Case 3
A 41-year-old Thai female from Bangkok
Chief compliant: Erythematous patch at left thigh for 2 months
Present illness: The patient presented with a 10- year history of erythematous patch on her right arm. Biopsy was done twice at other hospital and revealed cutaneous malignancy. Since the patient unfortunately lost to follow up, and denied the treatment. The lesion progressed. (Fig 2.2.1)

There was a new itching erythematous patch for 2 months on her left thigh (Fig 2.2.2). Few days after skin biopsy, she noticed multiple asymptomatic small erythematous papules on both arms and legs. (Fig 2.2.3)

Past history: She was previously healthy and not taking any medication.

Family history: nil
Physical examination:
VS: T 37 ^{0} C, RR 20/min, BP 125/85 mmHg, HR 80/min
GA: good consciousness, not pale, no jaundice
CVS: normal S1 S2, no murmur
RS: normal breath sounds
Abdomen: no hepatosplenomegaly
NS: intact all
LN: not palpable

Skin examination:
Rt arm- ill-defined poikilodermatous patch size 3x4 cm.
Lt thigh- ill-defined dry scaly erythematous patch with wrinkle surface size 4x6 cm.
Multiple discrete erythematous indurated papules on all extremities

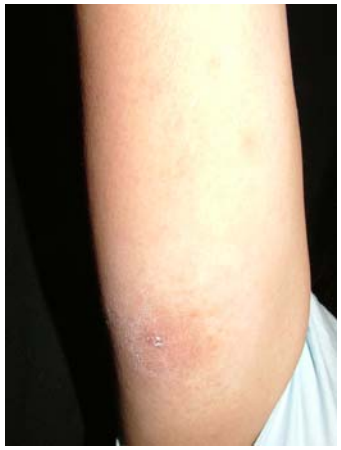
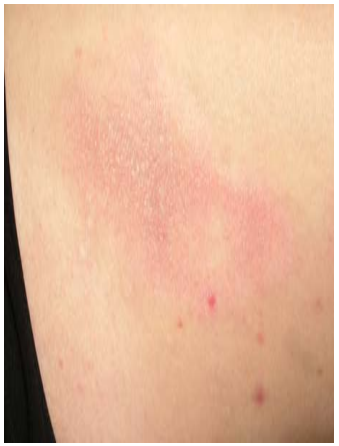


Fig. 3.1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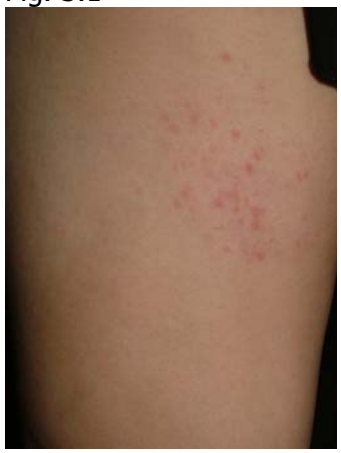
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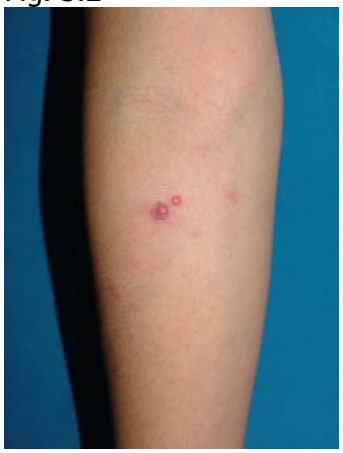
Fig. 3.4

Investigation:

CBC: Hb 13.7 g/dL, Hct 41.1%
WBC 7800/mm^3 (N 56%, L 32%, M 8%, E 3%, B 1%)
Platelets 293,000/mm^3
Serum LDH: 131 U/L (100-190)
Serum uric acid: 3.4 mg/dl
BUN & creatinine: 8/0.7 mg/dl
LFT: normal
Anti HIV: negative
Urinalysis: normal
Chest X ray: no mediastinal mass, no infiltration
CT chest and whole abdomen: no evidence of intraabdominal involvement of lymphoma, normal size of spleen and liver

Histopathology:

1). (S09- 2639A, B) (Fig)

- Dense superficial lichenoid infiltrate of lymphocytes, some with atypical nuclei in a thickened papillary dermis.
- Epidermotrophism of atypical lymphocytes in both solitary unit and small nests.

2). (Slide S09-003410A) (Fig)

- Diffuse infiltrate of lymphocytes, admixed with histiocytes, neutrophils, eosinophils and large atypical lymphocytes in the dermis.
- Scale-crust, mild epidermis hyperplasia and superficial ulcer in the overlying epidermis.
- Atypical lymphocytes positive for CD3 and CD30.

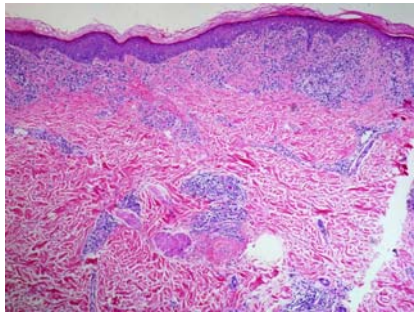
Fig. 3.5

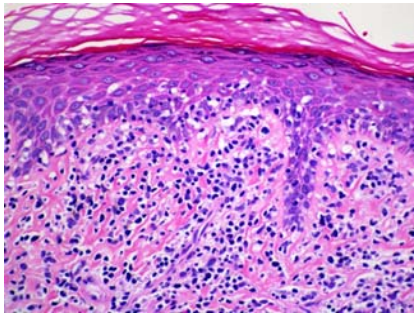
Fig. 3.5.1

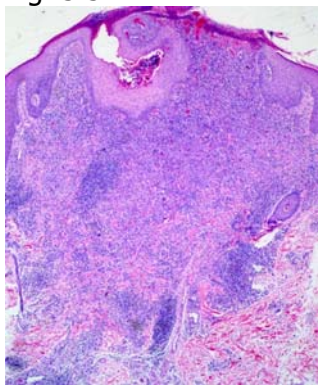
Fig. 3.6

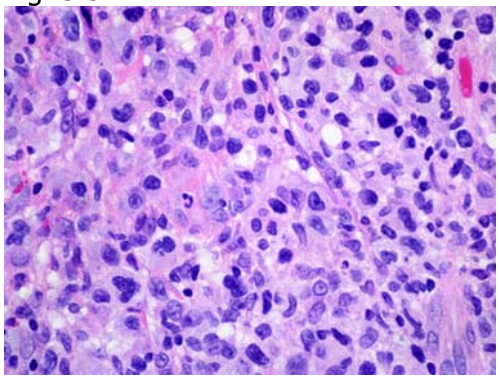
Fig. 3.6.1

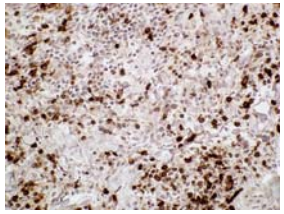
Fig. 3.6.2 CD3

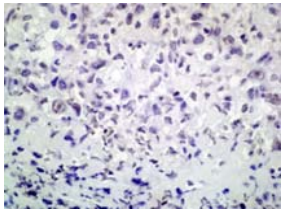
Fig. 3.6.3 CD20

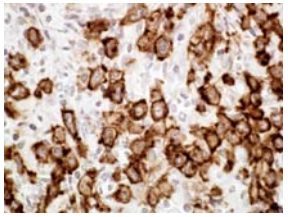
Fig. 3.6.4 CD30

Bone marrow aspiration: Normal bone marrow
Bone marrow biopsy: Normocellular bone marrow showing adequate trilinear hematopoiesis

Diagnosis: Mycosis fungoides (plaque type) stage 1A and lymphomatoid papulosis type C
Treatment: PUVA and consult hematologist -> CHOP regimen
Presenter: Pranee Wongkitisopon
Consultant: Natta Rajatanavin

Discussion:

Lymphomatoid papulosis (LyP) is a CD 30+ lymphoproliferative disorder in which papules and nodules evolve and involute spontaneously. It characterized by recurrent crops of papular, papulonecrotic, and/or nodular skin lesions at different stages of development, predominantly on the trunk and limbs. It has a variable appearance on microscopic examination, but its lesions characteristically contain large, atypical lymphocytes. LyP was defined as histologically malignant but clinically benign lymphoma-like condition with excellent prognosis. It is best regarded as a low-grade malignant CTCL.[1, 2]

The pathogenesis is unknown. It has been suggested that interactions between CD30 and its ligand (CD30L) may contribute to apoptosis of the neoplastic T cells and the subsequent regression of the skin lesions, but the exact mechanism is as yet unknown.[2] The incidence of LyP is 18% of all CTCL. It can affect patient at any age, with peak incidence during the fifth decade. The male to female ratio is approximately 1.5. [3]

The histologic picture of LyP is extremely variable. Three histologic subtypes of LyP (types A, B, and C) have been described.

In LyP type A lesions, (Hodgkin-like) Wedged shape initially non-epidermotropic multinucleated or Reed-Sternberg-like, CD30+ Tcells are intermingled with numerous inflammatory cells, such as histiocytes, small lymphocytes, neutrophils, and/or eosinophils.

LyP type B (MF-like) is uncommon (less than 10%) and is characterized by an epidermotropic infiltrate of small atypical cells with cerebriform nuclei similar to that observed in MF with CD3+ CD4+ but CD30-.

LyP type C lesions (ALCL-like) demonstrate a monotonous population or large clusters of large CD30+T cells with relatively few admixed inflammatory cells.

Histologically, LyP type C must be differentiated from CD30+ primary cutaneous anaplastic large cell lymphoma. The latter is characterized by nonregressing solitary or localized ulcerated tumours or nodules, with favorable prognosis. They are closely related conditions and are classified in primary cutaneous CD 30 positive lymphoproliferatve disorders by WHO/EORTC classification of primary cutaneous lymphoma as table 1.[1, 4, 5]

Patients with LyP have an increase risk for developing lymphoma (10-60%), most commonly mycosis fungoides (MF), Hodgkin's disease, and primary anaplastic large cell lymphoma.[6- 9] LyP can present before, with or after the lymphoma. In the patients presenting with LyP alone, 18% later developed lymphoma. Kunishige et al. found that men with LyP were 2.5 times to have lymphoma than were women and other risk factor could not be identified.[10] There was studies reported the lymphomatoid papulosis-associated MF carries a favorable prognosis.[4, 11]

Large cell transformation of MF is rare and is associated with an aggressive clinical course and poor prognosis. The 5- year survival from the diagnosis of transformation was 20.8%.[12] MF transformations is defined as the presence of large cell exceeding 25% of the infiltrate, or forming microscopic nodules.[13] LyP and large cell transformation probably exists in the same spectrum when they are associated with progressive stages of MF.[14]

Table 1. WHO-EORTC classification of cutaneous lymphomas with primary cutaneous manifestations

Indolent (low-grade/slow growing) clinical behaviour

- Mycosis fungoides (MF)
- MF variants and subtypes
  - Folliculotropic MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- **Primary cutaneous CD30+ lymphoproliferative disorders**
  - **Primary cutaneous anaplastic large cell lymphoma**
  - **Lymphomatoid papulosis**
- Subcutaneous panniculitis-like T-cell lymphoma
- Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma

Aggressive clinical behaviour

- Sézary syndrome
- Adult T-cell leukaemia/lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive CD8+ T-cell lymphoma
  - Cutaneous γ/δ T-cell lymphoma

The treatment of patients with LyP is unsatisfactory. Topical or systemic corticosteroids or antibiotics are not effective. Low-dose oral methotrexate (5-20 mg/week) is the most effective therapy for reducing the number of skin lesions however, the disease recurs within 1-2 weeks after discontinuing the medication.[15, 16] Beneficial effects have been reported with PUVA, topical nitrogen mustard or BCNU, topical MTX, topical imiquimod cream,[17] intralesional interferon, low-dose cyclophosphamide, chlorambucil, medium-dose UVA-1 therapy, excimer laser therapy,[18] and dapsone help disease suppression.

When larger skin tumors develop in the course of LyP, they can be observed for a period of 4 to 12 weeks for the possibility of spontaneous remission. If spontaneous resolution does not occur, such lesions can be excised or treated with radiotherapy. Because of the potential risk for developing a systemic lymphoma, long-term follow-up is required in all patients with LyP.

In our patients, both presented with persistent patch and recurrent erythematous papules. The diagnosis was cutaneous T cell lymphoma (primary cutaneous anaplastic large cell lymphoma and mycosis fungoides) coexisting with lymphomatoid papulosis. For LyP lesion, one received topical steroids, while the other one received PUVA therapy with good response. Despite of good prognosis, the long term follow up is needed.

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