

Association between pemphigus and psoriasis: a systematic review and meta-analysis

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Abstract

Pemphigus has been associated with other autoimmune and autoinflammatory disorders. Specifically, some case reports in the literature document coexistence of pemphigus with psoriasis, but this association is lacking larger scale investigation. With this in mind, we conducted a systematic review and meta-analysis to evaluate the association between pemphigus and psoriasis. In doing so, we found an association between the two conditions. Pemphigus was more common in patients with psoriasis than in controls (OR 2.64, 95% CI 1.24-5.59, P=0.01), with heterogeneity ($I^2=94\%$). We go on to propose pathophysiologic mechanisms and its relevance for diagnostic and management considerations.

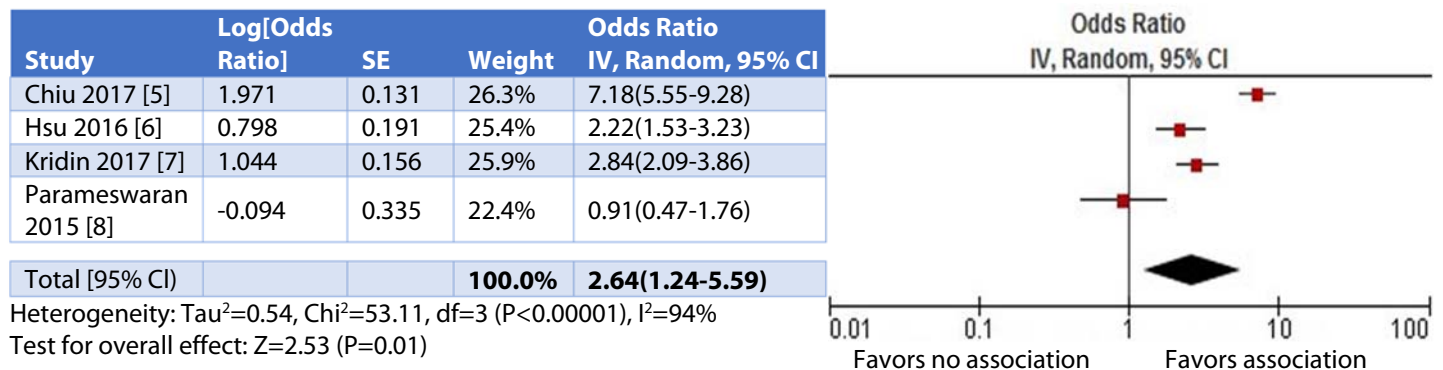
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To the Editor:

Pemphigus comprises IgG-mediated autoimmune blistering disorders targeting the squamous epithelium of skin mucous membranes, which manifests as debilitating intraepidermal blisters and erosions [1]. The autoimmune etiology and chronicity of pemphigus diseases has spurred investigation of its association with other autoimmune and autoinflammatory conditions. Some case reports note co-existence of pemphigus with psoriasis [1], but whether an association exists or not remains unclear. We conducted a systematic

review and meta-analysis to assess the association between pemphigus and psoriasis.

Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [2], online databases searched were: PubMed; Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Ovid Medline; ACP Journal Club; and Database of Abstracts of Review of Effectiveness. These were searched from their respective inception dates to August 2019. Search terms were: "pemphigus foliaceus," "pemphigus vulgaris," or "pemphigus" in conjunction with "psoriasis." Inclusion criteria specified investigations comparing psoriasis cases in pemphigus patients to controls. Pemphigus cases included pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, pemphigus erythematosus, and drug-induced pemphigus. Studies were excluded if pemphigus diagnosis was not confirmed by either direct or indirect immunofluorescence staining or enzyme-linked immunosorbent assay. Additionally, case reports, reviews, and studies without controls were excluded. The statistic used in analysis was the odds ratio (OR), which was calculated using random effects model considering the baseline study heterogeneity assessed with the I^2 statistic. As a supplemental statistic, a number needed to treat (NNT) was calculated using the OR and the global prevalence of psoriasis (1.30% to 2.20%) as a surrogate for the patient expected event rate (PEER), [3-4]. Statistical analyses were performed using Review Manager Version 5.3 (Cochrane Collaboration, Oxford, United Kingdom).

Figure 1. Forest plot representing the association between pemphigus and psoriasis ($P=0.01$).

We identified 658 references and after exclusion of duplicate or irrelevant references, a total of four studies were pooled in the meta-analysis [5-8]. Overall, 11,183 pemphigus cases were compared with 87,051,171 controls. Pemphigus was more common in patients with psoriasis than in controls (OR 2.64, 95% CI 1.24-5.59, $P=0.01$), with heterogeneity ($I^2=94\%$), (**Figure 1**). The NNT was calculated as 29 to 49 using global psoriasis prevalence rates as surrogate for PEER and the OR of 2.64.

The pathophysiologic mechanisms underlying the association between pemphigus and psoriasis is unclear. However, the association may be, in part, explained through several mechanisms. A fundamental genetic predisposition may be present as pemphigus and psoriasis are both associated with HLA DRB1 alleles [9]. Plausible mechanisms linking these two conditions may be altered T-lymphocyte function in psoriasis with rising autoantibody production and epitope spreading from chronic autoinflammation or autoimmune derangements [10,11]. Additionally, plasminogen activity in pemphigus results in acantholysis and elevated levels of plasminogen activation are present in

psoriatic lesions, serving as another possible link [12]. Other exogenous and endogenous triggers for both conditions (e.g. infection, trauma), cannot be excluded.

Limitations of our study include lack of data concerning immunopathological subtypes of both pemphigus and psoriasis, clinical features, disease severity, chronology of diagnosis (i.e. which diagnosis preceded the other), treatment-related outcomes, and a true PEER value to obtain a more accurate NNT. Additionally, different study types, cohort sizes, and patient demographics may influence statistics.

Dermatologists caring for patients with pemphigus should be cognizant of the association of pemphigus and psoriasis. However, further research is required to elucidate the molecular basis of this association, deem more specifically its clinical significance and prevalence, and possibly identify optimal therapeutic strategies for patients with coexistence of both conditions.

Potential conflicts of interest

The authors declare no conflicts of interests.

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