REVIEW

Diet and psoriasis, part II: Celiac disease and role of a gluten-free diet

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Patients with psoriasis have been shown to have a higher prevalence of other autoimmune diseases including celiac disease, a condition marked by sensitivity to dietary gluten. A number of studies suggest that psoriasis and celiac disease share common genetic and inflammatory pathways. Here we review the epidemiologic association between psoriasis and celiac disease and perform a meta-analysis to determine whether patients with psoriasis more frequently harbor serologic markers of celiac disease. We also examine whether a gluten-free diet can improve psoriatic skin disease. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.03.017.)

Key words: antigliadin; celiac disease; celiac sprue; diet; gluten-free; nutrition; psoriasis.

Psoriasis is a chronic inflammatory disease affecting about 2% of the population and characterized by well-demarcated, erythematous, scaly plaques.[1] The pathogenesis of psoriasis involves the interplay among multiple gene susceptibility loci, the immune system, and various environmental factors. Psoriasis is most commonly understood as a T-cell-mediated disease involving interferon-γ and tumor necrosis factor-alpha as key proinflammatory players. More recently, T cells expressing cytokine interleukin 17 have been found to play a major role in psoriasis.[2]

Patients with psoriasis are more likely to have autoimmune diseases than the general population. In a recent study conducted by Wu et al[3] examining the medical records of 25,341 patients with psoriasis from the Southern California Kaiser database, psoriasis was found to be significantly associated with 14 other autoimmune diseases. The link between psoriasis and other autoimmune diseases may result from the shared abnormalities in cytokine pathways[4,5] and genetic susceptibility loci.[6]

Abbreviations used:

AGA: antigliadin antibody
EMA: endomysial antibody
GFD: gluten-free diet
tTG: tissue transglutaminase antibody

The association between psoriasis and celiac disease has been of recent interest, and a number of studies have evaluated a possible therapeutic effect of a gluten-free diet (GFD) on psoriasis. Celiac disease is defined as a disease of the small intestine characterized by mucosal inflammation, villous atrophy, and crypt hyperplasia upon exposure to dietary gluten, which is mainly composed of two groups of proteins called "glutenins" and "gliadins." Serum antibody levels including IgA tissue transglutaminase antibody (tTG), IgA endomysial antibody (EMA), IgA antigliadin antibody (AGA), and IgG AGA are most commonly used as diagnostic markers for celiac

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disease, with IgA tTG and IgA EMA being the most sensitive and specific markers.[7-9] A large meta-analysis found that IgA tTG has a 96% sensitivity and 95% specificity for the diagnosis of celiac disease in adults, and that IgA EMA has an even higher 97% sensitivity and 100% specificity in adults.[10]

Here, we examine the evidence that patients with psoriasis are at increased risk for celiac disease and review studies evaluating the impact of a GFD on psoriasis improvement.

CAPSULE SUMMARY

- A gluten-free diet has been reported to be beneficial in some patients with psoriasis, particularly those who test positive for celiac disease markers.
- Our meta-analysis of 9 case-control studies showed that psoriasis is associated with an increased frequency of celiac markers (odds ratio 2.36, 95% 1.15-4.83).
- Patients with psoriasis should be questioned about celiac disease symptoms; those who are antibody positive may benefit from a gluten-free diet.

METHODS

We searched the electronic MEDLINE database via PubMed using search terms "psoriasis" combined with "celiac disease," "celiac sprue," and "gluten," respectively. We limited our search to articles available in English and those published between 1960 and 2012. Manual searches of bibliographies of the articles were also performed to identify additional studies to be included. We focused on population-based studies examining the co-occurrence of psoriasis and celiac disease, investigations of celiac disease antibody markers in psoriatic cohorts, and clinical trials examining the therapeutic benefit of a GFD in patients with psoriasis. In all, 28 articles met our inclusion criteria. For data analysis, we synthesized studies that reported on the number of patients with positive IgA AGA for psoriasis and control groups (n = 9 studies). In addition, we synthesized studies (n = 5) that reported on mean IgA levels in cases of psoriasis compared with controls. Meta-analysis was performed using a random effects model in Stata (STATA 12, StataCorp LP, College Station, TX).

RESULTS

Population studies

Several studies have found that patients with psoriasis are at increased risk for celiac disease. A retrospective cohort study comparing 25,341 patients with psoriasis with more than 125,000 matched control subjects in the US Southern California Kaiser Permanente database showed an odds ratio of 2.2 for the association of psoriasis with celiac disease.[3] Similarly, a case-control study comparing 12,502 patients with psoriasis with 24,285 age- and sex-matched control subjects using an Israeli medical database found the prevalence of celiac disease to be 0.29% in patients with psoriasis versus 0.11% in control subjects ($P < .001$), corresponding to an odds ratio of 2.73.[11] The converse question, whether patients with celiac disease have increased risk of psoriasis, has also been examined. A cohort of 28,958 patients from Sweden with biopsy-confirmed celiac disease was evaluated for risk of future psoriasis compared with 143,910 age- and sex-matched control subjects.[12] The authors found that individuals with celiac disease had a hazard ratio of 1.72 for development of future psoriasis.

Celiac disease markers in psoriasis

Seven studies have reported a positive association between psoriasis and celiac disease markers (Table I). All of these studies compared a group of patients with psoriasis with a nonpsoriatic control group, with the number of patients with psoriasis ranging from 37 to 302. Ojetti et al[13] evaluated 92 consecutive patients with psoriasis seen in an Italian dermatology department for the presence of celiac disease antibodies compared with 90 healthy control subjects. Four of the 92 patients with psoriasis (4.3%) were given a diagnosis of celiac disease based on positivity for IgA EMA antibodies and confirmatory small bowel biopsy specimens showing villous atrophy, compared with none of 90 control subjects ($P < .0001$). A Swedish study of 302 patients with psoriasis and 99 reference subjects found that patients with psoriasis had elevated IgA AGA levels compared with the reference group, but that IgG AGA did not differ.[14] Four additional studies in Turkey,[15] Egypt,[16] Poland,[17] and India[18] also found elevated IgA AGA levels in patients with psoriasis compared with control subjects, and elevated IgA tTG levels in the latter two studies. Beyond serologic testing, a case-control study found that malabsorption was present in 60% (33 of 55) of patients with psoriasis and only 3% (2 of 65) of control subjects.[19]

On the other hand, several studies did not find evidence of association between psoriasis and celiac disease (Table II). However, these studies were of smaller size and some did not use control groups.[20-24] A case-control study of 120 patients with psoriasis tested for both IgA and IgG AGA demonstrated no significant difference in prevalence