Gluteal Subcutaneous Extranodal Marginal Zone Lymphoma

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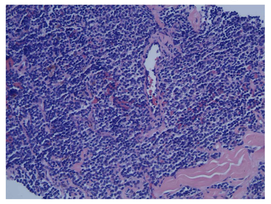
ABSTRACT

Both primary and metastatic involvement of subcutaneous adipose tissue due to extranodal Non-Hodgkin's lymphoma (NHL) are rare. The following case report describes the presentation of the most indolent subtype of NHL, marginal zone lymphoma, of the left buttock in a 50 year-old female with prior history of primary breast lymphoma s/p lumpectomy and chemotherapy 6 years prior. The aim of the following case report is to highlight the exceedingly rare case of subcutaneous marginal zone lymphoma, its CT imaging findings, and bring awareness to the need for future studies on disease progression, treatment approach, and the development of standardized surveillance guidelines.

CASE PRESENTATION

50 year-old Hispanic female referred to interventional radiology for biopsy of asymptomatic bilateral subcutaneous gluteal lesions with increased FDG avidity on PET/CT. Patient had a past medical history of primary breast lymphoma (PBL), of the marginal zone subtype, s/p lumpectomy and Rituximab chemotherapy six years prior. An initial FDG-CT/PET showed slight increase in activity in the gluteal region bilaterally two years prior to her presentation at our department. The left gluteal lesion was selected for biopsy and 3 core biopsy samples were obtained. The pathology report revealed diffuse infiltration by small lymphocytes with mature cytological features. Immunohistochemical stains revealed predominant B cells, positive for CD20, and uniformly positive for bcl-2; negative for CD3, CD5, CD10, bcl-6 and bcl-1, favoring low grade B-cell lymphoma of the marginal zone subtype (Fig. 1).



Treatment was not pursued at this time due to the patient having stable blood work results and remaining asymptomatic. Unfortunately, she was lost to follow up, but began to have pain in the buttock and was able to palpate a mass two years later. She sought medical attention and was found to have spread to subcutaneous tissues of an anterior thigh, abdomen, and arm. Patient is currently under treatment with the trial drug Acalabrutinib, with no significant decrease in size of the lymphomas. However, she remains minimally symptomatic, has undergone colonoscopy and endoscopy with no findings, and is on surveillance with 6 monthly CT scans.

INTRODUCTION

Lymphomas can originate in the lympho-reticular tissue, within any part of the system, comprising 10% of all malignant tumors and is divided into Hodgkin disease and NHL [1]. NLH is the most common type of lymphoma, with diffuse large B-cell lymphoma being its commonest subtype.

The NHL subtype of marginal zone lymphoma represents a group of lymphomas that have been classified together because they appear to arise from post-germinal center marginal zone B cells. They share the following immunophenotype: positive B cell markers CD19, CD20, and CD22, and negative for CD5, CD10, and usually CD23.

Subtypes are recognized in the WHO classification of lymphoid neoplasms:

- Extranodal marginal zone lymphoma (EMZL) of mucosa associated lymphoid tissue (MALT lymphoma)
- Nodal marginal zone lymphoma
- Splenic marginal zone lymphoma

With a median age at diagnosis of 66 years, EMZL accounts for 5 to 10 percent of NHLs in the US, but make up approximately half of lymphomas in sites such as the stomach, lung and ocular adnexa [2]. Primary breast lymphomas make up <1% of all NHL, 1.7–2.2% of all EMZL and 0.04–0.5% of all malignant neoplasms of the breast. Of primary breast lymphomas, marginal zone lymphoma makes for around 9% of cases [3].

EMZL tend to stay localized, but being that they are a clonal B cell neoplasm, they often recur locally and have potential to spread systemically, transforming to an aggressive B cell lymphoma on occasion. Historically, studies have suggested that their etiology overall is chronic immune stimulation, often due to bacterial, viral, or autoimmune stimuli. With acquisition of additional mutations, including the chromosome abnormalities, the tumor becomes antigen-independent and gains the capacity for systemic spread. Of note, loss-of-function studies in knockout mice show that FOXP1 deficiency leads to reduced B cell numbers, impaired T cell independent antibody production, and decreased B cell survival, possibly because of lowered expression of BCL-XL, an anti-apoptotic member of the BCL2 family [4].

IMAGING

While radiological modalities such as sonography, computed tomography (CT) and magnetic resonance (MR) imaging aid in the diagnosis of this disease, diagnosis using these modalities is not conclusive. A biopsy is necessary for a final and conclusive diagnosis.

CT pelvis WO demonstrate a soft tissue lesion in the lateral aspect of the superior left gluteal region which is isodense to musculature and mild surrounding fat stranding, measures 5.8 cm x 2.0 cm x 2.6 cm (AP X TV X CC). Below is the imaging of the CT guided biopsy performed.

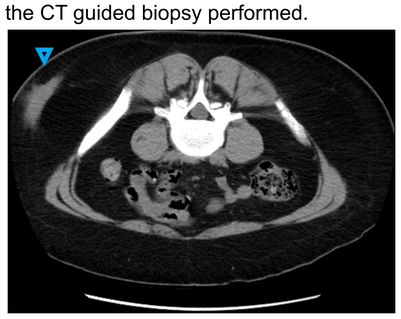


Figure 2A: Axial plane

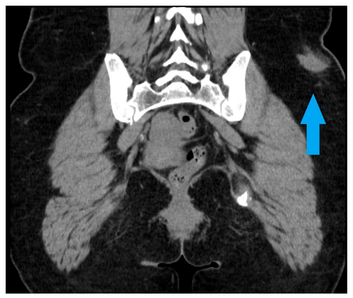


Figure 2B: Coronal plane

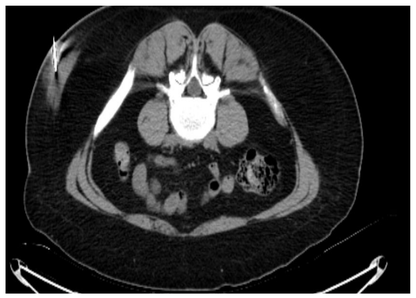


Figure 2C: CT guided biopsy

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CONCLUSION

The stomach is the site of origin in around 50% of patients presenting with extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT); it is known to be associated with *H. pylori* infection. However, very few cases have been reported to involve subcutaneous tissue in patients with gastric and non-gastric MALT lymphomas.
An Austrian retrospective study found 12/ 200 patients had subcutaneous spread from MALT-lymphoma, specifically of the ocular adnexa and the breast, which is congruent with our case. Given that most cases of subcutaneous involvement have been reported to be on the limbs and trunk, with only a select few occurring in the gluteal region, it is unknown whether local trauma such as from injections may predispose the proliferation of these lymphocytes [1]. On the other hand, the etiology of primary breast EMZL is unclear. Its progression, treatment approach, and response is less studied due to its rarity. A case report in 2020 of an asymptomatic 64 year old female with bilateral primary marginal zone lymphoma advanced to multiple organs claims breast EMZL can be managed with close observation so long as patients remain hemodynamically stable and asymptomatic. They cited the Surveillance, Epidemiology, and End Results (SEER) registry database, which reported that PBL has increased in incidence over the last four decades for younger women. There have been no prospective studies on this rare type of cancer [6]. Although indolent and less aggressive than other forms of breast lymphoma, it is important to keep a level of alertness to possible extra nodal involvement in the case of primary breast EMZL, as occurred with our patient with involvement of multiple subcutaneous sites. Although not presenting an imminent threat to life, it signifies an immense burden to patients in terms of procedures, imaging surveillance and medication side effects and costs. Both retrospective and prospective studies are needed to evaluate for possible etiologies, and medical and/or surgical treatment options, and their outcomes, respectively. Moreover, a multicenter meta analysis of surveillance intervals and lengths could set forth a standard of care for patients.

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