ORIGINAL ARTICLE

Lymphomatoid papulosis: Treatment response and associated lymphomas in a study of 180 patients

Iris Wieser, MD,[a,b] Chee Won Oh, MD,[a] Rakhshandra Talpur, MD,[a] and Madeleine Duvic, MD[a]
Houston, Texas and Salzburg, Austria

Background: Lymphomatoid papulosis (LyP) is a CD30$^+$ lymphoproliferative disorder, with a self-regressing clinical course and malignant histopathology.

Objective: The aim of this study was to evaluate characteristics, risk factors, associated malignancies, long-term outcome, and treatment of LyP in a large cohort representing the experience of the MD Anderson Cancer Center.

Methods: Patient charts and clinical and histopathologic data of 180 patients with LyP were retrospectively assessed.

Results: A total of 56.7% of patients was men. Histologic subtype A was found in 47.2%, type B in 17.2%, type C in 22.8%, type D in 7.8%, type E in 0.6%, and mixed subtype in 4.4% of the patients. One hundred fourteen lymphomas were observed in 93 patients, with mycosis fungoides (61.4%) and anaplastic large cell lymphoma (26.3%) being the most common forms. Risk factors for development of lymphoma included sex and histologic subtype. Number of lesions and symptom severity were not associated with lymphoma development. Patients with type D were less likely to have lymphomas. Treatment provided symptomatic relief but did not prevent progression to lymphoma.

Limitations: The limitation of this study is the retrospective study design.

Conclusion: Patients with LyP are at increased risk of associated lymphomas. Thorough patient counseling is needed and long follow-up periods are required to detect and treat secondary lymphomas. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.09.013.)

Key words: associated lymphomas; CD30$^+$ lymphoproliferative disorders; cutaneous T-cell lymphoma; lymphomatoid papulosis; lymphomatoid papulosis treatment.

INTRODUCTION

Lymphomatoid papulosis (LyP) is a rare CD30$^+$ lymphoproliferative disorder. The estimated worldwide incidence is 1.2 to 1.9 cases per 1.000.000 people[1] with a 10-year survival rate close to 100%.[2] Although the peak incidence is in the fifth decade, any age group can be affected. Men are more likely to have LyP than women.[3,4]

The first to report this disease was Dupont in 1965[5]; 3 years later, Macaulay introduced the term *lymphomatoid papulosis* and described it as benign, self-regressing erythematous papules with malignant histology.[6] By definition, LyP lesions are red or purple (sometimes pruritic) papules and nodules, measuring less than 2.0 cm. They occur as single or multiple crops and can affect any body part. In half of the patients, the lesions heal with scar formation.[3] The tendency to regress spontaneously is characteristic for the disease and crucial to establish a clinical diagnosis.[7] Larger nonregressing lesions, in contrast, would be expected in primary cutaneous anaplastic large cell lymphoma (ALCL) or mycosis fungoides (MF) tumor lesions with CD30$^+$ expression.[4]

From the Department of Dermatology, The University of Texas, MD Anderson Cancer Center[a] and the Department of Dermatology, Paracelsus Medical University.[b]

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Reprint requests: Iris Wieser, MD, Department of Dermatology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030-4095. E-mail: iris.wieser@hotmail.com.

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Over the years, the subclassification of LyP has become very precise and is a work in progress.[8] The most common LyP subtype is type A, characterized by a wedge-shaped infiltrate with neutrophils, eosinophils, and histiocytes. Type B has small- to medium-sized lymphocytes with cerebriform nuclei, simulating features observed in MF. Type C has sheets of large $CD30^+$ lymphocytes, resembling ALCL.[9] Other rare types include type D, with predominantly $CD8^+$ lymphocytic infiltrates[10] and type E, characterized by angiodestructive infiltrates of small- to medium-sized lymphocytes expressing CD30 and CD8.[11] A sixth, type F, is currently proposed and described as having a perifollicular infiltrate with folliculotropism.[12]

Previous smaller studies, including our first report of LyP patients 10 years ago, suggested a possible association of LyP and development of secondary lymphomas.[3,4,13-16] To date, no curative treatment for LyP is available.[17] Information regarding the potential of aggressive therapy on prevention of secondary lymphomas is lacking.

The purpose of this study was to define LyP characteristics, risk factors, associated malignancies, long-term outcome, and response to currently available treatment options in a large cohort from the MD Anderson Cancer Center, Clinic for Cutaneous T-cell Lymphomas.

CAPSULE SUMMARY

- LyP is a $CD30^+$ T-cell lymphoproliferative disease characterized by waxing and waning of lesions.
- LyP is associated with a high risk of secondary lymphomas; currently available treatments can suppress LyP lesions but cannot prevent lymphoma development.
- Patients with a $CD8^+$ phenotype are less likely to subsequently have an associated lymphoma.

METHODS

Patients

This was a retrospective study of patients with LyP seen at the MD Anderson Cancer Center, Houston between 1999 and 2015 aimed to bring continuity to our previously published cohort of 84 patients in the follow-up period from 1999 to 2005.[16] The study protocol was approved by the institutional review board (#PA15-0324). A total of 237 patients with LyP were identified, searching the MD Anderson Cancer Center cutaneous T-cell lymphoma database. The diagnosis of LyP was made according to the World Health Organization–European Organisation for the Research and Treatment of Cancer classification.[2] Patient charts and pathology reports were reviewed using electronic medical records and paper-based flow sheets. All patients' clinical and histopathologic data were re-evaluated: 11 patients with a clinical diagnosis of LyP were excluded because of lack of confirmatory biopsy, 46 patients were seen for a single consultation visit only without proper follow-up data. A total of 180 patients with both clinical and histopathologically proven diagnosis of LyP met the inclusion criteria.

Clinical data

The following data were collected: age at diagnosis, sex, ethnicity, time from symptom onset to biopsy, duration of follow-up, and status at follow-up. Lymphomas were counted before, concomitant to, and after LyP diagnosis; each lymphoma entity was counted only once, that is, relapse and disease progression were not counted as a new malignancy. MF Staging was made according to the modified International Society for Cutaneous Lymphomas/European Organisation for the Research and Treatment of Cancer revisions of the TNMB Classification of MF and Sézary syndrome.[18] Time from lymphoma to LyP diagnosis and time from LyP to secondary lymphoma were studied. Other nonhematologic cancers were documented. LyP severity was defined as mild (<12 lesions), moderate (12 to 50 lesions), and severe (>50 lesions) and was reported at the worst time point. History of positive/negative Epstein-Barr virus (EBV) IgG, EBV nuclear antigen, and lactate dehydrogenase levels obtained from laboratory tests at baseline presentation was recorded.

Treatment

Treatment history and treatment response were documented in all 180 subjects. Complete remission (CR) was defined as having no cutaneous lesions at follow-up and was only reported if the patient remained free of lesions until the last follow-up examination. Partial remission (PR) was defined as more than 50% reduction of skin involvement. No response (NR) was defined as less than 50% reduction, no change in disease or worsening of skin status at the next follow-up examination. A relapse was defined as recurrence of LyP lesions after CR.

STATISTICAL ANALYSIS

Basic summary statistics were used to describe demographic data, treatment types, and response.