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Case Report

Partial Response of Alopecia Areata to *Helicobacter Pylori* Eradication and Treatment with Low-Dose Naltrexone

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Abstract

Alopecia areata is an autoimmune disease of unknown origin. It has been proposed that it is a multifactorial disease with genetic, immunological, infectious, circulatory, and psychogenic factors being involved in its etiopathogenesis. Its association with other autoimmune diseases is frequent. The infection of *Helicobacter pylori* has been linked to multiple immuno-mediated extradigestive conditions including alopecia areata. There is scientific evidence of the usefulness of naltrexone in low doses (an opioid antagonist) in autoimmune diseases such as inflammatory bowel disease. We present the case of a patient with alopecia areata who partially responded to the eradication of *H. pylori* and initiation of treatment with naltrexone.

Keywords
Helicobacter pylori; alopecia areata; naltrexone; autoimmunity; molecular mimicry

1. Introduction

Alopecia areata is an autoimmune disease associated with hair loss and other autoimmune conditions. The etiology of this condition is unknown but it has been speculated to be caused by genetic, immunological, infectious, circulatory and psychogenic factors [1]. *Helicobacter pylori* infection has been associated with extra-digestive immune-mediated conditions such as Immune thrombocytopenic purpura (ITP), autoimmune thyroiditis, and psoriasis [2]. Likewise, *H. pylori* has also been linked to alopecia areata [1, 2], where healing after the eradication of infection was observed [2].

There is scientific evidence of the usefulness of naltrexone in low doses (an opioid antagonist) in autoimmune diseases such as inflammatory bowel disease [3] or chronic genetic skin diseases such as familial benign pemphigus (Hailey-Hailey disease) [4]. Earlier studies have also shown some effectiveness in the treatment of rheumatoid and seropositive arthritis (showing a reduction in medication use in patients taking low-dose naltrexone) [5].

Unlike the FDA-approved dose of naltrexone of 50 mg/day that antagonizes opioid receptors, low dose of naltrexone (less than 10 mg/day, usually 0.1 mg/kg/day) has been shown to have anti-inflammatory properties possibly through its action on Toll-like receptors (by selective blockade of opioid receptors on inflammatory cells peripherally through antagonism on Toll-like receptor 4) [6, 7] and also by inducing an elevation of endogenous opioids such as endorphins and enkephalins [3]. Naltrexone interacts with the opioid growth factor receptor (OGFr) on immune cells directly as an antagonist or modulates the amount of OGFr agonists like met-enkephalin, thus helping in the minimization of the exaggerated autoimmune response [5]. As it is a nonselective opioid receptor antagonist, it also interacts with other opioid receptors such as mu, kappa, and delta. Safety of this drug in pediatric patients has been established [3].

2. Case

Informed consent was obtained from the parents of the patient prior to the publication of this manuscript.

Here we present the case of a patient with alopecia areata partially ameliorated after the eradication of *H. pylori* and the initiation of naltrexone treatment. The patient was an 8-year-old girl who had a sudden onset of alopecia areata at the age of 5 with no known trigger. It was characterized as total alopecia affecting the entire scalp, eyebrows, and eyelashes.

The patient had a history of first-degree relatives with diabetes mellitus type 1 (father), autoimmune hypothyroidism (mother), and celiac disease (sister). The treatment with topical corticosteroids did not yield any positive effect. In addition, the treatment with locally injected corticosteroids was suggested but was dismissed by the parents.

A biopsy of duodenal mucosa without alterations carried out at a different center was available. The genetic susceptibility haplotype of celiac disease was positive (DQ2.5) in the patient. A gluten-

free diet was prescribed given the family and genetic history, as well as the existence of documented cases of alopecia areata in celiac patients with a response to a gluten-free diet [8]. However, the symptoms did not improve after following the diet for seven months.

A second digestive endoscopy was performed, which showed antral gastritis without other findings, resulting in a gastric biopsy compatible with chronic *H. pylori*-positive gastritis and a normal duodenal biopsy. The patient was asymptomatic for gastrointestinal symptoms including, nausea, vomiting, change in appetite or bowel habits.

H. pylori was eradicated with amoxicillin, metronidazole, and omeprazole treatment for ten days following the usual protocol. Likewise, the treatment was started with naltrexone at a dose of 0.1 mg/kg/day, administered orally, which was maintained indefinitely. Moreover, the post-treatment breath test was negative.

The patient began to show hair follicles in bilateral parietal regions two months after the eradication regimen and the initiation of naltrexone treatment. The response was very gradual, with subsequent hair follicles appearing on the eyebrows and eyelashes (Figure 1). Two and a half years after the start of the response, the patient showed considerable improvement, but still there were some alopecia plaques in the temporary regions, in which incipient hair follicles were observed (Figure 2).

The quantification of the degree of alopecia areata in our patient was performed via the manual Salt II score. We considered the affected area as 100% before the treatment, determined it to be 62% after one year of treatment, and 34% after two and a half years. However, even at this point, the outcome was still cosmetically unacceptable [9].

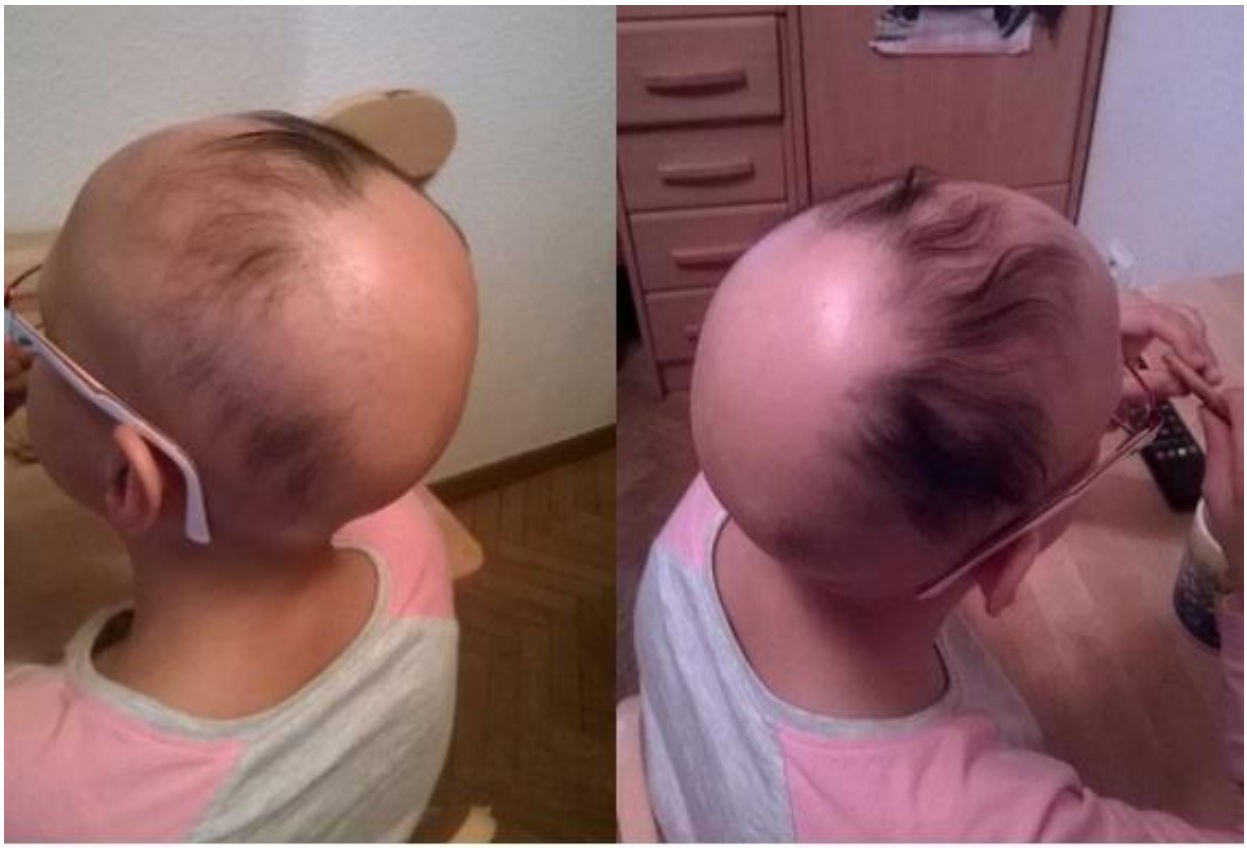

Figure 1 Evolution after one year of treatment.

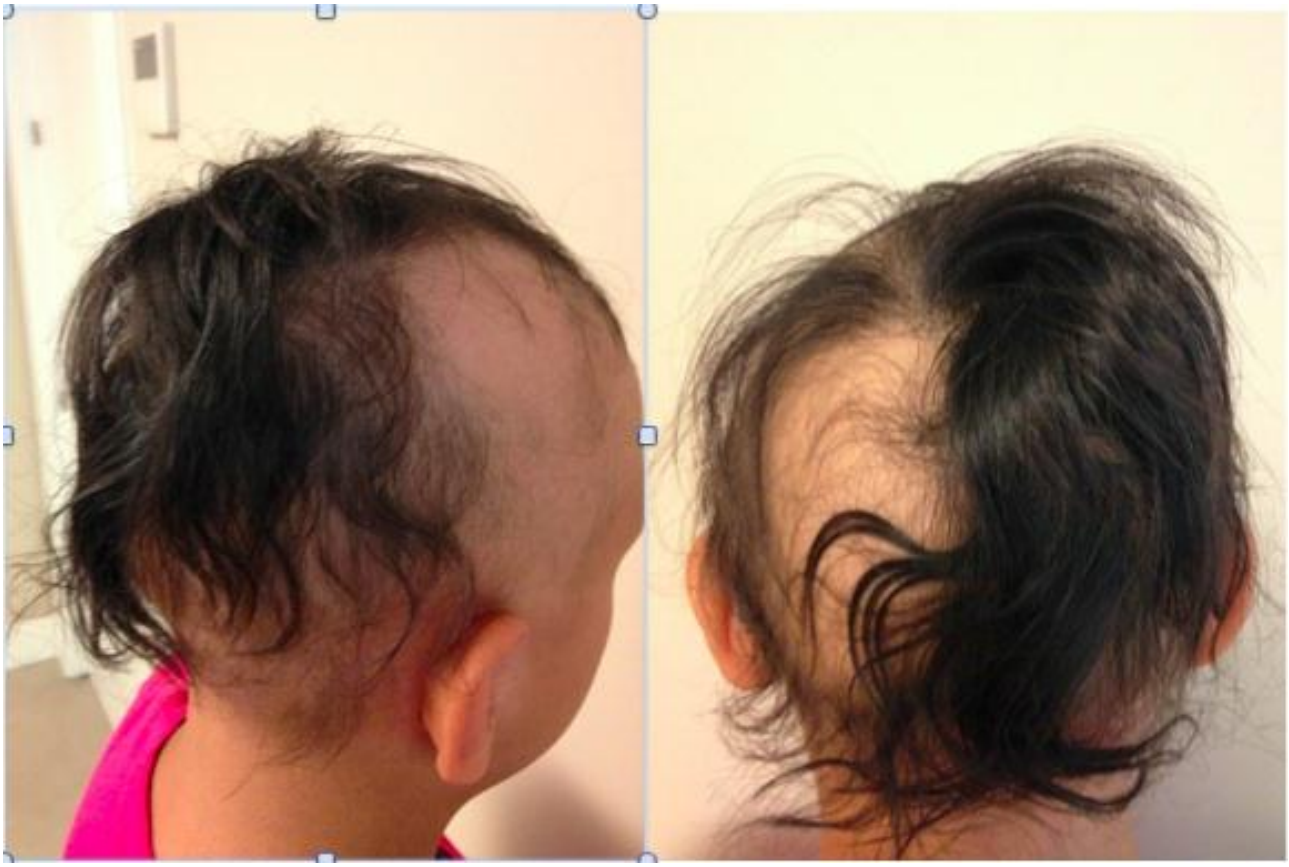

Figure 2 Evolution after two and a half years of treatment.

3. Discussion

There is no scientific evidence regarding the use of naltrexone in the treatment of alopecia areata. The mechanism of action of naltrexone prompted us to postulate that it could be equally beneficial in our patient since it has been shown to be helpful in other autoimmune diseases [3, 5].

In our case, the possible benefit of the patient to scientific interest was prioritized, so both measures (*H. pylori* eradication and naltrexone initiation) were carried out together. Therefore, it cannot be said whether the positive outcome was due to only one of these procedures or to a combination of both. Further, cases of spontaneous healing of alopecia areata have been described. However, in our case, such possibility is very improbable due to the temporal coincidence of the start of the aforementioned therapeutic measures with the clinical improvement, as well as the chronicity of the condition in our patient.

The fact that both the eradicating protocol of *H. pylori* and the treatment with naltrexone in low doses are innocuous to most patients suggests that they could be considered in cases of alopecia areata. The authors suggest the relevance of non-invasive screening for *H. pylori* infection in these patients. Infection as a trigger is frequent in multiple autoimmune diseases such as rheumatoid arthritis (related to infection by *Proteus mirabilis*), ankylosing spondylitis (infection by *Klebsiella pneumoniae*) or Guillain Barré syndrome (infection by *Campylobacter jejuni*, among others) [10].

We would like to recommend to our colleagues that while dealing with autoimmune, allergic, and oncological diseases, they should not overlook the possible role of infectious agents as an initiating or perpetuating factor.

Author Contributions

Laura Alonso Canal: main author of the research paper. Rest of authors contributed equally to this work.

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Competing Interests

The authors have declared that no competing interests exist.

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