Category: (A) Clinical Research

Histologic Features of Secondary Syphilis: A Systematic Review and Meta-Analysis

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Background: Syphilis is a sexually transmitted infection caused by *Treponema pallidum*. Secondary syphilis, often termed "the great imitator," presents with diverse manifestations, most commonly a maculopapular rash. If left untreated, lesions may resolve spontaneously, leading to a latent stage and potential recurrence, often mimicking other dermatologic conditions. Histopathologic examination plays a crucial role in early and accurate diagnosis, preventing delays in treatment. This study aimed to analyze the prevalence of histopathologic features of secondary syphilis to improve disease recognition and reduce diagnostic errors.

Methods: A systematic search was conducted in PubMed, Embase, and Cochrane databases up to January 2025, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search strategy included the terms (Syphilis OR "*Treponema pallidum*") AND ("Histologic features" OR "Histopathology" OR "Skin biopsy findings"). Statistical analyses were performed using R version 4.3.2. A random-effects model was performed to determine the proportion with a 95% confidence interval (CI). Heterogeneity was assessed using the Cochrane Q test and I^2 statistics. Leave-one-out analyses were performed to address high heterogeneity.

Results: A total of eight studies were included, encompassing 384 patients and 460 lesions. The mean age was 38.1 years, and approximately 24% of patients were female. The most common histologic features were endothelial swelling, reported by five studies, with a prevalence of 85% (95% CI 0.75–0.96; $I^2 = 82.6\%$), and moderate to dense plasma cell infiltration, reported by six studies, with a prevalence of 83% (95% CI 0.74–0.92; $I^2 = 90.7\%$). Acanthosis was observed in six studies, with a prevalence of 66% (95% CI 0.47–0.86; $I^2 = 96.0\%$), followed by perivascular inflammatory infiltrate, reported in five studies, with a prevalence of 64% (95% CI 0.37–0.90; $I^2 = 96.9\%$). Other histologic characteristics included lymphocytes with ample cytoplasm, described in three studies, with a prevalence of 53% (95% CI 0.31–0.75; $I^2 = 93.2\%$), and neutrophils in the epidermis, reported by five studies, with a prevalence of 51% (95% CI 0.16–0.85; $I^2 = 94.6\%$).

Conclusion: A combination of clinical history, presentation, and histopathologic findings should raise suspicion for secondary syphilis. Endothelial swelling and moderate to dense plasma cell infiltration were the most prevalent features, highlighting their diagnostic significance.