

# Lymphomatoid papulosis: A rare case report and review of literature

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**Abstract** Lymphomatoid papulosis (LyP) is a rare cutaneous condition characterized by chronic, recurrent, and self-regressing papulonodular skin eruptions. It belongs to the spectrum of primary cutaneous CD30+ lymphoproliferative disorders, along with primary cutaneous anaplastic large cell lymphoma (primary C-ALCL) with which it shares overlapping clinical and histopathologic features. The occurrence of LyP is extremely rare, with an estimated overall prevalence rate of 1.2 to 1.9 cases per 1 million population. Patients with LyP are at an increased risk of developing cutaneous or nodal lymphoid malignancies such as classic mycosis fungoides, ALCL, and Hodgkin lymphoma. Treatment includes use of topical steroids with or followed by phototherapy (psoralen-UVA light therapy [PUVA]) or oral low-dose methotrexate (MTX). Complications due to long-term treatment may also include a higher incidence of non-melanoma skin cancer (due to PUVA) or hepatic fibrosis (due to MTX). Here, we report a case of 48-year-old female, admitted with the complaints of multiple erythematous painless nonpruritic plaques and subcutaneous nodules over the right shoulder, both upper limbs, lower limbs, back and the abdomen for 4 months and a large ulcerated tumor over the medial aspect of left leg for 3 months. To the best of our knowledge, this is the first case of LyP to be published from Bangladesh.

**Key words**

Lymphomatoid papulosis, cutaneous CD30+ lymphoproliferative disorders

## Introduction

Lymphomatoid papulosis (LyP) is a chronic papulonecrotic or papulonodular skin disease with histologic features suggestive of a malignant lymphoma.<sup>1</sup> The term lymphomatoid papulosis originally was used by Macaulay in 1968 to describe "a self-healing rhythmical paradoxical eruption, histologically malignant but clinically benign." However, the classification system for cutaneous lymphomas has evolved rapidly, and, during consensus meetings in 2003-2004, the World Health Organization—European Organization for Research and Treatment of Cancer (WHO-

EORTC) classification grouped lymphomatoid papulosis among the indolent cutaneous T-cell lymphomas. These classifications were updated in 2008.<sup>2-4</sup> The rationale for classifying lymphomatoid papulosis as a cutaneous lymphoma is its association with other malignant lymphoproliferative disorders; however, some experts hesitate to classify this chronic skin disease as a true malignancy because of its spontaneous resolution and benign clinical course. LyP is part of a spectrum of CD30 (Ki-1)-positive cutaneous lymphoproliferative diseases (CD30<sup>+</sup> LPDs), including lymphomatoid papulosis, primary cutaneous anaplastic large cell lymphoma (pcALCL), and borderline CD30<sup>+</sup> lesions.<sup>5</sup>

The pathophysiology of CD30<sup>+</sup> LPDs, including LyP, is largely unknown.<sup>6</sup> CD30 signaling is known to have an effect on the growth and

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survival of lymphoid cells, and one hypothesis is that genetic instability and accumulated genetic defects may have a role in the development of LyP and the progression to associated neoplasms.<sup>7</sup> Genetic instability of tumor cells may lead to altered expression of apoptotic proteins and immune-regulatory molecules, such as transforming growth factor-beta (TGF- $\beta$ ).<sup>8</sup> Spontaneous regression of LyP is seen almost universally, whereas regression occurs in approximately 25% of pcALCL cases. Therefore, the higher apoptotic index found in LyP compared with pcALCL is not surprising. The proapoptotic protein Bax is also expressed at high levels in CD30<sup>+</sup> cutaneous lymphoproliferative diseases and may play a crucial role in mediating apoptosis of tumor cells.<sup>9</sup> The CD30<sup>+</sup> cutaneous lymphoproliferative disorders account for approximately 25% of cutaneous T-cell lymphoma cases.<sup>10</sup> Black persons may be less affected by lymphomatoid papulosis than persons of other racial groups. No consistent sex predominance is found in studies of LyP, but some studies have reported a male-to-female ratio of 1.5-2:1. LyP may develop at any age, but the peak incidence occurs in the fifth decade. Etiology is unknown. In some reports, a correlation has been found between the use of immunosuppressive medication e.g. antitumor necrosis factor (TNF) agents for the treatment of chronic inflammatory diseases.<sup>11</sup> LyP lesions develop as erythematous papules and nodules of less than 1.5-2 cm, grouped in clusters or disseminated throughout the body. Lesions may become necrotic in the center, show pigmentation and leave scarring. They spontaneously regress within 4 to 8 weeks but new lesions can occur at any time.<sup>1</sup>

The prognosis of LyP is good because most patients have a chronic, indolent course. Physicians are guardedly optimistic about the prognosis because estimates indicate that as

many as 4-25% of patients have a history of associated malignant lymphoma (ALCL, HD, MF) prior to, concurrent with, or subsequent to the diagnosis of LyP. Unfortunately, no clinical or histologic factors analyzed to date are predictive of worse outcomes in persons with LyP. A study suggested that fascin expression is increased in LyP cases associated with a malignant lymphoma.<sup>12</sup> Alterations in TGF- $\beta$  signaling are hypothesized to play a role in the progression of LyP to malignant lymphoma. pcALCL is more likely than MF to manifest as an ulcerated tumor and palpable lymph nodes. In most patients, the malignancy develops many years after the diagnosis of LyP.<sup>13</sup>

We, here, report a female case of LyP due to rarity of disease, first case from Bangladesh.

### **Case Report**

A 48-year-old, female, housewife, hailing from Faridpur was admitted at Department of Dermatology and Venereology in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh on 31 July 2016 with the complaints of multiple erythematous painless non pruritic plaques and subcutaneous nodules over the right shoulder, both upper limbs, lower limbs, back and the abdomen for 4 months and a large ulcerated tumor over the medial aspect of left leg for 3 months. According to the statement of the patient she was reasonably well 4 months back. Then she developed a painless erythematous patch on right shoulder along with mild burning sensation. After few days the patch became a palpable plaque and about one month later she noticed another erythematous nodule on the medial aspect of the left leg. For this problem she took some medications including oral and topical antibiotics without any significant improvement. Gradually she develops multiple erythematous plaques and nodules over both upper limbs, lower limbs,



**Figure 1** Erythematous tumor and plaques on the right shoulder, neck and upper chest area.



**Figure 2** Subcutaneous erythematous nodule on right side of abdomen with spontaneously regressive plaques left side of abdomen.



**Figure 3** Erythematous nodules over extensor surface of left upper limbs with some healed lesions.

back of the trunk and abdomen with progressive enlargement of the previous lesions. Some



**Figure 4** Multiple erythematous subcutaneous nodules over both lower limbs with edema of left leg.



**Figure 5** A large ulcerated tumor with overlying necrotic crust and oozing with erythematous surrounding skin on medial surface of right leg.

lesions healed spontaneously while others enlarged progressively. New lesions appeared as

erythematous plaques or nodules. They were round, variable in size with mildly elevated temperature, not painful except the larger lesions which were mildly painful. Some of the nodules spontaneously eroded with moist surface, crusted and healed with postinflammatory hyperpigmentation. With these problems, she got herself admitted with us for evaluation and management. After admission the tumor on the left leg become ulcerated, painful and progressively enlarged. New lesions appeared day by day in different parts of body. She had no history of fever and weight loss. Her bowel and bladder habits were normal. Ten years ago, she had history of breast abscess which was cured by medication. She was hypertensive for last 6 months. None of her family members was suffering from the same type of disease. She was nonsmoker, nonalcoholic, not having history of exposure and history of betel nut chewing. She belonged to a lower middle class family. Her menarche started on 13 years, her menstrual period was 4 to 5 years and cycle was  $28 \pm 2$  days. She is married for 30 years, she has 3 children and age of her last child is 17 years. In the course of the disease, she been treated with systemic and topical antibiotics.

On general examination, the patient was ill looking and anxious, cooperative, with an average built. Anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia were absent. Moderate leg edema was in left leg and mild edema in right leg and lymph node was just palpable on left posterior cervical chain. Her temperature was  $98^{\circ}\text{F}$ , pulse 64 beats/min, blood pressure 130/80 mm Hg and respiratory rate was 16/min on day of examination.

Cutaneous examination revealed multiple well-defined round, erythematous, subcutaneous nodules and tumors of variable diameter present on the right shoulder, both upper limbs, lower limbs, back of the trunk and abdomen, firm in

consistency with mildly elevated local temperature. Smaller lesions were non-tender but the larger and older lesions are mildly tender. A large round tumor on the medial aspect of the left leg measuring about  $7 \times 10$  cm in diameter, tender and firm in consistency with mildly elevated temperature and not fixed with underlying structure. Overlying skin of the tumor was ulcerated with irregular border and studded with necrotic crust and oozing. Surrounding skin of the tumor was erythematous with elevated temperature. Oral mucosa and hair were normal but nail showed onychomycosis with paronychia in the nails of right thumb and middle finger.

Complete blood count findings on 31.07.16 showed Hb - 11.7 gm/dl, ESR - 31 mm in 1<sup>st</sup> hour, WBC -  $8.0 \times 10^9/\text{L}$ , RBC -  $3.0 \times 10^{12}/\text{L}$ , platelet -  $460 \times 10^9/\text{L}$ . Complete blood count findings on 8.9.16 showed Hb - 10.9 gm/dl, ESR - 50 mm in 1st hour, WBC -  $7.0 \times 10^9/\text{L}$ , RBC -  $3.57 \times 10^{12}/\text{L}$ , platelet -  $380 \times 10^9/\text{L}$ . Blood film on 08.09.16 showed normocytic normochromic anemia. RBS : 5.2 mmol/L, serum creatinine: 0.64 mg/dL. Urinalysis, X-ray (chest), wound swab for culture and sensitivity, Mantoux (tuberculin test) showed no abnormality. X-ray left leg both view showed fairly large round dense opacity having irregular marginal filling defect noted in posterolateral aspect mid of left leg. Soft tissue swelling also noted around the ankle but ankle joint appeared normal and no obvious bony lesion was seen. USG of whole abdomen showed hepatomegaly (16 cm), mildly bulky uterus. Bone marrow examination on 10.09.16 showed normal active marrow with no bone marrow infiltration. Skin biopsy for histopathology (done on 01.08.16 on left leg) revealed dense infiltration of lymphocytes in the dermis, mostly around the blood vessels and adnexa. Infiltrate contained small number of histiocytes and few polymorphs. The lymphocytes had irregular

nuclei. This finding was compatible with cutaneous T-cell lymphoma. Skin biopsy for histopathology (right leg on 24.08.16) showed dense infiltrate of lymphocytes in the dermis and subcutis. Intraepidermal lymphocytes were present singly and in small groups compatible with diagnosis of mycosis fungoides. Immunohistochemistry revealed CD3: positive; CD4: small number of lymphoid cells positive; CD8: majority of the lymphoid cells positive; CD20: positive; CD30: negative, this report confirmed the diagnosis of LyP. The patient was treated symptomatically. Goal of treatment was to accelerate healing and to reduce or prevent frequency and severity of new crops for short time.

## Discussion

There have been case reports of LyP in dermatological literature. Wollina *et al.*<sup>14</sup> reported a 64-year-old woman with a 10-year history of chronic relapsing reddish-brownish papules on the limbs and the trunk, except the face. The papules were non-pruritic. Histopathologic examination showed a heavy broad dermal infiltrate consisting of lymphomonocytoid cells including large cells with atypical nuclei and mitoses. Immunostaining (PAAP) revealed positivity for CD30 (large cells), CD8, and T cell intracellular antigen TIA1 (only some cells), immunostains for fascin were negative. In addition granulocytes, especially eosinophils were intermingled. There was a slight increase of eosinophil counts (5.6%) and an increased ratio of T4/T8 by flow cytometry (3.7). No atypical cells were observed in the circulating blood. Ultrasound scan of pelvic and abdominal organs and X-ray of the thorax did not show any manifestation of the CTCL. The diagnosis of LP, type A, was made. They treated the case with cream PUVA which resulted in improvement of burning sensations and partial remission of LP.<sup>14</sup>

Wollina *et al.*<sup>14</sup> also reported a 42-year-old woman with relapsing papulonodular lesions on the limbs and the trunk for last 18 years. Previous treatments such as UVB and UVA irradiation, PUVA, dapsone, and vidarabine phosphate had only temporary and slight effects. Several skin biopsies were taken from these lesions that showed a dense dermal infiltrate composed of large, atypical lymphoid cells mixed with eosinophils and neutrophils. The immunophenotype was CD30-positive, CD3-positive, CD4- and CD8-negative. Fluorescent activated cell sorting analysis (FACS) showed an increased ratio of activated T-cells; however, no atypical cells were found in the peripheral blood. Patient was treated with PUVA and later with extracorporeal photochemotherapy (ECP). During ECP treatment, a rapid metastatic spread developed that could not be controlled by polychemotherapy. Eventually she died due to a central nervous system metastasis one year later.<sup>14</sup>

Obaidat *et al.*<sup>15</sup> reported a 23-year-old Jordanian female with a history of recurring skin lesions since the age of 2. 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, distributed mainly over her extremities, but also involved some parts of her trunk, lower abdomen, and buttocks. The rest of the clinical examination was unremarkable. Laboratory investigations were all within normal, and there were no atypical cells in the peripheral blood smear. Skin biopsy revealed extensive dermal edema with a diffuse dermal infiltrate containing large atypical cells, admixed with some eosinophils and neutrophils. 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, the differential including anaplastic large cell lymphoma (ALCL) and LyP. Due to the long and benign course of the disease, the diagnosis of LyP was made. The patient was treated with topical steroids alone for symptomatic relief as she declined phototherapy or other treatments.<sup>15</sup>

Sina *et al.*<sup>16</sup> were reported five new cases of LyP. This entity can apparently be divided into at least two subtypes. In one group of patients, papulopustular lesions resembling those of pityriasis lichenoides develop that resolve spontaneously within a few weeks. The lesions contain an epidermotropic dermal infiltration composed predominantly of abnormal lymphocytes. The other group of patients displays larger, more persistent lesions that contain a nonepidermotropic dermal infiltration composed predominantly of histiocytes. Lymphoma eventually develops in about 10% of the patients with LyP.<sup>16</sup>

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