Follicular lymphomatoid papulosis revisited: A study of 11 cases, with new histopathological findings

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Background: Follicular lymphomatoid papulosis (LyP) describes a variant of LyP with perifollicular infiltrates and some degree of folliculotropism of $CD30^+$ atypical lymphocytes. So far, only a few cases of follicular LyP have been described.

Objective: Our goal was to study the clinicopathologic features of follicular LyP in a series of 11 cases (9 male, 2 female; age range 7-78 years, mean age 50 years).

Methods: In all, 113 cases of LyP were reviewed to select cases showing follicular involvement. Histology was correlated with the clinical data to exclude cases of $CD30^+$ anaplastic large-cell lymphoma or folliculotropic mycosis fungoides.

Results: Six cases were classified as type C and 4 as type A, whereas the remaining case manifested epidermotropism of small lymphocytes in a background of a typical type A lesion (overlapping type A/B). Perifollicular infiltrates of $CD30^+$ atypical lymphoid cells were seen in all 11 cases, with infiltration of the follicular epithelium in 8 cases. Hyperplasia of the follicular epithelium was observed in 4 cases; ruptured hair follicles, in 3 cases; and follicular mucinosis, in 2 cases. In addition to hair follicle infiltration, atypical cells were recognized within sebaceous glands in 2 lesions. New findings were presence of numerous intrafollicular neutrophils in 2 patients, who clinically had pustules in addition to papules. Other histopathological features encountered included perieccrine infiltration (n = 5), focal subcutaneous involvement (n = 4), granulomatous inflammation (n = 3), epidermal hyperplasia (n = 2), and 1 each of infiltration of muscle bundles, numerous eosinophils in the infiltrate, and angiocentricity.

Limitations: This was a retrospective study.

Conclusions: Follicular LyP is a variant of LyP with involvement of hair follicles, mostly in the form of perifollicular infiltrate with variable degree of folliculotropism. Other changes including hyperplasia of the follicular epithelium, rupture of hair follicle, and follicular mucinosis are less common. Rarely, intrafollicular pustules can be seen in the follicular epithelium; such lesions manifest clinically as pustules. (J Am Acad Dermatol 2013;68:809-16.)

Key words: CD30; follicular mucinosis; lymphoma; lymphomatoid papulosis; skin.

Several clinicopathological variants of lymphomatoid papulosis (LyP) have been delineated, sometimes occurring in the same individual. The commonest histopathological variants are LyP type A and C, which are characterized by wedge-shaped or nodular infiltrates of large pleomorphic or anaplastic $CD30^+$ lymphoid cells arranged as scattered atypical cells in the background of eosinophils and neutrophils (type A) or in cohesive sheets/nodules with more than 50% of atypical cells (type C) imitating $CD30^+$ anaplastic large-cell lymphoma.[1] Less common forms are LyP type B and the recently described type D, both showing an epidermotropic infiltrate of atypical lymphocytes with

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variable expression of CD30, which histopathologically resembles mycosis fungoides and cutaneous aggressive epidermotropic $CD8^+$ cytotoxic T-cell lymphoma, respectively.[2,3] Cases with overlapping patterns have been reported.[1] Most recently, a new variant of LyP has been proposed, namely, type E characterized by a predominantly angioinvasive infiltrate and oligolesional presentation with eschar-type necrosis.[4]

The term "follicular lymphomatoid papulosis" was introduced in 1980 by Pierard et al[5] who reported 2 patients with LyP and perifollicular distribution of the infiltrate. Other changes related to hair follicles encountered in the biopsy specimens from the above patients were cystic dilatation of a hair follicle (infundibular cyst), rupture of a hair follicle, and hyperplasia of the follicular epithelium.[5] Since the original description, only a few more cases under the designation of follicular LyP have subsequently been described, mostly as isolated case reports, documenting, in addition to the above changes, rare instances of intrafollicular atypical cells (folliculotropism) and follicular mucinosis.[1,6-10] We present the first series, to our knowledge, of follicular LyP including 11 cases and describe a new feature: collections of neutrophils in the follicular epithelium presenting as pustules.

CAPSULE SUMMARY

- Lymphomatoid papulosis may present with unusual clinical and histologic findings.
- We present 11 cases of follicular lymphomatoid papulosis.
- Histology is characterized by perifollicular infiltrates of $CD30^+$ atypical lymphoid cells with variable degree of folliculotropism, follicular mucinosis, and neutrophils in the follicle. The follicular variant may occasionally manifest with pustules.

METHODS

After encountering 2 patients with folliculocentric LyP who had collections of neutrophils in the follicular epithelium, we retrieved cases of $CD30^+$ lymphoproliferative disease from our files to identify cases with follicular involvement. A search was performed for cases displaying any of the following: perifollicular distribution of the infiltrate, intrafollicular $CD30^+$ cells, cystic dilatation or rupture of a hair follicle, hyperplasia of the follicular epithelium, follicular mucinosis, and collections of neutrophils in the follicular epithelium. The main clinical data (age, gender, location, clinical presentation, treatment, and follow-up) were obtained from the medical charts and contributing clinicians and were correlated with histology to exclude cases of $CD30^+$ anaplastic large-cell lymphoma and mycosis fungoides with expression of CD30. A total of 113 LyP cases were reviewed, and 11 cases of follicular LyP were found. For each case only 1 biopsy specimen was available for review. The cases were classified into types A, B, and C according to the current histopathological classification of LyP.[11,12] In addition to the above changes related to hair follicles, we documented other alterations such as presence of granulomas, vessel involvement, and adipose tissue involvement. In all the cases, immunohistochemical studies (CD30) had been performed at the time of diagnosis.

RESULTS

Clinical findings

There were 9 male and 2 female patients ranging in age at time of diagnosis from 7 to 78 years (mean age 50 years, median age 59 years). All of them presented with widespread recurrent papules and nodules, usually involving several anatomic sites over the course of the disease. In 1 patient the distribution of the lesions was confined to the face, thus conforming to the concept of regional (localized) LyP (Figs 1 and 2).[13] One patient had a history of Hodgkin disease. The detailed information is included in Table I. Follow-up was available in 2 cases (cases 8 and 9). Both patients were alive with no evidence of disease at 40 and 26 months.

Histopathological findings

Of the 11 cases, 6 were classified as type C and 4 as type A. The remaining case manifested epidermotropism of small lymphocytes in a background of a typical type A lesion, thus matching the concept of so-called "overlapping type A/B."[1] Perifollicular infiltrates of $CD30^+$ atypical medium to large lymphoid cells were seen in all 11 cases, whereas infiltration of the follicular epithelium in 8 cases and usually only few atypical lymphocytes were noted to invade the hair follicles (Fig 3). Hyperplasia of the follicular epithelium was observed in 4 cases and ruptured hair follicles were present in 3 biopsy specimens (Figs 4 and 5). Follicular mucinosis was noted in 2 cases, and in 1 of them several hair follicles demonstrated mucin deposits (Figs 6 and 7). In addition to hair follicle infiltration, atypical cells were recognized within sebaceous glands in 2 lesions. In 2 cases, there were neutrophils in the infundibula of the hair