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Dermatopathic Lymphadenitis Mimicking Breast Cancer with Lymphatic Metastasis: A Case Report and Discussion

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 56
Final Diagnosis: Dermatopathic lymphadenitis
Symptoms: Lymphadenopathy
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Rare co-existence of disease or pathology
Background: Dermatopathic lymphadenitis is a rare benign lymphatic hyperplasia commonly associated with exfoliative or eczematoid dermatitis. Of interest, this condition can be confused with lymphatic metastasis in adults.
Case Report: In this report, we describe the case of a 56-year-old woman diagnosed with left breast invasive ductal carcinoma in remission, who presented with dermatopathic lymphadenitis mimicking breast cancer recurrence.
Conclusions: Dermatopathic lymphadenitis is a benign entity that needs to be considered in the differential diagnosis of lymphadenopathy. Pursuing extensive workup in asymptomatic patients with a similar presentation and initial negative tests for malignancy recurrence is not recommended.

MeSH Keywords: Breast Neoplasms • Lymphadenitis • Recurrence • Triple Negative Breast Neoplasms

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Background

Dermatopathic lymphadenitis is a distinctive reaction pattern in lymph nodes, characterized by paracortical hyperplasia composed of interdigitating dendritic cells (IDC), Langerhans cells (LC), macrophages containing melanin pigment, and small T cells. Dermatopathic lymphadenitis is believed to represent an exaggerated response to increased antigenic stimulation in the skin [1].

Dermatopathic lymphadenitis is often seen in patients with skin diseases, especially mycosis fungoides/Sézary syndrome [2]. DLN has also been associated with several viral diseases, especially Human Immunodeficiency Virus (HIV) [3] and Human Papilloma Virus HPV [4].

Although DLN is a benign entity, its uncommon concurrence with cancer may lead physicians to pursue unsolicited aggressive diagnostic and therapeutic measures. Hence, DLN should be included in the differential diagnosis of lymphadenopathy in malignancies.

Case Report

A 56-year-old Hispanic female patient with past medical history of stage III-B left breast invasive ductal carcinoma triple-negative was diagnosed in 2010. She underwent modified radical mastectomy, axillary lymph node dissection, and neoadjuvant TAC (docetaxel plus doxorubicin plus cyclophosphamide), and radiation completed in 2010.

Review of her medical history was significant for diabetes mellitus type II, hypertension, dyslipidemia, normocytic anemia, and right brachiocephalic vein thrombosis managed with Coumadin.

In 2016, the patient presented with diffuse lymphadenopathy involving bilateral axillary and inguinal lymph nodes, suspicious for recurrence of malignancy. No fever, chills, or skin lesions were reported. Complete review of systems was not contributory.

Lab values were: hemoglobin: 11.6 g/dL, Hct: 36.2%, MCV: 88.1 fL, WBC: $4.85 \times 10^3/\mu\text{L}$, and PLT: $219 \times 10^3/\mu\text{L}$. Vitals were: t: 37.3°C, BP: 128/72, P: 97, RR: 18.

On physical examination, generalized lymphadenopathy was noted, which was more pronounced on the right axilla. No skin lesions or organomegaly were appreciated.

The patient underwent multiple imaging modalities. Following the initial presentation, a PET scan was performed, showing hypermetabolic lymph nodes in the right axillary and subpectoral

region, worrisome for malignancy: a lateral right axillary lymph node measured 1.4×1.1 cm with an SUVmax of 6.0, and a subcentimeter right interpectoral lymph node showed SUVmax of 3.6. These lymph nodes were contralateral to the patient's left breast carcinoma. Subcentimeter mildly FDG-avid lymph nodes were seen in the left axilla. A millimetric left axillary lymph node showed SUVmax of 1.8. Mildly FDG-avid bilateral level IIA cervical lymph nodes were seen, the more prominent one on the right, showing SUVmax of 3.6 and measuring 7 mm in short axis.

Multiple hypermetabolic lymph nodes were seen in the retroperitoneum (left paraaortic region, left common iliac chain, and left external iliac chain). A hypermetabolic node along the posteromedial aspect of the left psoas muscle measured 1.5 cm in diameter, with an SUVmax of 8.3. A left external iliac lymph node measured 2.1×1.5 cm with an SUVmax of 5.2. The pattern of nodal disease was very suggestive of lymphoma, which may be an incidental finding in this patient with a history of breast cancer.

Interestingly, diffuse mildly increased tracer uptake was seen throughout the spleen, which may have been related to extramedullary hematopoiesis secondary to anemia or lymphomatous infiltration.

Hence, a subsequent right axillary lymph node needle core biopsy was performed and revealed follicular and interfollicular lymphoid hyperplasia, without malignancy. The lymphadenopathy persisted, so a follow-up abdomen and pelvis CT scan with contrast was done and showed slightly enlarged left common iliac lymph nodes (Figure 1), with subcentimeter paraaortic lymph nodes (Figure 2).

A PET scan done at 4-month interval revealed progression of lymph nodes above and below the diaphragm, with stable diffuse increased uptake in the spleen, which could represent lymphoproliferative disorder, or an infectious or inflammatory process.

Concurrent left inguinal lymph node needle core biopsy demonstrated follicular and interfollicular hyperplasia (Figure 3), scattered pigmented macrophages (Figure 4), and rare eosinophils, suggestive of dermatopathic lymphadenitis without malignancy.

A scheduled screening right breast mammogram showed no evidence of right breast malignancy, with interval enlargement of intramammary lymph nodes in the upper outer quadrant related to known lymphoproliferative process, with stable right axillary lymphadenopathy. Follow-up chest, abdomen, and pelvis CT scans revealed minimal interval increase in size of left axillary lymph nodes, as well as stable mildly enlarged retroperitoneal and left external iliac lymph nodes.

Figure 1. CT abdomen and pelvis showing slightly enlarged left common iliac lymph nodes.

Figure 2. CT abdomen and pelvis showing one of several subcentimeter paraaortic lymph nodes.

Four months later, a PET scan showed significant interval improvement of the previously avid lymph nodes, with interval resolution of the previously noted diffuse increased uptake of tracer by the spleen. A final right axillary lymph node needle core biopsy confirmed the diagnosis of dermatopathic lymphadenitis without malignancy. Spontaneous resolution of dermatopathic lymphadenitis was achieved without any further intervention or treatment.

Discussion

Dermatopathic lymphadenitis (also known as lipomelanotic reticulosis, or Pautrier–Woringer disease) is a rare type of benign lymphatic hyperplasia associated with a variety of exfoliative or eczematoid type inflammatory erythrodermas. The axillary

Figure 3. Lymph node with follicular (arrows) and interfollicular (arrow head) hyperplasia.

Figure 4. Pigmented-laden macrophages (arrow) compatible with dermatopathic lymphadenitis.

and inguinal regions are most commonly affected, although occasionally it can present in the head and neck as well [5].

DLN is often seen in patients with skin diseases, especially mycosis fungoides and Sézary syndrome, but has rarely been described in the absence of clinical skin disease. DLN was first coined by Hurwitt et al. The relationship between lymph node hyperplasia and cutaneous disease was first described by Wise et al., although it was later established by Pautrier and Woringer as lipomelanotic reticulosis [6,7].

In adults and children, there is a range of non-neoplastic, non-infectious etiologies for lymphadenopathy. These include reactive lymphoid hyperplasia (RLH), dermatopathic lymphadenitis (DLN), Rosai–Dorfman disease, Castleman disease, Kimura disease, Kikuchi–Fujimoto disease, and lymphadenopathy associated with autoimmune and metabolic/storage disease. Differentiating between these nodal entities and diagnosing DLN is mostly based on the lymph node biopsy, FNA. [8] ^{18}F -FDG PET/CT, as a sensitive and noninvasive whole-body imaging technique, can also be used as a valuable aid in the diagnostic workup [9]. In a review by Hu et al. of F-FDG PET/CT characteristics in malignancies vs. benign lymphadenopathy, the SUV(max) of malignant tumors (6.3 ± 2.4) was significantly greater than that of benign lesions (2.9 ± 2.0) ($P < 0.001$). Receiver-operating characteristic curve analysis showed that the SUVmax cutoff value of 3.5 had a

high sensitivity (92.6%) and specificity (76.9%) for the diagnosis of malignancies [10].

Morphologic features found to be helpful in the diagnosis of DLN on fine-needle aspiration cytology include melanin-laden macrophages with variable pigment; large, histiocytic clusters with blood vessels at the center; characteristic histiocytes with elongated vesicular nuclei, nuclear grooves, crumpled and convoluted nuclei, and pseudonucleoli; and absence of or very few tingible body macrophages. Positivity on immunostaining for S-100 and negativity for CD68 aid in the diagnosis [11].

In our case, distinguishing DLN and breast cancer lymph node involvement depended on multiple characteristics: PET scan findings of higher SUVmax in malignancies compared to benign lymphadenopathy, and the tendency of breast cancer to metastasize to regional axillary lymph nodes in contrast to the tendency of DLN to have widespread involvement of lymph nodes.

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Conclusions

This case report highlights a non-malignant etiology of lymphadenopathy in the setting of a history of breast cancer, mimicking cancer recurrence. This should be taken into consideration when evaluating lymphadenopathy in patients with a cancer history, as this presentation may not always be due to infection or malignancy, but can be due to a reactive condition such as DLN [6], making the differential diagnosis of DLN an important entity to keep in mind, even in the absence of skin lesions.

This case also suggests that extensive workup in an asymptomatic patient with initial negative findings for malignancy recurrence is of low diagnostic yield due to the benign course and spontaneous resolution of this disease.

Conflicts of interest

None.