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LETTER

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Helicobacter pylori infection in Turkish children with familial Mediterranean fever: is it a cause of persistent inflammation?

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Familial Mediterranean fever (FMF) is characterized by recurrent, self-limited attacks of fever and serosal inflammation [1]. *Helicobacter pylori* infection, an established cause of chronic gastritis and peptic ulcer disease, is another cause of recurrent abdominal pain [2]. A high prevalence of FMF as well as *H. pylori* infection in association with recurrent abdominal pain has been shown in the Turkish population [1, 3, 4]. In this study we aimed to determine whether *H. pylori* infection might be a causative factor in FMF attacks.

The study included 85 patients (aged 5–22 years) with FMF. Eighteen (21.2%) did not have the mutations that were routinely screened for, 11 (12.9%) had one mutation, and 56 (65.9%) had two mutations (same or different) in both alleles (homozygote or compound heterozygote). They had no recent FMF attacks and no gastrointestinal complaints. Patients with symptoms of other infections were excluded. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and fibrinogen levels were obtained to evaluate inflammation.

H. pylori IgG was investigated by using an ELISA. When seropositivity was detected, a ^{13}C urea breath test (UBT) was performed. In patients with positive serology and UBT, an upper gastrointestinal endoscopy was performed to confirm *H. pylori* infection. After treatment they were re-evaluated with a UBT and acute-phase reactants were re-assessed. The results were expressed as medians. Comparisons of measurable data between two groups were done using the Mann–Whitney *U* test. Proportions were compared by using χ^2 test or Fisher's exact χ^2 test when expected frequencies were < 5.

Forty-three (50.6%) of the patients were *H. pylori* IgG positive. Their median ESR, CRP and fibrinogen levels (25 mm/h, 1.1 mg/dl, 360 mg/dl, respectively) were significantly higher than those in *H. pylori*-seronegative FMF patients (15 mm/h, 0.2 mg/dl, 300 mg/dl, respectively, $p < 0.05$).

Thirty-one (72%) seropositive FMF patients also had a positive UBT. Upper gastrointestinal endoscopy could be performed in 13 UBT-positive FMF patients. All of them showed abnormal endoscopic and histopathologic findings compatible with *H. pylori* infection. Percentages of both seropositivity of *H. pylori* and UBT positivity in subjects with the homozygote M694 V mutation were significantly higher than in those with compound heterozygote mutation and no detected mutation (Table 1). All the acute-phase reactants returned to normal limits after treatment in patients with *H. pylori* gastritis ($p < 0.05$).

FMF is a disease of innate immunity. Although attacks are precipitated by stress and infections in general, this is the first time an environmental factor has been demonstrated to affect the inflammatory response in this single gene disease; we have shown that acute-phase reactants were significantly modified in FMF patients with the presence of an infectious agent, *H. pylori*.

In conclusion, recurrent abdominal pain may be due to both FMF and *H. pylori* infection in children. Furthermore, it may occur in the same patient. If a patient with FMF shows elevated levels of acute-phase reactants without a recent FMF attack, *H. pylori* may be one of

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Table 1 Percentages of *H .pylori* seropositivity and UBT positivity in subjects with homozygote M694 V mutation, compound heterozygote, and no detected mutation

	Homozygote for M694 V mutation (%) ($n = 34$)	Compound heterozygote (%) ($n = 22$)	No mutation (%) ($n = 18$)
H. pylori seropositivity	44.2[a]	25.6	20.9[b]
UBT positivity	51.6[a]	19.4	19.4[b]

[a] $p < 0.05$ homozygote M694 V mutation vs compound heterozygote
[b] $p < 0.05$ homozygote M694 V mutation vs no mutation

the infectious causes to investigate, as ongoing subclinical inflammation is a major risk for morbidity. Whether other specific infectious triggers have the same role awaits further investigations.

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