Case 12
A 46 year-old Thai female from Bangkok

Chief complaint: Multiple erythematous papules on trunk and extremities for 2 weeks

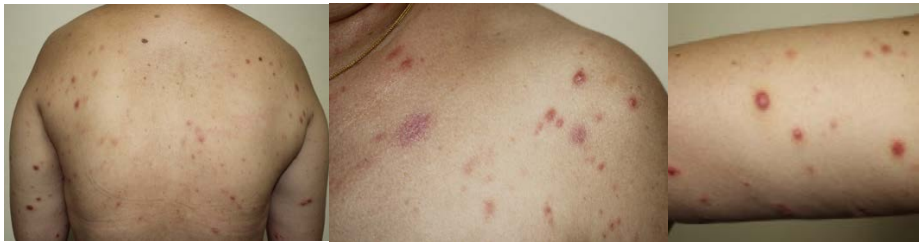

Fig. 12.1

Present illness:
She presented with a 2-week history of multiple pruritic, mild tender, erythematous papules located on her trunk. She had no fever or any systemic symptoms. The rash progressively extended to her arms and thighs. Topical steroids, oral antibiotics and antihistamine was prescribed without improvement. She had prior experienced of similar rash 1 year ago which was spontaneously resolved within a few weeks.

Past history: She has underlying disease of glaucoma.

Family history:
Her cousin had a history of breast cancer.
There was no family history of similar lesion.

Physical examination:
No hepatosplenomegaly or lymphadenopathy
Others: WNL

Dermatological examination: (Fig. 12.1)

Multiple discrete erythematous papules and few small plaques with some scale crusts on face, trunk, and all extremities

Histopathology: (S17-039957A, skin, right forearm) (Fig. 12.2)

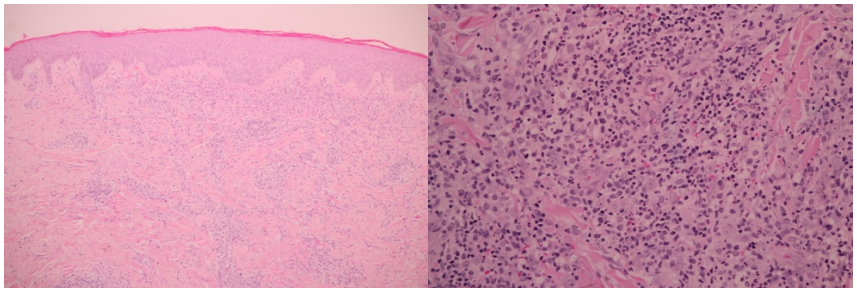

Fig. 12.2

- Dense perivascular and nodular inflammatory cells infiltrate in the superficial to deep dermis
- Numerous large atypical lymphoid cells intermingle with lymphocytes, eosinophils, and neutrophils

Immunohistochemistry: (Fig 12.3)

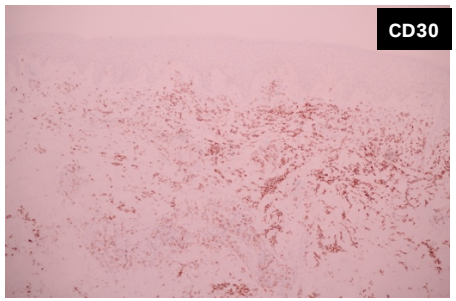

Fig. 12.3

- Positive CD 3, CD4, focally positive CD8

- Positive CD30 of large atypical lymphocytes

Laboratory investigations:

- CBC: Hb 14.2 g/dL, Hct 42.4%, MCV 86.5 , Plt 448,000/mm^3, WBC 9,270 /mm^3 (N 71%, L22%, M5%, Eo 2%)
- BUN/Cr: 9/0.82 mg/dL
- LFT: AST 19 U/L, ALT 45 U/L, ALP 124 U/L, GGT 100 U/L, TP 76.7 g/L, albumin 36.5 g/L, TB 0.4 mg/dL, DB 0.2 mg/dL
- LDH: 162 U/L
- UA: pH 7, Sp.gr. 1.009, protein and glucose: negative, WBC 0-1 /HPF, RBC 3-5 /HPF, squamous epithelium 0-1 /HPF
- CXR: WNL
- CT chest and whole abdomen: WNL

Diagnosis: Lymphomatoid papulosis type A

Treatment: PUVA phototherapy

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Discussion:

Lymphomatoid papulosis (LyP) is the most common $CD30^+$ lymphoproliferative disorders (LPD), first described by Macaulay in 1968.[1-3] LyP is benign and characterized by recurrent self-healing crops of red to violaceous papulonodules, usually on trunk and extremities.[2,4] There are approximately 1.2 to 1.9 cases per million persons of Lyp in the United States.[2] It occurs more often in men with an average age of onset between 35-45 years.[3]

LyP usually runs a chronic course from years to decades with recurrent crops of papules or nodules, then resolve within a few weeks or months, leaving varioliform scars.[2,4,5] Although the main clinical features are papules (90%) and nodules (20 %) which are up to 2 cm in size, [4,6] it may be plaques (12%), tumors (7%), or eczematous lesion (5%).[4] Eczematous lesions are significantly associated with a poorer response to treatment.[4] The lesion may develops central hemorrhage, necrosis or crust.[2] It is generally asymptomatic but it may be pruritic or tender secondary to ulceration, crusting, or necrosis.[2] The main differential diagnoses of Lyp include pityriasis lichenoides, arthropod bite reaction, and cutaneous lymphoma. Diagnosis of Lyp is based on the characteristic clinical presentation as well as typical histopathological findings.

Nowadays there are 7 histologic subtypes of Lyp (A-F, DUSP-IRF4 type).[3,7] Lyp type A is the most common histologic manifestation, accounting for 70% of all, characterized by wedge-shaped infiltrate with large pleomorphic or anaplastic CD30+ T-cells resembling Reed–Sternberg cells and numerous background eosinophils and neutrophils as in our case.[3,4,7] However, patients could have more than one histologic subtypes. Immunohistochemical examination was also sent for establish diagnosis of Lyp. In Lyp, CD30+ tumor cells express CD4 in most cases, CD45RO are expressed with variable loss of pan-T-cell antigens (CD2, CD3, CD5). ALK typically absent in Lyp and also in primary cutaneous anaplastic large cell lymphoma (PC-ALCL) as opposed to systemic ALCL.[8]

Although Lyp is benign, it could increase risk of secondary malignancy for 5%-30%, especially hematologic malignancy (mostly mycosis fungoides, anaplastic large cell lymphoma (ALCL), and Hodgkin's disease).[2,9] The median onset of secondary malignancy is 42 months.[4] Delay onset may be as long as 36 years.[4] Therefore, long term follow-up is warranted. The risk factors included male sex, history of EBV infection, histologic subtypes B and C, clonal T-cell receptor gene rearrangement, and advanced age.[2,9,10] Histologic subtype D were less likely to have lymphoma.[11] No further laboratory testing, including imaging or bone marrow biopsy is necessory, especially patients with typical clinical manifestation of Lyp without any systemic symptoms or lymph nodes enlargement.

The management of Lyp depends on the clinical severity and symptoms.[2] Because of benign clinical course with spontaneous resolution, Treatment in cases with limited disease is unnecessary.[2]

To date, treatment can not alter the course of the disease or prevent secondary malignancy. However, topical corticosteroids, phototherapy, in particular PUVA, and low dose methotrexate are commonly used and effective in treating patient with numerous or disseminated lesions.[4,5,8] A retrospective study of 252 patients found that overall median time to complete response between these treatment were not different and 78% of complete responders showed cutaneous relapse.[4] Overall estimated median disease-free survival (DFS) is about 11 months.[5] Patients who undergone phototherapy (PUVA and UVB) had longer DFS.[5] Recently, brentuximab vedotin (BV), CD30 antibody-drug conjugate, was shown to be effective in treating refractory Lyp.[12] Multiagent chemotherapy should be avoided due to risk for secondary lymphoid neoplasm.[5]

PUVA phototherapy[8,13] was started in our patient at dose 0.5 J/cm^2 twice weekly, then dose increment of 0.5 J/cm2 per week with maximum fixed dose at 4 J/cm^2. Cetirizine 10 mg daily, also prescribed to relieve pruritus. Topical mupirocin ointment was applied on crusting erosive lesions. After 34 sessions of phototherapy, the lesions were improved, leaving postinflammatory hyperpigmentation. However, long term follow-up is required.

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