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DOI: [10.1159/000182263](https://doi.org/10.1159/000182263)**Chronic Erythema Nodosum Circumstantially Linked with *Helicobacter pylori* Infection: Where Is the Evidence?**

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The association of *Helicobacter pylori* infection (*HpI*) with several skin disorders is a matter of dispute [1]. A putative association between *HpI* and chronic recurrent erythema nodosum (EN) [2] has not yet been described. Patient 1 was a 21-year-old woman seen by the author in 2003 after her ninth EN recurrence and 2 admissions to hospital in 4 years. Patient 2 was a 38-year-old man who came for consultation in 2005 after 3 EN relapses in 1 year. Both patients had been repeatedly and thoroughly studied for EN causes [2] without appreciable results. They were otherwise in good health, and their medical history was unremarkable as to significant diarrhea or enteritis. Investigations aimed at *H. pylori* demonstration were prompted by the clinical clue of vague reflux-like dyspepsia. Patients resulted positive to urea breath test, *H. pylori* serology and fecal antigen test. Adequate triple therapy (see below) led to the disappearance of the EN, as well as to the persistent negativization of urea breath test and fecal antigen test. They remained free from EN in the follow-up (5 and 3 years, respectively), with confirmed eradication of *H. pylori*.

HpI and EN: where is the evidence? Applying a commonly used set of causal criteria [3], we find that the following ones are fulfilled by the present cases:

(1) Plausibility: *Campylobacter* spp., which are biologically related to *H. pylori*, are recognized causes of EN [2].

(2) Analogy: *Helicobacter cynaedi* bacteremia can present with an EN-like eruption in immunosuppressed patients [4]. EN-like lesions of Behçet's disease substantially disappeared in patients treated for concomitant *HpI* [5].

(3) Coherence: *HpI* is a chronic, creeping disease, with recognized systemic implications, such as antigen shedding and activation of the immune system [1, 5, 6]. Typical EN ensues from similarly disturbed settings [2]. One case of EN associated with confirmed *HpI* in a patient with rectal MALT lymphoma has been reported [6]. Both diseases improved after *HpI* treatment. Even

lymphomas can rarely cause EN as well [2, 7], including 1 case of gastric centrofollicular lymphoma [7]. However, this was reported in 1989, when laboratory investigations for *HpI* were not readily available.

(4) Semi-experimental evidence: EN disappeared after triple treatment of *HpI*. Other causes of EN (either infectious or noninfectious ones), which, being sensitive to clarithromycin, metronidazole or lansoprazole, could act as hypothetical confounders, have never been demonstrated in these patients.

(5) Temporality: this is an unarguable criterion [3]. Given the fact that it has not been demonstrated that *HpI* cannot precede EN, the current hypothesis that *HpI* can cause EN cannot be dispensed with to date.

This topic clearly needs further studies. Practical clinicians could contribute to address stronger causality tenets [3] from an observational viewpoint, by prescribing relatively inexpensive *H. pylori* laboratory investigations and therapy to patients presenting with unexplained EN.

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