JPDS Journal of the Philippine Dermatological Society

CASE REPORT

Lupus panniculitis in an ANA-negative systemic lupus erythematosus patient: A case report

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ABSTRACT

INTRODUCTION Lupus panniculitis (LP) is an unusual type of cutaneous lupus erythematosus (CLE) wherein the cutaneous inflammatory reaction involves primarily the deeper dermis and subcutaneous fat. It is characterized by the appearance of recurrent, mostly asymptomatic, firm, nodules or plaques, involving the face, upper limbs, and buttocks.

CASE REPORT In our case, a 30-year-old female presented with a non-tender, non-movable nodule on the left breast, 6 weeks prior to her admission. She had fever, chills, and joint pains. The patient later developed hyperpigmented plaques on the infraclavicular area, and left flank extending to the abdomen. Urinalysis showed proteinuria, and RBC cast. She also had leukopenia, and anemia on CBC. Chest computerized tomography (CT) scan revealed a heterogeneously enhancing soft tissue mass in the base of the neck at the right infraclavicular region with malignant features. ANA titer was normal, while skin biopsy on two sites and direct immunofluorescence studies were compatible with lupus panniculitis. She was managed as a case of systemic lupus erythematosus (SLE) using a combination of hydroxychloroquine, and oral corticosteroids, which afforded temporary relief of symptoms. The patient however was lost to follow-up and opted for alternative medicine, and subsequently succumbed to the complications of SLE.

CONCLUSION This case highlights the importance of a carefully made assessment after an accurate clinicopathological correlation was done. This case also emphasizes that although LP if associated with SLE may signify a milder condition, judicious monitoring and follow-up must still be undertaken since management is based on the disease activity.

KEYWORDS Chronic cutaneous lupus erythematosus, lupus panniculitis, lupus mastitis

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Conflict of interest
None

Source of funding
None

INTRODUCTION

Lupus panniculitis (LP) is a clinical variant of cutaneous lupus erythematosus (CLE). It may present as exclusive cutaneous condition, or it may coexist with discoid lupus erythematosus (DLE), or systemic lupus erythematosus (SLE). Although LP is more frequent in women, it may affect both genders and the median age of presentation is 41 years old.[1] The condition consists of a tender, indurated, subcutaneous nodules or plaques with or without surface changes. Surface changes may include erythema, atrophy, hyper or hypopigmentation, hyperkeratosis, telangiectasia, ulceration, necrosis, or follicular plugging. Typical sites involved are the proximal extremities, buttocks, trunk, scalp, and face. The condition runs a chronic and relapsing course and lesions tend to resolve with lipoatrophic depressions.[1,2] A rarer variant is called lupus mastitis, defined as the extension of LP to the mammary gland.[3]

CASE REPORT

This is a case of a 30-year-old female who presented with a firm, approximately 2x3 cm, non-tender, non-movable nodule over the left breast, six weeks prior to admission, without any accompanying symptoms. She then developed irregularly shaped, hyperpigmented, indurated plaques on the infraclavicular area and left flank. At that time, the patient experienced high-grade fever and chills. Consult was done, and the assessment was soft tissue infection. She was prescribed with sultamicillin 750mg/tablet,[1] tablet twice a day for 7 days, which provided no relief of her symptoms.

Four weeks prior to admission, the patient noted the development of a hyperpigmented plaque overlying the nodule. Because of this, consult with another physician was done and an ultrasound of the left breast revealed soft tissue swelling. Ciprofloxacin 500mg/capsule, twice a day, and amycin 300mg/capsule, twice a day, for

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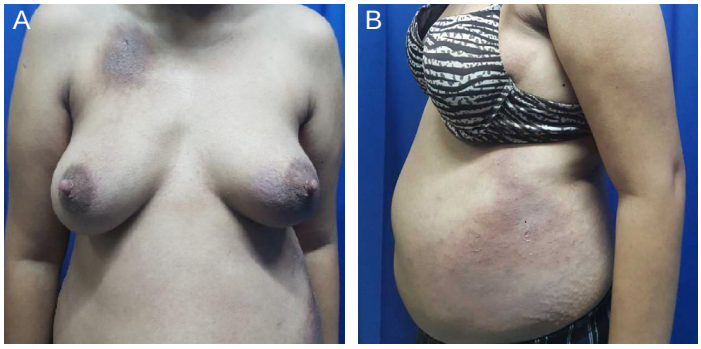

Figure 1. **A.** Showing the round, well-demarcated, hyperpigmented to dusky plaque on the right infraclavicular area and the left breast. **B.** Showing the irregularly shaped, ill to well-defined hyperpigmented plaque on the left flank extending to the lower left abdomen.

10 days were given but these did not provide resolution of her symptoms.

In the interim, the patient still experienced intermittent high-grade fever and increase in the size of the lesions.

Patient was admitted under the Internal Medicine Department and was referred to the Dermatology service. On physical examination, there were well-demarcated, hyperpigmented, plaques on the right infraclavicular and left breast. At the time of examination, there were no palpable breast nodules, or axillary lymphadenopathies. There was also an irregularly shaped, hyperpigmented plaque on the left flank, extending to the lower abdomen (Figure 1). Complete blood count (CBC) revealed leukopenia and anemia, while the antinucleur antibody (ANA) test was within normal limits. Both erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated, while urinalysis revealed proteinuria (+++) and red blood cell (RBC) casts. Computed tomography (CT) scan of the chest showed soft tissue tumor on the right infraclavicular region with malignant features. The patient was also referred to the Surgery Department for the evaluation of the breast lesion. However, during the time of examination, there was no palpable breast mass, hence the surgeons opted to wait for the result of the skin biopsies.

Skin biopsies from the dusky plaque on the right supraclavicular area, and left flank were obtained and both sections revealed basal layer vacuolization, mild to moderately dense superficial and deep perivascular and peri-appendageal lymphocytic infiltrates admixed with few plasma cells (Figures 2 and 3). In addition, the lesion on the flank showed lymphocytic infiltrates with occasional plasma cells extending into the subcutaneous lobules wherein hyaline necrosis of the fat and nuclear dust within the infiltrates were noted. (Figure 2B and 2C) These findings were consistent with LP. The Surgery Department was notified of the result of the skin biopsies and decided to defer the biopsy on the left breast. They noted however that they will proceed with the contemplated procedure if the patient will not

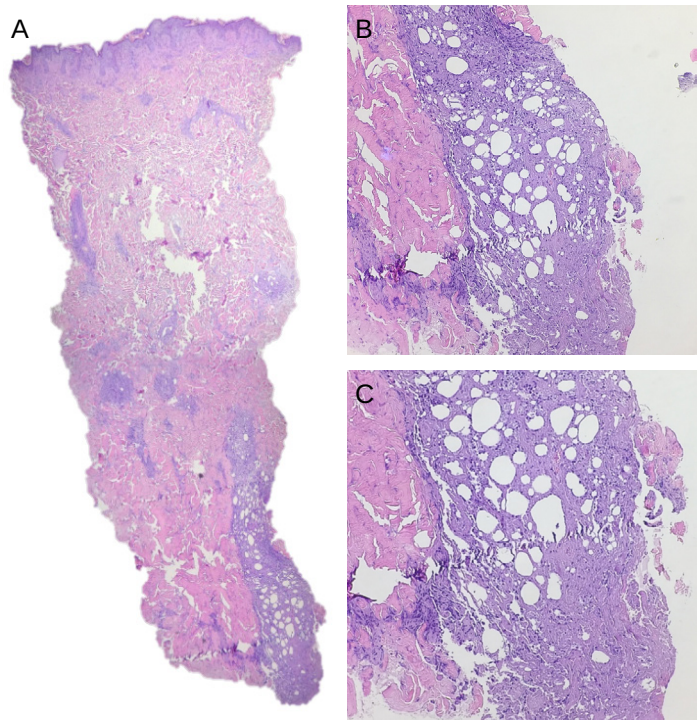

Figure 2. Skin punch biopsy on the flank. **A.** Scanning view. **B.** LPO: Lesion on the flank showed lymphocytic infiltrates with occassional plasma cells extending into the lobules of the subcutaneous fat, the blue tinge indicates presence of mucin. **C.** HPO: necrosis of the fat towards the base of the section in the subcutaneous fat, and nuclear dust within the infiltrate. These findings were consistent with lupus panniculitis.

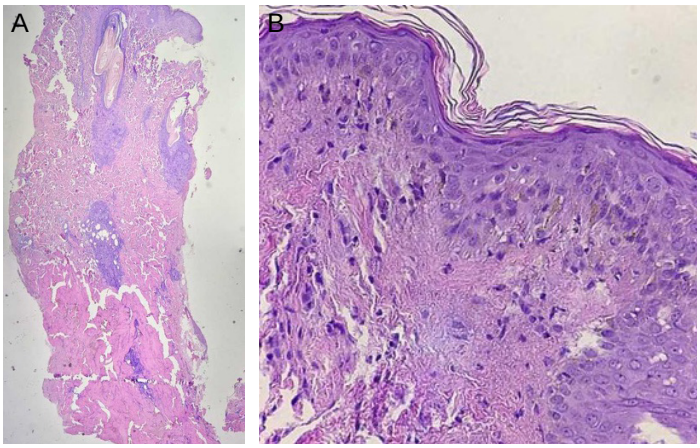

Figure 3. Skin punch biopsy on the clavicular area. **A.** Scanning view. **B.** HPO view showing basal layer vacuolization, follicular plugging, mild to moderately dense superficial and deep perivascular and peri-appendageal lymphocytic infiltrates admixed with few plasma cells.

respond well with the initial treatment. Direct immunofluorescence revealed presence of granular basement membrane zone deposition of IgG, C3, IgM and fibrin, consistent with a connec-

tive tissue disease. Further work up showed normal C3 and Anti-Ds DNA levels, while Anti-Sm and direct coomb's test were not done.

On review of system, patient reported absence of weight loss, non-scarring alopecia, malar rash, oral ulcerations, and photosensitivity. She however reported occasional joint pains involving both her elbows and knees.

Considering the clinical features including fever, joint pains, the discoid rash proven to be LP, urinalysis findings of proteinuria and RBC casts, and CBC findings of anemia and leukopenia, the patient fulfilled the American College of Rheumatologists (ACR) criteria for SLE. However, due to the negative ANA, normal C3 and anti-Ds DNA; and other immunologic markers not provided, it is difficult to classify her using the Systemic Lupus International Collaborating Clinics Classification (SLICC) Criteria for SLE.

The patient was managed as a case of SLE with LP and was given hydroxychloroquine 200mg/tablet OD with clearance from Ophthalmology service. She was also given prednisone 30mg/day (0.5mkd) and Vitamin D + calcium once a day. She was asked to apply clobetasol propionate 0.05% ointment twice daily on the indurated plaques. She was also advised rigorous sun protection measures and regular follow-up with her physicians. The patient was signed out as discharged improved and stable. However, she was lost to follow-up, and physicians were informed that she opted to seek alternative medicine which resulted to the patient succumbing to the complications of SLE.

DISCUSSION

LP is an uncommon subset of CLE. It can occur as a single manifestation of the disease, or it may be associated with DLE or SLE. The condition, LP, may emerge at the same time, before, or after the appearance of other signs and symptoms of DLE or SLE.[1]

The frequency of association of LP with SLE varies depending on the series. Arai and Katsuoka noted in their study that 40% were associated with SLE, while reports by Mastens et al and Massone et al showed only 10% and 22.2% association respectively.[4,5] Fraga et al observed that the coexistence of LP with SLE signified a marker for a less severe variant of SLE.[1]

ANA is often negative in cases of LP alone.1 A retrospective study by Ng et al noted only 27% of the cases of LP revealed a positive ANA; and it was emphasized that the presence of ANA positivity in a patient with LP signifies a high likelihood of systemic involvement. However, this finding is not universal as other studies did not find any association.[2] A study by Tarazi et al highlighted that although a positive ANA is a sensitive marker in identifying patients with SLE, ANA may not always be present in patients with significant disease. The study also discovered that ANA status can change over time, thus if ANA positivity will be required for a diagnosis of SLE, some cases might be missed.[5] This case also highlights the role of dermatologists in complex cases such as SLE. They are at the forefront of doing a thorough investigation about lupus-specific mucocutaneous findings, as these findings are part of both the ACR and SLICC diagnostic criteria for SLE. Because of the complexity of SLE, a multi-disciplinary approach is necessary to provide the best management.

The diagnostic procedure of choice for CLE is skin biopsy. The two most important histopathologic criteria for diagnosis of LP are the presence of lymphocytic infiltrate involving fat lobules and hyaline necrosis of the fat lobule.[1] Direct immunofluorescence is also a valuable tool and shows deposits of IgG, IgM and C3 at the dermoepidermal junction.[6,7] These are all consistent with the direct immunoflurescence findings of our patient.

Since this patient presented with a lesion on the breast initially perceived as a nodule, it is important to note that a rarer subtype of LP called lupus mastitis (LM) exists. It is the extension of the lupus panniculitis on the mammary gland, and presents clinically as a mass, or may present with cutaneous involvement such as thickening and discoloration, as observed in our patient. Just like LP, LM, may present before, during, or after a diagnosis of SLE is made. The diagnosis of LM may be established by doing skin biopsy, core needle biopsy, fine needle aspiration, or open surgical biopsy. Major histopathologic criteria includes hyaline fat necrosis, lymphocytic infiltration with lymphoid nodules surrounding the necrosis, periseptal or lobular panniculitis, and microcalcifications.8 Moreover, in some case reports, imaging modalities such as mammography and magnetic resonance imaging (MRI) helped in verifying the diagnosis.[3,8] In the literature review done by Voizard et al, there was no distinct investigation algorithm established. On mammography, LM often presents as an ill-defined mass, or either a focal or diffuse asymmetry. Other mammographic findings include large dystrophic calcifications and axillary lymph node enlargement that may be suggestive of a neoplastic process. 3 While a biopsy is necessary to rule out carcinoma, the procedure can possibly exacerbate the inflammatory process. Cho et al in their report therefore recommended that a trial pharmacological treatment be given first to avoid diagnostic biopsy or surgery.[8]

First-line treatment for both LP and LM is hydroxychloroquine, and effects may take up to 3 months.[1,3,4] Systemic corticosteroids may be combined with the anti-malarial drug during the initial therapy of patients presenting with extensive inflammatio.[4] For patients with LM, surgical intervention is the last option if pharmacological treatment fails to improve the symptoms.[8] In patients with systemic involvement, associated adverse side effects of chronic steroid use is of paramount consideration. As such, glucocorticoids are believed to be a bridge therapy. To minimize SLE-associated organ damage, the goal is to control active inflammation, reduce steroid dose, and eventually use long term immunosuppressives such as mycophenolate mofetil, azathioprine, and methotrexate.[1]

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CONCLUSION

Lupus panniculitis is a rare variant of CLE. A rare subtype of LP is LM that may present clinically as breast mass, and on imaging as a carcinoma. The frequency of association of LM and LP with SLE is variable, both may emerge simultaneously, after, or prior to the onset of SLE. This case highlights how complex lupus is that it presented with a number of diagnostic dilemmas. Therefore, a multi-specialty approach, and proper clinicopathologic correlation are needed to arrive at an appropriate diagnosis and management plan. Lastly, since SLE is characterized by a chronic course of remissions and flares, vigilant surveillance of disease progression is recommended as long-term treatment is designed depending on the disease activity.

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