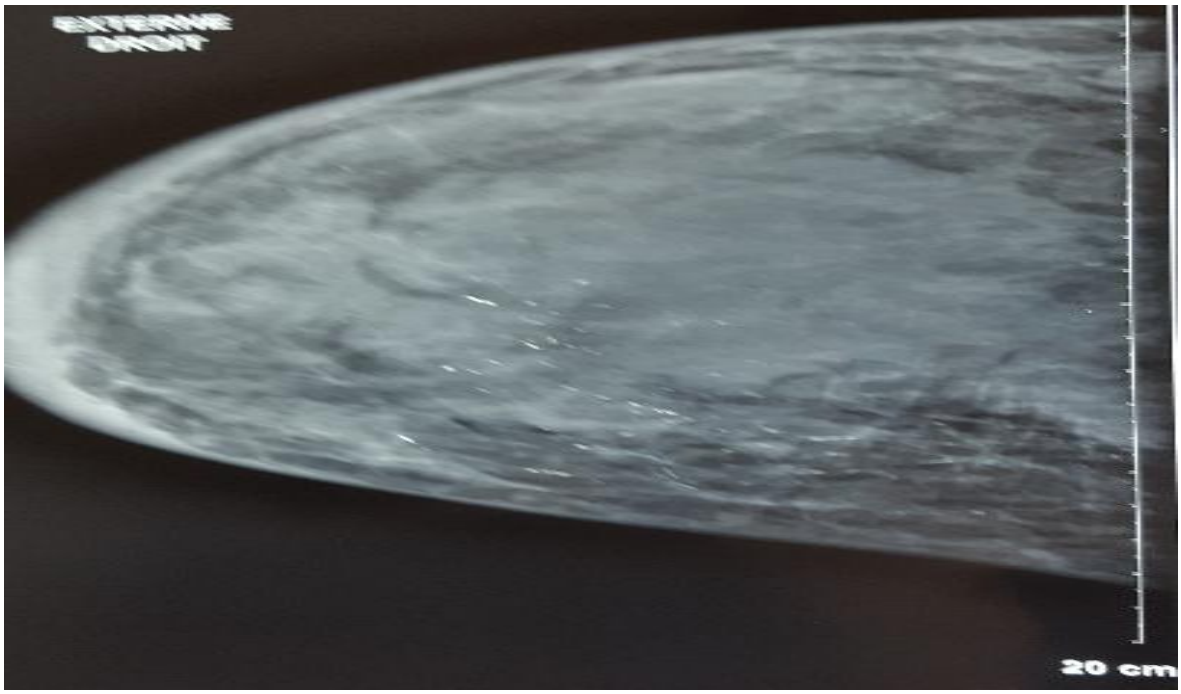

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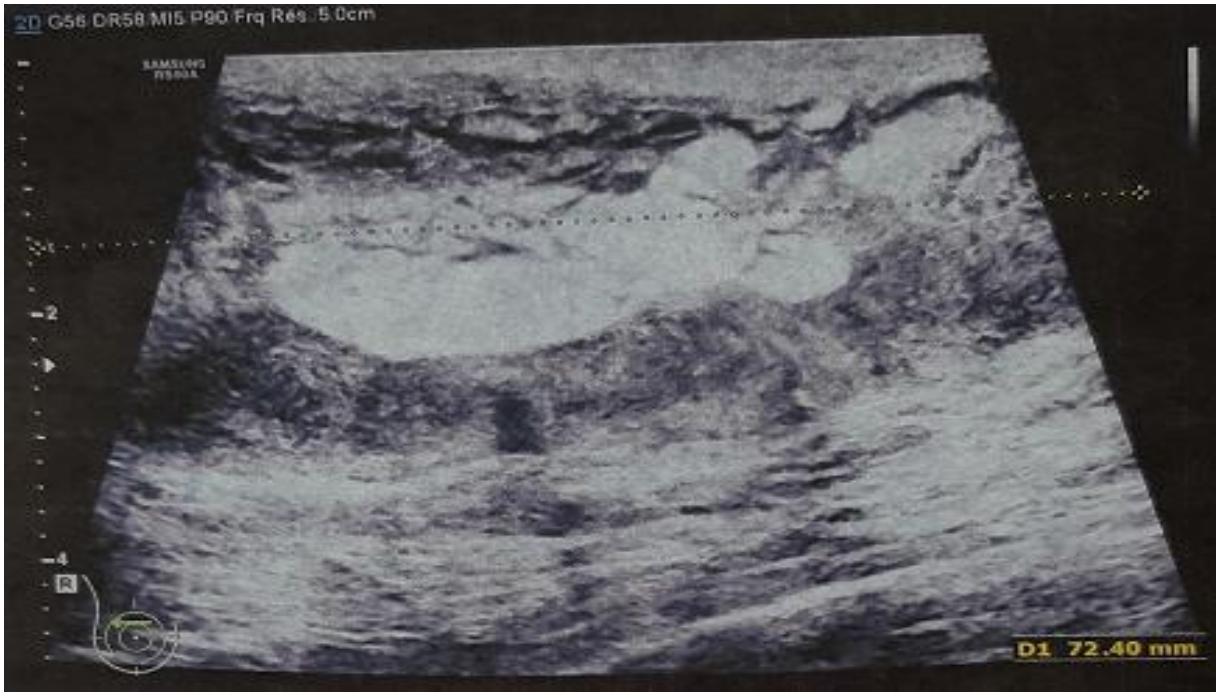

Figure 5

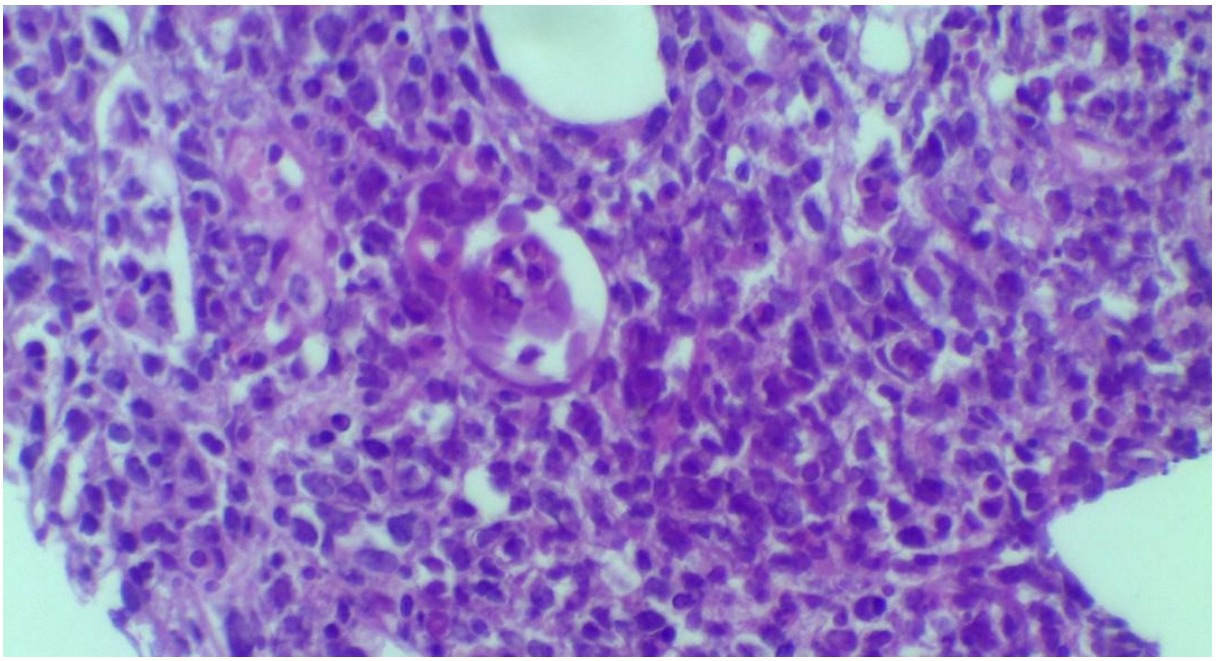

Figure 6

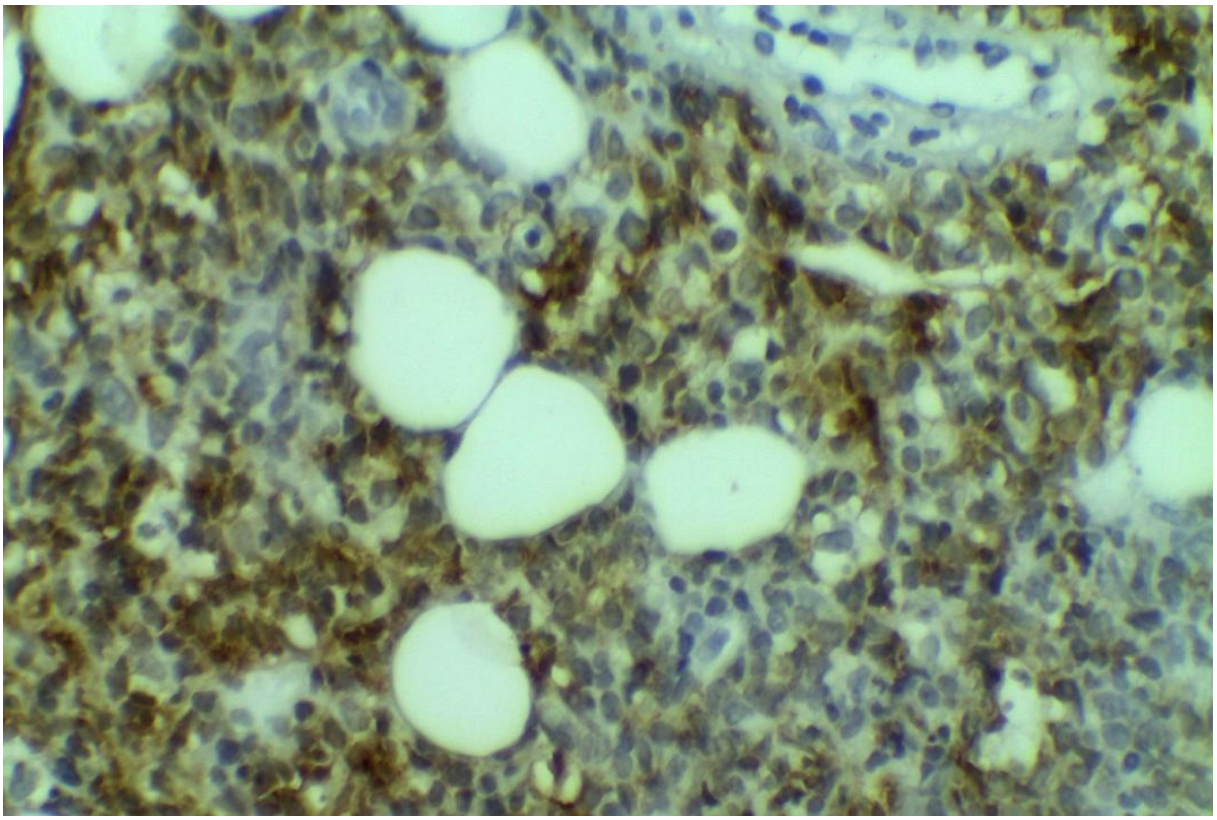

Figure 7