Helicobacter Pylori Association in Multiple Dermatological Presentations

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Abstract
Helicobacter pylori (H. pylori) is a human-associated organism, colonizing the stomach. It is a slowly growing microaerophilic microorganism. It needs enriched growth medium, rich in blood or its derivatives. H. pylori infection is estimated to affect more than half of the adult population worldwide. The presence or absence of H. pylori infection may influence the risk of developing several autoimmune conditions, including immune-mediated dermatological diseases. The immunomodulatory role of H. pylori infection in Chronic Urticaria (CU) is a subject of intensive studies. For instance, IgG and IgA antibodies generated against H. pylori were found to play a role in the pathogenesis of CU. H. pylori have been reported to cause or correlate with different dermatological diseases such as: vasculitis, autoimmune bullous diseases, Sweet’s syndrome, and Vitiligo.

Keywords: Helicobacter Pylori (H. Pylori), Dermatological diseases

Helicobacter pylori
1.1 Background
Helicobacter pylori (H. pylori) is a human-associated organism, colonizing the stomach. It is a slowly growing microaerophilic microorganism. It needs enriched growth medium, rich in blood or its derivatives. H. pylori is considered a causative agent of chronic gastritis, with an important role in the development of peptic ulcer and non-cardia adenocarcinoma of the stomach. Although the way the infection is transmitted is still unclear, interpersonal transmission appears to be the main route. Epidemiological evidence also suggests the possible role of waterborne transmission (1).

H. pylori is a Gram-negative helical microaerophilic organism with multiple sheathed flagella at each pole of the bacterial cell. The cells are 2 to 4 μm long and 0.2 to 1.0 um wide. H. pylori is catalase-positive and has a potent urease enzyme, which has particular importance in cytoplasmic pH homeostasis. This ability enables its survival in the strongly acidic gastric mucosal environment and colonization of the stomach (2).

H. pylori infection usually starts in the early childhood and remains as a chronic persistent infection for decades. Interestingly, only a minority of infected individuals actually develop gastric diseases. Various gastrointestinal and extra-gastrointestinal diseases are reported to be associated with H. pylori in children and adolescents (3).
1.2 Epidemiology
H. pylori infection is estimated to affect more than half of the adult population worldwide. Approximately, one-third of adults in North Europe and North America carry H. pylori, whereas in south and east Europe, South America, Africa and Asia, the prevalence of H. pylori is often higher than 50%. Wide variations in the prevalence and incidence between regions and population groups exist (1).

1.3 Mode of transmission
There are two possible routes of transmission of H. pylori: oral-oral and fecal-oral. The oral-oral route is well established and is the most likely route of infection in childhood. The presence of the bacterial antigens and DNA in the feces of infected people is common (4). However, molecular techniques have successfully been applied to detect H. pylori in the environment. This organism contaminates water mainly through human excreta. H. pylori can be identified more readily in human feces with antigen tests and PCR than with culture. The presence of H. pylori in feces reinforces the possibility of the fecal-oral transmission route. As well, the presence of H. Pylori in sewage water has been confirmed by some studies (5).

1.4 Diagnosis of helicobacter pylori infection
a- Urea Breath Test (UBT)
UBT is a suitable method with many advantages (simple, noninvasive and safe) to detect H. pylori infection in pediatric patients. The accuracy of UBT in pediatric patients is not as good as it used in adult patients, especially for children younger than 6 years old, having 75% to 100% sensitivity and specificity (6).

b- Stool antigen test
Stool antigen test (SAT) is noninvasive method in the diagnosis of H. pylori infection, with good sensitivity and specificity, 94% and 97% respectively in global meta-analysis (7).

c- Antibody-based tests
Numerous serological tests based on the detection of anti-H pylori IgG antibody are widely available for H. pylori diagnosis and enzyme immunoassay (EIA) test is the most common and accurate technique among them. However, serological test is not a reliable test to assess eradication therapy because antibody levels can persist in the blood for long periods of time even after successful eradication (8).

d- Polymerase chain reaction (PCR)
PCR has been used extensively for the diagnosis of H. pylori from gastric biopsy specimens, saliva, stool, gastric juice and variable specimens. PCR provides excellent sensitivity and specificity, greater than 95%, as compared with other conventional tests and has more accurate results in detecting H. pylori in patients with bleeding (9).

e- Culture
Culturing of H. pylori from gastric biopsy specimen is a highly specific but less sensitive method. In general, culturing has almost 100% specificity, but the sensitivity of culture shows significant variation, between 85%-95%. Because of the delicate and fastidious nature of H. pylori, the cultivation in vitro requires particular transport medium, growth medium and incubation environment (10).

1.5- Immunomodulatory mechanisms of H. Pylori in autoimmune diseases
Various mechanisms have been proposed in an attempt to explain the extraintestinal autoimmune manifestations of H. pylori infections. Autoimmune diseases are characterized by dysregulation of the...
The inflammatory response to H. pylori infection can lead to the development of antigen-antibody complexes or cross-reactive antibodies resulting in autoimmunity. H. pylori induced molecular mimicry can also result in both humoral and cell-mediated autoimmune reactions. The chronic character of H. pylori infections increases the risk of initiation or maintenance of H. pylori related pathological disorders triggered by the host immune mechanisms during infection (12).

Infection with H. pylori elicits a significant immunomodulation, that are typically triggered by chronic inflammation and results in a primarily Th1 T-cell response, resulting in the production of interleukin (IL)-2 and interferon gamma. This chronic infection is also characterized by higher local and systemic levels of proinflammatory cytokines such as tumor necrosis factor-α, IL-6, IL-10, and IL-8. H. pylori chronic infection can also result in uncontrolled growth and proliferation of CD5+ B-cells, which produce poly-reactive and auto-reactive IgM and IgG3 antibodies (13).

H. pylori antigens were found to activate cross-reactive T cells and induce autoantibodies production. Also, microbial heat shock proteins (HSP) play an important role in the pathogenesis of autoimmune diseases because of the high level of sequence homology with human HSP (14).

Based on these observations, Blaser et al., (15) suggested that the presence or absence of H. pylori infection may influence the risk of developing several autoimmune conditions, including immune-mediated dermatological diseases.

1.6- Helicobacter pylori and dermatological diseases

H. pylori and chronic urticaria

Urticaria is widely regarded as a heterogeneous group of diseases that share a distinct skin reaction pattern. Chronic spontaneous urticaria (CSU) is defined as wheals arising spontaneously without any external physical stimuli and the disease lasts more than 6 weeks. It is accepted that autoimmune mechanisms are involved in the pathogenesis of CU. Different pathogenic autoantibodies may also result in a release of histamine, after reaction with IgE epitopes, or with the α-chain of FceRI receptors (16).

Assessment of these autoantibodies in clinical practice is performed by the autologous serum skin test (ASST) and by immunoassay, while a positive ASST correlates with CU exacerbation. The role of H. pylori infection in CU is still a matter of debate, although the association between CU and H. pylori has been found by some research groups (17).

The pathogenetic mechanisms by which H. pylori may induce urticaria are far from being clear and several hypotheses have been developed regarding the link with the bacteria and CU. The immunomodulatory role of H. pylori infection in CU is a subject of intensive studies. For instance, IgG and IgA antibodies generated against H. pylori were found to play a role in the pathogenesis of CU (18).

When IgA-, IgG-, and IgE- mediated immune responses against H. pylori antigens were analysed, some bacterial immunoresponsive proteins were identified in cases of CSU (19).
H. pylori and psoriasis
Psoriasis is an autoimmune disease which affects 1%-3% of population. Latest immunological studies have increased our understanding of the pathogenesis of psoriasis. Recently, it has been suggested that H. pylori infection might be a triggering factor in psoriasis. H. pylori infections were considerably more common in psoriasis patients than in healthy controls. Several investigators reported cases in which psoriatic lesions cleared up following the eradication of H. pylori infections (20).

H. pylori and alopecia areata
Alopecia areata (AA) is an autoimmune T-cell mediated disease directed against the hair follicle, with an estimated lifetime risk of 1.7% among the general population. While one group of investigators found higher prevalence of H. pylori infection in patients with AA, other studies failed to confirm this association. However, a case of a 43-year-old man with an 8-months history of AA of the scalp and beard and concomitant H. pylori infection was presented, with complete remission from AA after H. pylori eradication (21).

H. pylori and vasculitis
There is some evidence of an association of H. pylori infection with various forms of vasculitis. Behçet’s disease (BD) is a multisystem inflammatory disorder characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. The etiology of the disease remains unknown, but epidemiologic findings suggest that an autoimmune process is triggered by an infectious or environmental agent in a genetically predisposed individual. As for the most other autoimmune disorders, the Th1-type polarization is significant in BD with increased numbers of activated T. lymphocytes (22).

Schoenlein-Henochpurpura (SHP)
(SHP) is a leukocytoclastic vasculitis of small vessels and is characterized by IgA deposition in the affected tissues. SHP is the most common vasculitic disorder affecting children, but it is less common in adults. In general, the relationship of H. pylori infection and SHP may be underestimated. Randomized controlled trials are necessary to confirm a relationship between H. pylori and SHP and to evaluate the usefulness of H. pylori eradication therapy in SHP (23).

H. pylori and autoimmune bullous diseases
Autoimmune bullous diseases (AIBD) are a heterogeneous group of disorders, which includes pemphigus, pemphigoid, epidermolysis bullosa cquisita, dermatitis herpetiformis, linear immunoglobulin A disease, and multiple autoimmune syndromes. AIBD are characterized with a genetic predisposition, which promotes the production of autoantibodies targeted against different components of the epidermal desmosome and hemidesmosome (24).

In a study looking at serological evidence of various infectious agents in patients with AIBD (Pemphigus and bullous pemphigoid), H. pylori IgG antibodies were reported to be more common in patients as compared to controls. Clinical trials are necessary to confirm preliminary observations (25).

Helicobacter pylori and rosacea
Rosacea is a common chronic facial dermatosis in adults which primarily affects those aged 30 to 60 years, with women being more often affected than men, especially in the early disease stages. It is characterized by transient or persistent central facial erythema, visible blood vessels, and often, papules
and pustules (26).

The skin manifestations progress in stages. The disease lasts for years, with episodes of improvement or exacerbation. Alcohol, sun exposure, and consumption of coffee and other products containing caffeine, as well as hot or spicy food, may precipitate disease exacerbation. Four subtypes of the disease have been recognised: erythematotelangiectatic, papulopustular, phymatous, and ocular rosacea (27).

Although rosacea is a common disease, its cause remains unknown. Endocrinological, pharmacological, immunological, infectious, climatic, thermal, and alimentary factors are implicated as triggers in its etiology (28).

Helicobacter pylori and sweet’s syndrome
Sweet’s syndrome or acute febrile neutrophilic dermatosis, is characterised by the acute onset of fever, leukocytosis, and erythematous plaques infiltrated with neutrophils. It has been associated with inflammatory and neoplastic diseases, but most cases are idiopathic. An association between H. pylori and Sweet’s syndrome has been proposed (26).

References


