Subcutaneous panniculitis-like T-cell lymphoma of the breast in an adolescent female: An Uncommon presentation

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Abstract

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of peripheral T-cell lymphomas (PTCL) and is extremely uncommon in the pediatric population. We present a case of a 15-year-old girl with SPTCL and an unusual involvement of the breast. The FDG-PET/CT showed avid uptake of 18F-FDG in the breast predominantly involving the subcutaneous tissue that improves post treatment. To our knowledge, this is the first case of breast SPTCL reported in pediatric patient. A study published by Goto-et-al in 2019 [(1)](#ref-0001), found only 27 cases of SPTCL under 15 years, including four infants and none of them shown breast involvement.

TITLE PAGE

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Abbreviations key:

Number	Abbreviations	Full form
1	SPTCL	Subcutaneous panniculitis-like T-cell lymphoma
2	PTCL	Peripheral T-cell lymphoma
3	ALCL	Anaplastic large cell lymphoma
4	NHL	Non-Hodgkin lymphoma
5	EORTC	European Organization for Research and Treatment of Cancer

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Abstract :

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of peripheral T-cell lymphomas (PTCL) and is extremely uncommon in the pediatric population. We present a case of a 15-year-old girl with SPTCL and an unusual involvement of the breast. The FDG-PET/CT showed avid uptake of 18F-FDG in the breast predominantly involving the subcutaneous tissue that improves post treatment. To our knowledge, this is the first case of breast SPTCL reported in pediatric patient. A study published by Goto-et-al in 2019 (1), found only 27 cases of SPTCL under 15 years, including four infants and none of them shown breast involvement.

Case Report:

A 15-year-old female presented to family physician with a 4-months history of left breast swelling. According to the patient, she felt a lump in the left breast that was slowly increasing in size causing some discomfort and burning sensation. There was no complaint of pruritus or discharge from the nipple. On examination, a violaceous thickened cutaneous plaque was noted without any excoriation or ulceration. The patient was referred to the breast clinic where an ultrasound-guided biopsy of the breast parenchyma and axillary node was performed, that revealed chronic inflammatory changes (mixed infiltrate of lymphocytes, histiocytes, and occasional plasma cells with stromal hyalinization) with negative histology for bacterial/fungal stains. A diagnosis of morphea profunda was favored, and patient was referred to the morphea clinic at our hospital. After a thorough evaluation, it was concluded that her symptoms and presence of histiocytes on biopsy were not consistent with morphea and possibility of non-specific inflammation was entertained, particularly in view of a preceding covid vaccination in the ipsilateral arm. Clarithromycin was prescribed and inflammatory markers (ESR, CRP, ANA) were done and found to be non-diagnostic. Ultrasound was repeated to assess any interval change and revealed extensive soft tissue edema of the left breast and enlarged axillary lymph

nodes, concerning for lymphoproliferative disorder (Fig-1a). In view of the ultrasound findings and interval progression, an MRI of the breast was done that revealed marked and diffuse inflammation of the left breast predominantly involving the subcutaneous soft tissue with questionable nipple retraction (Fig-1b). Repeat MRI with contrast after 2 weeks (Fig-1c) demonstrated mild interval progression with predominant subcutaneous enhancement and enhancing axillary lymph nodes without any discrete parenchymal mass. The right breast and axilla were normal.

An ultrasound-guided punch biopsy of the subcutaneous soft tissue of the left breast (Fig-1d) demonstrated fibroadipose tissue with lobular panniculitis-like lymphoid cell infiltrate, background fat necrosis, karyorrhexis, and histiocytes containing karyorrhectic debris. Atypical lymphoid cells were mildly enlarged and have irregular and hyperchromatic nuclei. A helpful diagnostic feature was the rimming of atypical lymphoid cells surrounding the individual adipocytes (Fig-1e). By immunohistochemistry, the atypical/alipotropic lymphoid cells expressed TCR beta-F1, CD8, and cytotoxic molecules (TIA1 and granzyme-B) were negative for CD4 and CD56. Epstein-Barr-encoding region in-situ hybridization was negative. PCR analysis showed TCRD gene clonal rearrangement. The overall findings were in keeping with a diagnosis of SPTCL. The expression of beta-F1 by the atypical cells and negative staining for CD56 facilitated the distinction from primary cutaneous gamma/delta (γ/δ) T-cell lymphoma. Additionally, the negative staining for CD30 together with morphology didn't support diagnosis of primary cutaneous-Anaplastic large cell lymphoma (ALCL).

Subsequently, the patient developed a new lesion in the right breast. FDG PET-CT (Fig-2a,b,c) was performed and revealed asymmetrical increased activity predominantly affecting the subcutaneous soft tissue of the left breast (SUVmax-8.7) and left axilla (SUVmax-10.5) as well as hypermetabolic axillary lymph nodes. Some patchy subcutaneous soft tissue activity was also noted in the medial aspect of the right breast, concerning for bilateral disease.

The oncology team discussed the diagnosis and management plan with the patient and family and started immunosuppressive therapy with prednisone (60mg/m2/day PO divided BID) and cyclosporin (6mg/kg/day PO divided BID). CT scan of the neck and chest was repeated after four weeks of therapy showed resolving left breast cutaneous and subcutaneous thickening and inflammatory-like changes as well as resolved left axillary lymphadenopathy. The prednisone dose was tapered to 30mg/m2/day divided BID. Repeat FDG-PET/CT (Fig 2c,d,e) for response assessment at 8-weeks of the therapy revealed significant improvement, SUV max falls from 8.7 to 3.5 in the left breast and from 10.5 to 3.02 in the left axilla. No activity was perceived in the right breast. Currently, the patient is on tapering doses of prednisone with a goal to decrease it to 2.5 mg daily to complete one year of therapy.

Discussion:

SPTCL is one of the rarest subtypes of non-Hodgkin lymphoma (NHL) in children, constituting less than 1% of the NHL and the cutaneous lymphomas (2,3) with limited literature in the pediatric population (4,5). No definite gender predilection is noticed, but a slight female predilection is reported by a few studies and is usually associated with good outcomes (5).

Historically, the SPTCL has two subtypes based on T-cell phenotypes – alpha/beta (α/β) with better prognosis and gamma/delta (γ/δ) with poor outcome (3). The European Organization for Research and Treatment of Cancer (EORTC) classification (2005) modified this categorization and advocated the use of α/β T-cell phenotype for SPTCL only and described γ/δ T-cell phenotype as a distinct cutaneous T-cell lymphoma (6). On immunochemistry, the malignant T-cells in SPTCL are CD8+ve, CD3+ve, beta-F1+ve, CD4-ve, and CD56-ve. The γ/δ T-cell phenotype cutaneous T-cell lymphoma is CD56+ve, while beta-F1-ve, and CD4 and CD8 are negative in most cases (3). Histopathology with immunohistochemistry is the gold standard for the diagnosis and is confirmatory in almost all cases (5).

The histological findings include T-cells and macrophages infiltrating subcutaneous fat lobules with relative sparing of the dermis and epidermis simulating panniculitis. The malignant T-cell infiltration of the hypodermic soft tissue in SPTCL incites an inflammatory response very similar to panniculitis (7,8). The

inflammatory change can involve a single site or be multicentric, presenting as soft tissue nodules, plaques, edema, discoloration, and itch (5). Compared to young infants, older children with SPTCL present frequently with fever and weight loss (90% vs 40%) and have a higher association with HLH (45.5% vs 20%) (1).

Ultrasound is the initial imaging modality of choice owing to the superficial location and typically demonstrates vague inflammatory changes with or without regional lymphadenopathy (9). CT/MRI may help to determine the extent of inflammatory changes, evaluate deeper structures, underlying masses, and loco-regional lymphadenopathy (3,10). FDG-PET is considered the most useful imaging modality, integrating both anatomical and functional assessment. (11,12). FDG-PET demonstrates the distribution and uptake of the FDG at the primary site and any involvement of the distant sites, visceral organs, and lymph nodes, allowing for accurate pre-treatment staging (3,11). It can also help to guide the optimal biopsy site based on the metabolic activity and FDG avidity (12). Post-therapy FDG-PET is useful in determining the treatment response, degree of residual disease, and any signs of recurrence (3,11,12).

The management of SPTCL in the pediatric population is variable and largely depends on the histopathological diagnosis and institutional preferences. Potential treatment modalities include observation, immunosuppression, chemotherapy, and radiotherapy (4,13). Similar to the adults, pediatric case series have shown good treatment outcomes with dual immunosuppression (cyclosporin-A and prednisolone) in childhood SPTCL, particularly in the absence of HLH (4). One of the largest reviews of pediatric PTCL shows the best treatment outcome in SPTCL with maximum 5-years survival compared to the other pediatric PTCL (14).

Conclusion :

Clinically, the SPTCL often mimics the panniculitis from a benign dermatological disease; initial imaging and histopathological findings can also be non-diagnostic and a high index of suspicion is required to reach an accurate diagnosis. FDG-PET has emerged as an excellent imaging tool that can provide a road map for the diagnosis and management of the SPTCL by accurately guiding the biopsy site, eluding false-negative examinations, and by identifying the multicentricity of the disease. Our case represents the first case of breast SPTCL in the pediatric population and describes the role of FDG-PET in the evaluation of the lesion, determining the multicentricity of the disease, and loco-regional lymphadenopathy.

Conflict of Interest statement: No affiliations to any organization.

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Figures & Legends

Figure 1: Ultrasound of the left breast (a) shows diffuse inflammatory changes predominantly affecting the subcutaneous soft tissue. No definite mass or focal lesion noted. Axial FS-T2W MR image (b) shows marked and diffuse hyperintensity and inflammatory changes of the left breast predominantly involving the subcutaneous soft tissue. Repeat MRI with contrast (c) after 2 weeks demonstrates mild interval progression of the disease with prominent subcutaneous enhancement and enhancing left axillary lymph nodes. No focal mass noted. Histology revealed adipocytes rimmed by mildly enlarged lymphoid cells with irregular and hyperchromatic nuclei (d). Karyorrhexis and histiocytes containing nuclear debris in background. Mitotic figures are evident. Hematoxylin and eosin stain, X200 (e): CD8 staining highlights the atypical lymphoid cells rimming the adipocytes. Immunohistochemistry for CD8, X40

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Figure-2: Pre-treatment whole-body FDG-PET/CT (a,b,c) reveals asymmetrical increased activity mostly affecting the subcutaneous soft tissue of the left breast and axilla with hypermetabolic axillary lymph nodes (black arrows in a,b). Some patchy soft tissue activity also noted along the medial aspect of the right breast (yellow arrow in a). Follow-up whole-body FDG-PET/CT (d,e,f) reveals significantly decreased activity in the subcutaneous soft tissue of the left breast and axillary lymph nodes (black arrows in d,e). There is near complete resolution of the activity in the right breast.

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