Cutaneous Pseudolymphoma Due to Lamotrigine: First Reported Case

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Cutaneous Pseudolymphoma Due to Lamotrigine: First Reported Case

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Case Presentation:

Patient: 8 year-old Caucasian female.

History of Present Illness: The patient presented with new onset of three pink papules on the scalp, which were mildly painful to palpation and gradually increasing in size. She denied any insect bites or trauma to the area. She did report switching from oxcarbazepine to lamotrigine for her seizure disorder six months prior to onset of the lesions and was gradually escalating the dosage. Review of systems was negative for fever, weight loss, nausea, lymphadenopathy or night sweats. She gradually developed a total of nine lesions over a course of a few months following her initial presentation, but remained otherwise asymptomatic. The lamotrigine was suspected as the causative agent. Upon its discontinuation, the lesions involuted completely within weeks, without recurrence at nine months follow-up.

Medical History/Surgical History: seizure disorder, keratosis pilaris, seborrheic dermatitis.

Current Medications: lamotrigine, ketoconazole 2% shampoo

Physical Examination: nine well-circumscribed, mildly scaly, pink, indurated 0.5-1cm nodules on the frontal and vertex scalp (Figures 1 & 2). No lymphadenopathy.

Laboratory Data: CBC, immunoglobulin assay, bone marrow transplant panel, CMP, lactate dehydrogenase, inflammatory markers and viral testing- WNL, bacterial and fungal skin cultures negative.

Biopsy: *Health Network Labs* (AD13-02642, 03/13/2013) Right crown of scalp: Lymphohistiocytic infiltrate, nodular (Figures 3 & 4).

Health Network Labs (AD13-03460, 04/03/2013) Right lateral crown of scalp: Atypical dermal lymphoid infiltrate (Figures 5 & 6).

Immunohistochemical studies revealed small BCL2+ lymphocytes with a 2:1 mixture of CD3+ T-cells and CD20+ CD79a+ B-cells. The T-cells expressed CD2, CD5, and CD43 and a subset with loss of CD7. The CD4:CD8 ratio was 10:1. No follicular dendritic networks were noted with CD21 and CD23. Rare, scattered medium sized CD30 cells were noted. CD10, Bcl6, ALK, EBER1, IgD and IgM were negative. The plasma cells had kappa:lambda ratio of 2:1. Ki-67 was positive in 15% of lymphoid cells. Gene rearrangement by PCR revealed a peak at 228bp in a predominantly polyclonal background.

Treatment: Discontinuation of lamotrigine

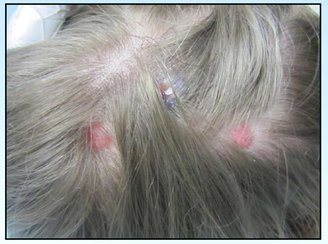

Figure 1: Three, well circumscribed, pink nodules on the scalp.

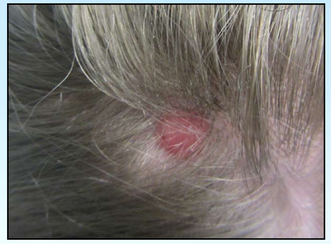

Figure 2: Close-up view of a scalp nodule.

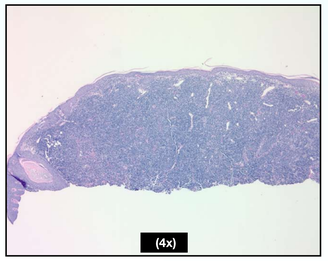

Figure 3: H&E 4x shave biopsy of right crown of scalp showing a dense, nodular lymphohistiocytic infiltrate.

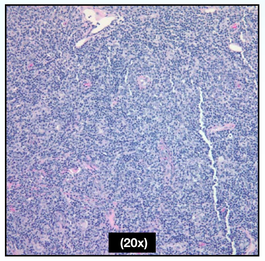

Figure 4: H&E 20x shave biopsy of right crown of scalp with a closer view of lymphohistiocytic infiltrate.

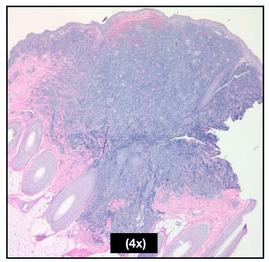

Figure 5: H&E 4x punch biopsy of right lateral crown of scalp showing an atypical dermal lymphoid infiltrate.

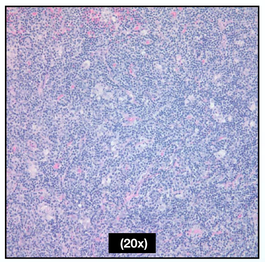

Figure 6: H&E 20x punch biopsy of right lateral crown of scalp showing a closer view of atypical dermal lymphoid infiltrate.

REFERENCES:

1 Ploysangam T, Breneman D, Mutasim D. Cutaneous pseudolymphomas. *J Am Acad Dermatol.* 1998; 38(6): 877-898.
2 Bergman R. Pseudolymphoma and cutaneous lymphoma: Facts and controversies. *Clinics in Dermatology.* 2010; 28:568-574.
3 Braddock S, Harrington D, Vose J. Generalized nodular cutaneous pseudolymphoma associated with phenytoin therapy. *J Am Acad Dermatol.* 1992; 27(2):337-340.
4 Cogrel O, Beylot-Barry M, Vergier B, et al. Sodium valproate-induced cutaneous pseudolymphoma followed by recurrence with carbamazepine. *British Journal of Dermatology.* 2001; 144:1235-1238.
5 Cheuk W, Lee K, Chong L, Yuen S, Chan J. IgG4-related sclerosing disease: A potential new etiology of cutaneous pseudolymphoma. *Am J Surg Pathol. 2009;* 33(11):1713-1719.
6 Marchesi A, Parodi P, Brioschi M, et al. Tattoo ink-related cutaneous pseudolymphomas: A rare but significant complication. Case report and review of the literature. *Aesth Plast Surg.* 2014; 38:471-478.
7 Gonzalez J, Sanz A, Martin T, Samaniego E, Martinez S, Crespo V. Cutaneous pseudolymphoma associated with molluscum contagiosum: a case report. *Int J of Dermatol.* 2008; 47:502-504.
8 Altamura D, Calonje E, Llau J, Rogers M, Verdolini. Diffuse cutaneous pseudolymphoma due to therapy with medicinal leeches. *JAMA Dermatol.* 2014; 150(7):783-784.
9 Imafuku S, Ito K, Nakayama J. Cutaneous pseudolymphoma induced by adalimumab and reproduced by infliximab in a patient with arthopathic psoriasis. *British Journal of Dermatology.* 2011;166:675-678.
10 Meyer S, Vogt T, Obermann EC, Landthaler M, Karrer S. Cutaneous pseudolymphoma induced by Cimicifuga racemosa. *Dermatology.* 2007;214:94-96.
11 Pathak P, McLachlan R. Drug-induced pseudolymphoma secondary to lamotrigine. *Neurology.* 1998;50:1509-1510.
12 Prabu V, Shivani A, Pawar V. Idiopathis cutaneous pseudolymphoma: An enigma. *Indian Dermatol Online J.* 2014;5(2):224-226.

Discussion:

Cutaneous pseudolymphoma is a term used to describe a heterogeneous group of benign reactive T- cell, B-cell or mixed cell type lymphoproliferative processes that resemble cutaneous lymphomas clinically and/or histopathologically.[1] Historically, these types of proliferations were classified under many alternative names and originally served to describe only B-cell type proliferations. The advent of T-cell type pseudolymphoma identification and description occurred more recently, in the 1980s.[1] With advances in immunohistochemistry allowing for more specific cell marker identification, cutaneous pseudolymphomas are often found to contain a mixture of T-cell and B-cell populations.[2]

The appearance of cutaneous pseudolymphoma is variable, from discreet nodules or papules to even confluent erythroderma in certain cases.[2] The high clinical variability further complicates diagnosis. While our case presented with nine individual nodular lesions, this alone would not be sufficient to have high suspicion for cutaneous pseudolymphoma without including a much broader differential diagnosis.

The primary concern regarding a diagnosis of cutaneous pseudolymphoma is the clinician's ability to effectively differentiate this entity from a true malignant lymphoma. Immunostaining has some value by identification of heterogeneous cell type populations with a mixed T-cell and B-cell infiltrate more characteristic of a benign reactive process. Subsequent PCR analysis can detect the presence or absence of monoclonal rearrangement of either the T-cell receptor gene or Ig heavy chain.[3] If these monoclonal rearrangements are absent, a benign diagnosis is favored. However, these rearrangements have also been shown to exist in certain cutaneous pseudolymphomas that earned their final diagnosis when removal of the offending agent led to spontaneous lesion regression.[4]

Many different entities have been described as causative factors for the development of pseudolymphoma. Of those that have been considered causative, simple categories emerge: endogenous, exogenous, and iatrogenic. A recently described endogenous etiology is IgG4-related disease.[5] A multitude of exogenous causes have been reported including several cases of cutaneous pseudolymphoma developing in a previous tattoo site.[6] Viruses, specifically molluscum contagiosum, have also been implicated, and reports of cutaneous pseudolymphoma development at previous sites of herpes zoster lesions have been described.[7] Development of cutaneous pseudolymphoma in a vaccination site has also been reported, and more obscure inciting events such as leishmaniasis donovani infection and medicinal leech therapy have been considered causative.[8]

A significant number of reported cases of cutaneous pseudolymphoma have been attributed to drugs including monoclonal antibodies,[9] herbal supplements,[10] and a multitude of other medications.[1] As a class, anticonvulsants are considered more likely to cause a lymph node pseudolymphoma than a strictly cutaneous pseudolymphoma.[11] However, many drugs in this class of medication have been described in the development of cutaneous pseudolymphoma.[3] There have been several reports implicating phenytoin, and through extensive research of the PubMed index we have found papers on the development of cutaneous pseudolymphoma after administration of the following: phenytoin, carbamazepine, mephenytoin, trimethadone, phenobarbital, primidone, butobarbitol, methsuximide, phensuximide, and valproic acid.[1]

To the best of our knowledge, this report represents the first published case of a strictly cutaneous pseudolymphoma caused by administration of lamotrigine. Our case describes a clear temporal relation between the cessation of lamotrigine and rapid and spontaneous disappearance of cutaneous lesions. Lamotrigine has been deemed causative in one prior case of pseudolymphoma with only lymph node involvement and no cutaneous lesions.[11]

The significance in proper diagnosis of cutaneous pseudolymphoma lies not only in its initial differentiation from true malignant lymphoma but also to allow for appropriate follow up and vigilant surveillance. Cases have been reported of progression from cutaneous pseudolymphoma to true lymphoma, necessitating follow up for these patients.[1,2] It is recommended that watchful follow up for these patients be carried out until at least 5 years after the diagnosis of cutaneous pseudolymphoma to rule out the possibility of malignant transformation, particularly in idiopathic cases.[12]

Conclusion:

Our patient represents the first case, to our knowledge, of strictly cutaneous pseudolymphoma due to lamotrigine. This is based on her negative systemic workup for underlying malignancy and development of lesions after starting the medication, with rapid resolution of the lesions after its discontinuation.