DERMATOPATHOLOGY

Histologic features of secondary syphilis: A multicenter retrospective review

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Background: Secondary syphilis has a wide spectrum of clinical and histologic manifestations.

Objective: We sought to determine the frequency of histopathological features characterizing secondary syphilis, and which are most common in specimens displaying few diagnostic findings.

Methods: In a multicenter, retrospective analysis of biopsy-proven secondary syphilis, cases were subcategorized by the number of histologic characteristics present.

Results: The 106 cases mostly had 5 to 7 of the features studied. Many features were scarcer in cases with 5 or fewer features, including endothelial swelling (87.7% overall vs 72.4% ≤5 features), plasma cells (69.8% vs 48.3%), and elongated rete ridges (75.5% vs 27.6%). Specimens with 5 or fewer features were more likely to be truncal (61.1% vs 34.4% overall), demonstrate rete ridge effacement (44.8% vs 19.8%), and have pityriasis rosea (33.3% vs 17.2%) or drug eruption (33.3% vs 10.9%) in the clinical differential. An interstitial inflammatory pattern was the most common characteristic of specimens with 5 or fewer features (75.9%).

Limitations: This was a retrospective review.

Conclusion: The independent value of many histologic features of syphilis may be overestimated. Combinations of endothelial swelling, interstitial inflammation, irregular acanthosis, and elongated rete ridges should raise the possibility of syphilis, along with the presence of vacuolar interface dermatitis with a lymphocyte in nearly every vacuole and lymphocytes with visible cytoplasm. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.08.062.)

Key words: dermatopathology; endothelial swelling; infectious diseases; interstitial inflammation; plasma cells; rete ridge effacement; secondary syphilis; sexually transmitted diseases.

The incidence of primary and secondary syphilis in the United States has more than doubled since its lowest recorded rate in 2000. The most recent data show the incidence of syphilis is roughly 5.3 cases in 100,000, with the majority occurring in men who have sex with men, regardless of race and ethnicity.[1] The clinical presentations of syphilis, coined "the great imitator" by Sir William Osler, are protean and the diagnosis is often not suspected clinically at the time of biopsy.[2] Atypical clinical presentations and false-negative laboratory tests are more common in patients with HIV infection.[3,4] Inevitably, the increased incidence of the disease coupled with inconsistently reliable serologic tests translates to increases in dermatopathological specimens for the diagnosis of syphilis.

The histopathological features of syphilis also exhibit a wide spectrum, from interface dermatitis to granulomatous disease.[5-8] We sought to determine the frequency of histopathological features characterizing the papulosquamous eruption of secondary syphilis, and to determine which are most common

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in specimens displaying few diagnostic findings by conducting a multicenter retrospective analysis of biopsy-proven secondary syphilis cases. Knowledge of these features would be particularly valuable to practicing dermatopathologists who must suspect the diagnosis of syphilis in specimens that lack well-known features such as plasma cells and endothelial swelling.

METHODS

Using electronic and written medical records, 106 biopsy specimens of secondary syphilis diagnosed between 2000 and 2014 were obtained from Ackerman Academy of Dermatopathology, State University of New York Downstate Medical Center, Kings County Hospital, and Dermpath Diagnostics New York. The diagnosis in each case was confirmed by immunostaining, silver staining, or serology. Approval was obtained from institutional review boards of the State University of New York Downstate Medical Center and Kings County Hospital.

The cases were reviewed by a board-certified dermatopathologist (D. E. or Q. X.) and categorized as having or lacking the following histologic characteristics: neutrophils in the stratum corneum; effacement of the dermoepidermal junction; regular psoriasiform or irregular acanthosis; elongated rete ridges; vacuolar, lichenoid, and/or interstitial patterns of inflammation; endothelial swelling; plasma cells; reactive lymphocytes with ample cytoplasm; and positive silver or immunohistochemical stains, if performed. The cases were then also subcategorized by the number of the above characteristics that were present for further comparison.

Clinical characteristics gathered included age at time of diagnosis, gender, site of biopsy, and prebiopsy differential diagnosis.

CAPSULE SUMMARY

- Secondary syphilis has widely varying clinical and histopathological presentations.
- Some of the well-recognized histologic characteristics are not consistently seen in cases with fewer histologic findings.
- The combination of interstitial inflammation, endothelial swelling, irregular acanthosis, and elongated rete ridges should raise the possibility of syphilis, even when no clinical suspicion exists.

RESULTS

Overall 106 cases were collected from the designated centers, of which 66 had at least partial clinical data available. As noted in Table I, no biopsy specimen demonstrated only a single feature, but as few as 2 or as many as 10 could be present in a given slide. As noted in Table II, an interstitial inflammatory pattern (Fig 1), endothelial swelling (Fig 2), irregular acanthosis (Fig 3, *A*), and elongated slender rete ridges (Fig 3, *B* and *C*) were the most common findings overall, although all studied characteristics were present in varying degrees (Figs 1-6). In cases with 5 or fewer features, interstitial inflammation, endothelial swelling, a vacuolar pattern with equal vacuoles and lymphocytes, plasma cells, and effacement of the rete ridge pattern were the most common findings, as noted in Table III. Interstitial inflammation was the most common finding seen in cases with 2 to 4 features. The clinical features of all cases and those cases with 5 or fewer features are listed in Tables IV and V, respectively.

Table I. Number of diagnostic features present

Total cases	106
No. of features	No. of cases (%)
1	0 (0)
2	2 (1.9)
3	5 (4.7)
4	7 (6.6)
5	15 (14.2)
6	30 (28.3)
7	28 (26.4)
8	14 (13.2)
9	4 (3.8)
10	1 (1.0)

Table II. Overall frequency of features

Feature	No. of cases (%)
Interstitial inflammation	97 (91.5)
Endothelial swelling	93 (87.7)
Irregular acanthosis	82 (77.4)
Elongated rete ridges	80 (75.5)
Vacuolar pattern (equal vacuoles and lymphocytes)	77 (72.6)
Plasma cells	74 (69.8)
Lymphocytes with ample cytoplasm	58 (54.7)
Neutrophils in stratum corneum	34 (32.1)
Lichenoid pattern	25 (23.6)
Effacement	21 (19.8)
Vacuolar pattern (more vacuoles than lymphocytes)	15 (14.2)
Psoriasiform acanthosis	3 (2.8)