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CASE REPORT

Cure of alopecia areata after eradication of *Helicobacter pylori*: A new association?

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Abstract

Alopecia areata is a disease of the hair follicles, with strong evidence supporting autoimmune etiology. Alopecia areata is frequently associated with immune-mediated diseases with skin manifestations such as psoriasis and lichen planus, or without skin manifestations such as autoimmune thyroiditis and idiopathic thrombocytopenic purpura. *Helicobacter pylori* (*H. pylori*) infection is present in around 50% of the world's population and has been associated with a variety of immune-mediated extra-digestive disorders including autoimmune thyroiditis, idiopathic thrombocytopenic purpura, and psoriasis. A case of a 43-year old man with an 8-mo history of alopecia areata of the scalp and beard is presented. The patient was being treated by a dermatologist and had psychiatric support, without any improvement. He had a history of dyspepsia and the urea breath test confirmed *H. pylori* infection. The patient went into remission from alopecia areata after *H. pylori* eradication. If such an association is confirmed by epidemiological studies designed for this purpose, new therapeutic options could be available for these patients, especially in areas where infection with *H. pylori* is highly prevalent.

INTRODUCTION

Alopecia areata is a disease of the hair follicles, with strong evidence supporting an autoimmune origin[1], although the exact pathogenesis of the disease is not clear. Alopecia areata has a frequency ranging from 0.7% to 3.8% in patients attending dermatology clinics, affects both sexes[2], and a familial occurrence is often reported[3,4]. The pattern of hair loss can vary and can affect any part of the body. Alopecia areata frequently occurs in association with other autoimmune diseases, including autoimmune thyroiditis[5], psoriasis[6-8] and Sjögren syndrome[9], among others.

Helicobacter pylori (*H. pylori*) is a microaerophilic Gram-negative bacterium that colonizes the gastric mucosa[10] and is present in around 50% of the world's population[11], with varying prevalence rates between 7% in the Czech Republic and 87% in a South African population[12]. In the case of Medellín, Colombia, prevalence of *H. pylori* infection in children under 12 years is 60.9%[13] and in adults, it is 77.2%[14]. *H. pylori* infection has been associated with the pathogenesis of gastric disorders such as gastritis, duodenal and gastric ulcers, gastric cancer, mucosa-associated lymphoid tissue lymphoma[10], and a variety of

extra-digestive disorders, many of them clearly identified as immune-mediated[15], such as idiopathic thrombocytopenic purpura[16,17], autoimmune thyroiditis[18,19], Sjögren's syndrome[20,21], rosacea[22] and psoriasis[23,24].

A case of a 43-year-old man with patchy alopecia areata and *H. pylori* infection is presented. The patient had hair regrowth after bacterial eradication.

CASE REPORT

A 43-year-old man presented with an 8-mo history of patchy hair loss in the scalp and beard (Figure 1A-C). He had consulted a dermatologist who prescribed 0.25% desoximetasone and 5% minoxidil, according to the guidelines for the management of alopecia[25], and had psychiatric support with escitalopram 5 mg/d, without any response other than progression of the condition.

The patient had a history of dyspepsia, therefore, he underwent analysis to determine *H. pylori* status. Urea breath test (^{13}C-UBT) (6.95 $\delta^{13}CO_2$; negative, < 1)[26], and *H. pylori* IgG antibodies (IgG index: 52.4; negative, < 9) were positive. Subsequent laboratory evaluation included normal values of ultrasensitive thyroid stimulating hormone, free thyroxine and free tri-iodothyronine; and negative antinuclear, antithyroid peroxidase and intrinsic factor antibodies. The patient was prescribed first line *H. pylori* eradication with proton pump inhibitor (omeprazole) 20 mg twice daily, amoxicillin 1000 mg twice daily, and clarithromycin 500 mg twice daily for 14 d, according to recommendations from the Maastricht Ⅲ Consensus Report[27], and was followed photographically every 2 wk. He was instructed not to take or apply any medications for alopecia areata. *H. pylori* eradication was confirmed 6 wk after treatment with a negative result of the ^{13}C-UBT (0.81 $\delta^{13}CO_2$).

Figure 1 shows the photographic sequence of the lesions before and after *H. pylori* eradication. From week 4, there was evidence of hair regrowth in the scalp and beard (Figure 1D-F). To date, the patient continues in complete remission from alopecia areata, as shown in Figure 1M-O.

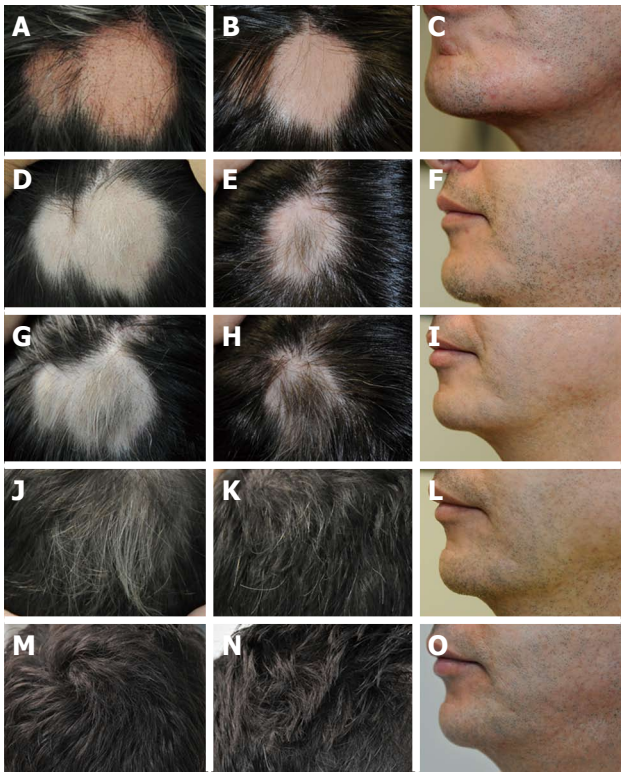

Figure 1 Photographic sequence of lesions before and after *Helicobacter pylori* eradication. A-C: Alopecia areata of the scalp (A and B) and beard (C) at baseline visit (week 0) before *Helicobacter pylori* (*H. pylori*) eradication. Positive ^{13}C-UBT (6.95 $\delta^{13}CO_2$); D-F: Evidence of hair regrowth at week 4; G-I: Hair regrowth at week 8. Negative ^{13}C-UBT (0.81 $\delta^{13}CO_2$); J-L: Hair regrowth at week 16; M-O: Hair regrowth at week 44. Negative ^{13}C-UBT (0.67 $\delta^{13}CO_2$).

DISCUSSION

H. pylori infection has been associated with numerous immune and non-immune disorders including dermatological conditions, such as chronic urticaria[28-30], rosacea[22,28,31-39], psoriasis[23,24], Schönlein-Henoch purpura[40-46], Behçet's disease[47,48], prurigo nodularis[49], chronic cutaneous pruritus[50], progressive systemic sclerosis[51-54], Sjögren's syndrome[20,21,55-57], and Sweet's syndrome[58]; many of them improving or going into remission after eradication of *H. pylori* infection[24,30,49,59-61]. Several mechanisms have been suggested to mediate the systemic effects of *H. pylori* infection, including the development of antigen-antibody complexes and cross-reactive antibodies (by molecular mimicry)[61-63], where antibodies developed against *H. pylori* cross-react with autoantigens to cause tissue damage, as has been reported in atrophic gastritis[62,64], chronic gastritis[65-67], chronic idiopathic thrombocytopenic purpura[16,17,68-70], Hashimoto's thyroiditis[19], atherosclerosis[71], arterial hypertension[72], unstable angina pectoris[73], ischemic heart disease[74,75], Alzheimer's disease[76], systemic sclerosis[77,78], central serous chorioretinopathy[79], iron deficiency[80,81], autoimmune pancreatitis[82-86], and chronic urticaria[87].

Alopecia areata has been described to be of autoimmune origin[88], with the presence of inflammatory cells around and within the human hair follicles. Alopecia areata has been associated with other autoimmune disorders including thyroid disease[89-93], psoriasis[6,7], and celiac disease[94-97]; conditions that have also been associated with *H. pylori* infection.

In the literature, there is ample evidence to suggest an association between *H. pylori* and alopecia areata that could explain the cure in this patient after eradication of infection. There is concurrent alopecia areata with immune diseases that are also concurrent with *H. pylori* infection. There are three different scenarios: immune-mediated skin diseases associated with *H. pylori* infection and alopecia areata, including psoriasis[6,7,23,24,98-103] and lichen planus[101,104-109]; immune-mediated non-skin conditions associated with *H. pylori* infection and alopecia areata, including autoimmune thyroiditis[18,19,110-115], celiac disease[94-97,116-118], idiopathic thrombocytopenic purpura[119,120], and autoimmune pancreatitis[82,84,85,121-124]; and laboratory findings that show the immunological nature of the conditions that are found in *H. pylori*-infected patients as well as in alopecia areata patients, including parietal cell antibodies[117,125-127] and thyroid antibodies[90,128].

After reviewing the medical literature, an association between *H. pylori* infection and alopecia areata has not been clearly demonstrated; only three reports have explored such association and had different results[129-131]. Abdel Hafez *et al*[131] have compared 31 patients with alopecia areata with 24 healthy controls and have found no significant difference in the *H. pylori* status, as determined by an antigen stool test. Rigopoulos *et al*[130] have compared *H. pylori* seroprevalence in 30 patients with alopecia areata and 30 healthy controls, and found no significant difference between the groups, whereas Tosti *et al*[129] have found, in a group of 68 patients with alopecia areata, that the seroprevalence of *H. pylori* infection was higher than in matched controls. It is of note that the presence of IgG antibodies against *H. pylori* does not confirm current infection and is only an indicator of previous exposure to the bacterium[132]. However, none of the studies tried to eradicate the infection and evaluate posterior hair regrowth.

Here, I have described the case of one patient who had patchy hair loss of the scalp and beard. The patient's condition started to improve within 4 wk of completing *H. pylori* eradication (Figure 1D-F). By week 16 (Figure 1J-L), the patient had completely reversed the hair loss, and by week 44 (Figure 1M-O), he remained *H. pylori*-negative and completely cured of alopecia areata. Although prior studies have only reported the prevalence of *H. pylori* infection in alopecia areata patients, to the best of my knowledge, this is the first documented case of reversed hair loss after *H. pylori* eradication.

There have been a few early studies in which antibiotic treatment was used in an attempt to cure alopecia areata, but in no case was there information on whether the patients were infected with *H. pylori*. Dapsone was used unsuccessfully[133,134]. There was one case of a 13-year-old girl with multiple autoimmune diseases who was successfully treated for alopecia areata with co-trimoxazole, a drug with antibiotic properties and immunomodulatory effects that could have been responsible for hair regrowth. Finally, there was one case in the literature describing the occurrence of alopecia areata after antibiotic treatment with rifampicin[135]. However, further case-control studies could be useful to rule out this possibility completely.

Hence, a common denominator in various autoimmune diseases is *H. pylori* infection; therefore, *H. pylori* status could be determined in several autoimmune conditions, and if positive, eradication treatment could follow as an initial step. More studies are needed to clarify the reality of the proposed association.

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