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ORIGINAL ARTICLE

Lymphomatoid papulosis in association with mycosis fungoides: A clinical and histopathologic review of five Taiwanese cases

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ABSTRACT

Background/Objectives: Lymphomatoid papulosis (LyP) is a cutaneous CD30+ lymphoproliferative disorder characterized by recurrent, self-healing lesions with a chronic clinical course. Approximately 10–20% of the patients have lymphomas, including mycosis fungoides (MF). LyP in association with MF is not well documented in Taiwan. We aimed to describe the clinicopathologic characteristics of LyP with MF in a Taiwanese case series of LyP.

Methods: A retrospective clinicopathologic study was performed on cases of LyP with MF diagnosed in our Department during the period 1990–2012. The diagnosis of LyP and MF were based on their characteristic clinical and pathologic features as well as correlation with the clinical course of the specific skin lesions.

Results: A total of 24 cases of LyP (10 males and 14 females, age 18–63 years, mean 40.4 years) were included. Multiple biopsies were often done in individual patients during the clinical course to establish the diagnosis of LyP and MF. LyP was further classified pathologically as type A ($n = 16$), B ($n = 3$), C ($n = 3$), and mixed type with A&B ($n = 1$) and A&C ($n = 1$). Five cases (21%) also had MF; two had juvenile-onset LyP and three had juvenile-onset MF (one with hypopigmented MF, one with hyperpigmented MF, two with CD8+ LyP, and two with CD8+ MF). In the case of juvenile-onset hypopigmented CD8+ MF, the patient developed CD8+ LyP 25 years after the onset of MF and died of aggressive epidermotropic CD8+ lymphoma involving the skin and lung.

Conclusion: MF occurred in five of the 24 cases (21%) in the present series of LyP. These five cases had several unusual clinical and pathologic features, including subtle or uncommon skin manifestation of MF and more frequent juvenile-onset and CD8 phenotype of LyP and/or MF lesions. Long-term follow-up and repeated biopsy of selected skin lesions are necessary for correct diagnosis and proper treatment of both diseases.

Introduction

Primary cutaneous CD30+ lymphoproliferative disorders (PC-CD30+LPDs) are the second most common group of cutaneous T-cell lymphomas (CTCLs), next to mycosis fungoides (MF), and account for about 30% of CTCLs.[1] The spectrum of PC-CD30+LPDs comprises primary cutaneous anaplastic large cell lymphoma (C-ALCL), lymphomatoid papulosis (LyP), and borderline cases.

LyP is a chronic, recurrent, self-healing papulonodular or papulonecrotic skin disease with infiltration of atypical CD30+ lymphocytes histologically. Clinically, the skin lesions of LyP typically wax and wane with spontaneous resolution in 3–12 weeks. The histologic findings of LyP are variable and three histologic subtypes (types A, B, and C) have been recognized with overlapping features; all three types may be observed in the same patient. Moreover, the age of the individual skin lesion at the time of biopsy also contributes to variability of histopathologic findings.

LyP type A (histiocytic) lesions are characterized by infiltration of scattered or small clusters of large, sometimes multinucleated, or Reed-Sternberg-like CD30+ cells intermingled with numerous inflammatory cells, such as histiocytes, small lymphocytes, neutrophils, and/or eosinophils. LyP type C (ALCL-like) lesions demonstrate a monotonous population or large clusters of large CD30+ T cells with relatively few inflammatory cells. LyP type B

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(MF-like) is uncommon (less than 10%) and is characterized by an epidermotropic infiltrate of small atypical lymphocytes with cerebriform nuclei similar to that seen in MF.

Two new variants of LyP have recently been described.[2,3] LyP type D is characterized histopathologically by infiltration of medium-sized, CD8+/CD30+ pleomorphic, atypical, lymphocytes with marked epidermotropism in a pagetoid reticulosis-like pattern, mimicking primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma. LyP type E is characterized by self-healing, oligolesional papulonodules with necrotic eschar clinically, and an angiocentric/angiodestructive infiltrate of small- to medium-sized CD30+, and frequently CD8+, atypical lymphocytes.

In up to 20% of patients, LyP may be preceded by, associated with, or followed by malignant lymphomas, with MF, Hodgkin's disease, and CD30+ large cell lymphomas comprising 90% of the associated lymphomas.[1] In patients with LyP associated with MF, including three of 15 cases in the study by Basarab et al,[4] and two cases each by Wood et al[5] and Chott et al,[6] identical clones have been reported in both types of lesions.

Reports of MF in association with LyP from Taiwan are rare.[7,8] In this study, we aim to describe the clinicopathologic characteristics of cases of LyP with MF affecting Taiwanese.

Materials and methods

Cases of LyP diagnosed during the period 1990–2012 in the Department of Dermatology, National Cheng Kung University Hospital were retrieved from the Department's Crux database system. In each case, the medical record, clinical photos, and pathology slides were reviewed. Specifically, the morphology (papules, nodules, patches, or plaques), onset and distribution of skin lesions, evolution of individual lesions (waxing and waning versus persistent) as well as the overall clinical course and treatment response were analyzed. Follow-up data were obtained from medical records, the Crux database, or via telephone contact with patients. All skin biopsy specimens were processed for routine histopathologic study. LyP lesions were classified as type A, B, or C based on the features delineated in the literature. Immunohistochemical stainings for CD3 (DakoCytomation Denmark A/S, Denmark), CD4 (BioSB, USA), CD8 (DakoCytomation Denmark A/S, Denmark), CD20 (DakoCytomation Denmark A/S, Denmark), CD30 (Dako Denmark A/S, Denmark), and granzyme B (Fremont, CA, USA) were performed in selected cases.

Results

Clinical presentations, clinical course, histology, and treatment

There were a total of 24 cases of LyP, consisting of 10 males and 14 females with age ranging from 18 years to 63 years (mean 40.4 years). Three patients had juvenile-onset LyP (defined by disease onset before 18 years of age). The LyP lesions were papulonodules, some with crusted or necrotic centers. The skin lesions were widespread over the limbs and trunk in 18 patients (75%) and were more limited to the limbs and/or penis in six patients. Most of the LyP lesions waxed and waned, lasting for about 1 week in smaller lesions or up to 1 month in larger lesions. The clinical and pathologic features were summarized in Table 1. Of the 24 cases, LyP was classified as type A in 16 (67%), type B in three (13%), type C in three (13%), and two cases had more than one type: Case 1 with both type A and type B lesions, and Case 5 with both type A and type C lesions.

Of these 24 patients, five (21%) also had MF and their LyP was type A in three (60%), type B in one (20%), and mixed type A + B in one (20%). The clinical presentations of these five cases are summarized in Table 2 and briefly described as follows.

Case 1

The patient was an 18-year-old male who had concurrent onset of both LyP and MF at 9 years of age. He first presented to us at the age of 18 years with a 9-year history of recurrent, self-healing

Table 1 Clinical and pathologic features of a series of 24 lymphomatoid papulosis (LyP) cases.

Patient	Sex/age of diagnosis (y)	LyP lesions	Distribution	Type/T-cell type	Associated lymphoma	Follow-up (mo)	Main therapy	Outcome[a]
1	M/18	P/N	G	A&B	MF	49	MTX	Under control
2	F/36	P/N	L (lower extremities)	B	MF	45	UVB311	Under control
3	M/32	P/N	L (upper extremities)	A	MF	2	MTX	Under control
4	M/37	P/N	G	A	MF; peripheral T-cell lymphoma	108	Systemic retinoids, CHOP	Death due to systemic involvement
5	F/31	P/N	G	A&C	MF	302	PUVA, topical steroids	Under control
6	M/55	P/N	G	A	—	0.5	obs	N/A
7	F/55	P/U	G	A	—	—	N/A	N/A
8	F/50	P/N	G	A	—	3	UVB	Under control
9	F/32	P/N	G	A	—	10	MTX	Under control
10	F/31	P/U	G	A	—	—	N/A	N/A
11	F/48	P/N	G	A	—	1	UVB311	Under control
12	F/49	P/U	G	C	—	0.5	MTX	Under control
13	M/55	P/U	L (penis)	A	—	3	Topical steroids	Subsided
14	M/42	P/N	G	B	—	165	Neotigason	Under control
15	F/43	P/N	G	A	—	7	Topical steroids, obs	Under control
16	M/36	P/N	G	A	—	0.5	Topical steroids, obs	Under control
17	F/33	P/N	L (extremities)	A	—	2	Topical steroids	Under control
18	M/41	P/N	G	B	—	302	MTX	Under control
19	F/18	P/N	G	A	—	12	Topical steroids	Under control
20	F/42	P/U	G	C	—	36	MTX	Under control
21	M/35	P/N	L (lower extremities)	A	—	—	N/A	N/A
22	M/48	P/U	G	C	—	8	MTX	Under control
23	F/63	P/U	G	A	—	—	N/A	N/A
24	F/42	P/N/U	L (extremities)	A	—	—	N/A	N/A

F = female; G = generalized; L = localized; M = male; MF = mycosis fungoides; MTX = methotrexate; N = nodule; N/A = not applicable; obs = observation; P = papule; PUVA = psoralen ultraviolet A; U = ulcer; UVB = ultraviolet B.

[a] Under control: new lesions can be suppressed, only sporative small new papules popped out.