

# Lymphomatoid Papulosis: A Case Report.

*Nidal Obaidat,\* Anwar Masri and Ahlam Awamleh*

## Abstract

A 23-year-old female presented with recurring papulo-nodular erythematous eruption, mainly on the extremities, since the age of 2. Histological examination of a representative lesion showed morphologic and immunohistochemical features of lymphomatoid papulosis (LyP). This is a distinctive and very rare type of cutaneous lymphoproliferative disorder, which has an apparently malignant histology, but clinically behaving in a benign fashion. LyP might accompany or precede the development of cutaneous T-cell lymphoma or systemic Hodgkin's disease. To the best of our knowledge, this is the first case of LyP to be published from Jordan.

**Keywords:** Lymphomatoid papulosis, CD30+ cutaneous lymphoproliferative disorder, case report.

*(J Med J 2006; Vol. 40 (2): 137- 141)*

Received

Accepted

---

## Introduction

Lymphomatoid papulosis (LyP) is typically a recurring, continuous, self-healing eruption characterized by papular, papulonecrotic, or varioliform lesions. The intriguing feature of this disease is its benign clinical course combined with aggressive cytological and morphological characteristics closely resembling lymphoma. Since the first case of LyP was described by Macaulay in 1968, there has been continuous discussion as to whether LyP is a malignant, premalignant, or benign condition.<sup>1,2</sup>

Currently, LyP is considered as a form of cutaneous lymphoproliferative disorder according to the most recent classification by the World Health Organization (WHO),<sup>3</sup> being classified under primary cutaneous CD30+ T-cell lymphoproliferative disorders. LyP comprises approximately 12% of primary cutaneous T-cell lymphomas as seen in a large study of 755 cases in the USA.<sup>4</sup> The occurrence of LyP is extremely rare, with an estimated overall prevalence rate of 1.2 to 1.9 cases per 1 million population.<sup>5</sup>

From the Departments of Dermatology and Pathology, King Hussein Medical Center, Amman, Jordan.

\* Correspondence should be addressed to:

Dr Nidal Obaidat

P.O.Box 3174, Amman 11953 Jordan.

Email: nobaidat@yahoo.com

## Case

A 23-year-old Jordanian female presented to the dermatology clinic at Prince Rashed Hospital (PRH) in April 2004, with a history of recurring skin lesions since the age of 2. The lesions were only slightly itchy, and not accompanied by fever or systemic ill-health. Each lesion would last for few weeks, later healing by some hyperpigmentation and minimal scarring. The patient was otherwise healthy and her family had no similar illness. On presentation, she had generalized papular erythematous eruption, with necrotic crusting center (figure 1). The lesions were distributed mainly over her extremities, but also involved some parts of her trunk, lower abdomen, and buttocks. The patient also had some residual hyperpigmented macules from previous lesions, with minimal scarring. There was no fever or palpable peripheral lymph nodes. Abdominal examination did not reveal organomegaly, and the rest of the clinical examination was unremarkable. The differential diagnosis included pityriasis lichenoides et varioliformis acuta (PLEVA), LyP, and chronic folliculitis.

Laboratory investigations were all within normal, and there were no atypical cells in the peripheral blood smear. In addition, a skin biopsy was taken from a representative lesion, revealing extensive dermal edema with a diffuse dermal infiltrate containing large atypical cells, admixed with some eosinophils and neutrophils (figures 2 and 3). The atypical cells were T-lymphocytes (positive for leucocyte common antigen (LCA) and CD45RO) and stained positively with CD30. The final histopathologic diagnosis was that of a CD30-positive lymphoproliferative disorder according to the WHO classification,<sup>3</sup> the differential including anaplastic large cell lymphoma (ALCL) and lymphomatoid papulosis. The patient was then referred to King Hussein Medical Center (KHMC) for further investigations to rule out systemic lymphoma. She had chest, abdomen and pelvic computerized tomography that were reported as normal. A bone marrow aspirate and biopsy were also normal. Since there was no systemic lymphoma, and due to the long and benign course of the disease, the diagnosis of lymphomatoid papulosis was made.

The patient is currently using topical steroids alone for symptomatic relief, and she declined phototherapy or other treatments. At the time of submitting this report, the patient was still under regular follow up at the clinic with no evidence of malignant transformation after 6 months from her initial presentation.

***Figure 1. Erythematous papules and plaques with necrotic centers over thigh.***

**Discussion:**

LyP may occur at any age, but is most common between 35 and 45 years of age. The disease is more common in men with a ratio of approximately 2:1.<sup>2</sup> Lesions are mostly red-brown asymptomatic papules and nodules, frequently progressing to have a varioliform appearance with a hemorrhagic crust. Subsequently, they slowly involute with or without treatment over a period of 3-8 weeks, sometimes leaving hyper-/hypo-pigmentation and/or minimal scarring.<sup>2, 3</sup> Lesions may be generalized, but usually they are located predominantly on the extremities or the trunk. Only rarely are lesions confined to the head and neck or involve the mucous membranes. LyP can occur in children, and in this group, association with malignancy is extremely rare.<sup>6</sup>

***Figure 2. A vaguely wedge-shaped dense dermal infiltrate.***

Clinically, LyP most closely resembles PLEVA and biopsy may be needed to differentiate the two. Histologically, LyP demonstrates a wedge-shaped infiltrate associated with perivascular lymphocytic inflammation and hemorrhage (figure 2). The infiltrate is mainly in the papillary and mid dermis and less concentrated in the reticular dermis or panniculus.<sup>7</sup> Exocytosis of lymphocytes, polymorphonuclear cells, and erythrocytes into the epidermis is present in 90 % of cases. The lymphocytic infiltrate typically contains large histiocytic-appearing cells likened to Reed-Sternberg cells (type A LyP). Less often the infiltrate consists entirely of small cerebriform lymphocytes (type B LyP). The remainder of cases are a mixture of type A and B. Eosinophils and neutrophils are admixed with lymphocytes in up to 50% of cases. Endothelial swelling in blood vessels and dermal hemorrhage is commonly seen, but true vasculitis is rare.<sup>3, 7, 8</sup>

***Figure 3. A high power view of the dermal infiltrate, showing large and atypical lymphocytes.***

The immunophenotype of the lymphocytic infiltrate in LyP consists mainly of T-cells with admixed B-cells. Characteristic T-cell antigens expressed include CD2, CD3, and CD4 with sparse staining for CD7 and CD8. The large Reed-Sternberg-like cells express CD30, and other lymphocyte activation markers including HLADR, CD25. They stain sparsely or negatively for CD15.<sup>7, 8</sup> In contrast to ALCL, LyP does not express ALK-1 (p80) or clusterin.<sup>9</sup>

The pathogenesis of LyP is largely unknown. Although a viral etiology is repeatedly suggested, studies for an etiological role for HTLV-1, EBV, and human herpesvirus subtypes 1, 2, 6, 7 and 8 were negative.<sup>10</sup> Common T-cell clones have been reported in patients with LyP, Hodgkin's disease, and mycosis fungoides.<sup>11</sup> Although this latter evidence strongly suggests linkage between LyP and lymphoma, results of DNA flow cytometry and molecular genetics studies have failed to predict which patients may develop lymphoma.<sup>8</sup>

The diagnosis of LyP is primarily a clinical one based on the characteristic morphology of the lesions as described above. This condition may mimic or even coexist with several other conditions including PLEVA, mycosis fungoides, or other cutaneous lymphomas including ALCL. The characteristic histopathological and immunopathological findings are essential to the correct diagnosis. On occasion multiple biopsies and long-term follow up are required to confirm the diagnosis.<sup>3, 6, 7</sup>

Treatment of LyP is generally unsatisfactory and not uniformly effective.<sup>6</sup> Topical and systemic steroids or antibiotics are usually not useful, and other treatments have variable efficacy. In many patients, it appears that phototherapy utilizing UVB or PUVA may be the most effective therapy.<sup>6, 8</sup> Case reports have documented response to systemic chemotherapy or total skin electron beam irradiation. However, LyP lesions may persist or recur within weeks-months of therapy. Since a curative treatment is not currently available, such aggressive therapy does not seem indicated, especially considering that the natural course of the disease is not affected by the currently available modalities.<sup>12</sup> In severe cases, with scarring or numerous papulo-nodular lesions, low dose oral methotrexate (5-20 mg/week) seems to be effective.<sup>13</sup>

Overall, the duration of the disease might range from a few months to more than 40 years. Many researchers estimate that in 10-20 % of cases, LyP may be preceded, accompanied or followed by the development of lymphoma, generally MF, CD30+ large T-cell lymphoma or systemic Hodgkin's disease<sup>2,5,6,11,12</sup>. However, the overall prognosis is usually excellent. In a recent study of 118 patients with LyP, only five patients (4%) developed a systemic lymphoma, and only two patients (2%) died of systemic disease over a median follow up period of 77 months.<sup>14</sup>

In conclusion, this case presentation illustrates the importance of diagnosing patients with LyP due to the possible link with other cutaneous and systemic lymphoproliferative disorders.

**References:**

1. Macaulay WL. Lymphomatoid papulosis. A continuing self-healing eruption, clinically benign-histologically malignant. *Arch Dermatol* 1968; 97:23-30.
2. Zackheim HS, Jones C, LeBoit PE, Kashani-Sabet M, McCalmont TH, and Zehnder J. Lymphomatoid papulosis associated with mycosis fungoides: A study of 21 patients including analyses for clonality. *J Am Acad Dermatol* 2003; 49:620-623.
3. Ralfkiaer E, Delsol G, Willemze R, and Jaffe ES. Primary cutaneous CD30-positive T-cell lymphoproliferative disorders. In: World Health Organization Classification of Tumors: Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Edited by Jaffe ES, Harris NL, Stein H and Vardiman JW. IARC Press, Lyon, 2001; 221-224.
4. Zackheim HS, Vonderheid ED, Ramsay DL, LeBoit PE, Rothfleisch J, and Kashani-Sabet M. Relative frequency of various forms of primary cutaneous lymphomas. *J Am Acad Dermatol* 2000; 43:793-796.
5. Wang HH, Lach L, and Kadin ME. Epidemiology of Lymphomatoid papulosis. *Cancer* 1992; 70:2951-57.
6. Liu HL, Hoppe RT, Kohler S, Harvell JD, Reddy S, and Kim YH. CD30+ cutaneous lymphoproliferative disorders: The Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. *J Am Acad Dermatol* 2003; 49:1049-1058.
7. LeBoit PE and McCalmont TH. Cutaneous Lymphomas and Leukemias. In Elder D. (Editor-In-Chief): *Lever's Histopathology of the Skin*, eighth edition. Lippincott-Raven publishers: Philadelphia, 1997; 805-846.
8. El-Azhary RA, Gibson LE, Kurtin PJ, Pittlekow MR, and Muller SA. Lymphomatoid papulosis: A clinical and histopathologic study of 52 cases with leukocyte immunophenotyping, DNA flow cytometry, and T-cell receptor gene rearrangements. *J Am Acad Dermatol* 1994; 30:210-218.
9. Gascoyne RD, Aoun P, Wd D, et al. Prognostic significance of anaplastic lymphoma kinase (ALK) protein expression in adults with anaplastic large cell lymphoma. *Blood* 1999; 93:3913-3921.
10. Kempf W, Kadin ME, Kutzner H, et al. Lymphomatoid papulosis and human herpesviruses--A PCR-based evaluation for the presence of human herpesvirus 6, 7 and 8 related herpesviruses. *J Cutan Pathol* 2001; 28:29-33.
11. Basarab T, Fraser-Andrews EA, Orchard G, Whittaker S, and Russel-Jones R. Lymphomatoid papulosis in association with mycosis fungoides: A study of 15 cases. *Br J Dermatol* 1998; 139:630-638.
12. Bekkenk MW, Geelen FA, van Voorst Vader PC, et al. Primary and secondary cutaneous CD30 (+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. *Blood* 2000; 95:3653-61.
13. Vonderheid EC, Sajjadian A, Kadin ME. Methotrexate is effective therapy for lymphomatoid papulosis and other primary cutaneous CD30- positive lymphoproliferative disorders. *J Am Acad Dermatol* 1996; 34:470-81.
14. Beljaards RC, Willemze R. The prognosis of patients with lymphomatoid papulosis associated with malignant lymphomas. *Br J Dermatol* 1992; 126:596-602.