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CASE REPORT

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# Eradication of *Helicobacter pylori* heals atrophic corpus gastritis caused by long-term treatment with omeprazole

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**Abstract** Long-term treatment with proton pump inhibitors in patients with *Helicobacter pylori* gastritis can lead to atrophic changes in the corpus mucosa. What is still unclear, however, is whether this atrophy can regress in response to *Helicobacter pylori* eradication. We report on a male patient with *Helicobacter pylori* gastritis receiving long-term treatment (4 years) with omeprazole for gastro-oesophageal reflux disease, who developed autoaggressive gastritis with progressive atrophy, hypochlorhydria, hypergastrinaemia and nodular ECL-cell hyperplasia. To determine whether these changes might be induced to regress, *Helicobacter pylori* eradication therapy was administered. Ten months after *Helicobacter pylori* eradication autoaggressive lymphocytic infiltrates were no longer detectable, and the glands in the corpus mucosa had normalised despite continued treatment with omeprazole – a finding that was confirmed at two further follow-up surveys performed at 6-month intervals. This case report shows that atrophy of the corpus mucosa developing under long-term treatment with a proton pump inhibitor can be cured by eradicating *Helicobacter pylori*.

**Key words** Atrophy · Gastritis · *Helicobacter pylori* · Proton pump inhibitors

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## Introduction

Acid suppression treatment may aggravate pre-existing *Helicobacter pylori* (*H. pylori*) gastritis in the corpus [1–4]. In some of these patients, progression to atrophic corpus gastritis may occur [3, 4].

Two questions that have yet to be answered are why partial atrophy develops in some, but not all, patients with *H. pylori* gastritis, and whether this atrophy will regress following eradication of *H. pylori*.

## Clinical history and pathological findings

In 1978 a large axial hiatal hernia associated with ulcerous reflux oesophagitis (Savary-Miller stage III) was diagnosed in a 44-year-old male patient. In 1982, endoscopy and a histological work-up revealed Barrett's mucosa and a Barrett's ulcer. Because treatment with a daily dose of 600 mg ranitidine proved unsuccessful, a fundoplication was carried out in 1985. Despite this procedure and continued long-term treatment with ranitidine, the ulcerative reflux oesophagitis failed to heal. In May 1987, treatment was changed to a daily dose of 40 mg omeprazole, and the reflux oesophagitis healed. Since a renewed attempt to change the treatment to an $H_2$-blocker (famotidine) resulted in recurrence of the reflux oesophagitis, long-term treatment with a daily dose of 20 mg omeprazole was instituted in November 1987.

Histological investigation of the gastric mucosa (in accordance with the Sydney System [2]) was carried out for the first time in September 1988. Massive colonization with *H. pylori*, and medium-grade chronic active gastritis were found in both the antrum and corpus, together with moderate activity but no atrophy or intestinal metaplasia. In 1989, chronic active *H. pylori* gastritis was again detected, but no atrophy or intestinal metaplasia,. During the further course of the disease, which is shown in Table 1, lasting elimination of the *H. pylori* from the antrum was achieved, with only low-grade, inactive gastritis persisting. Although the density of *H. pylori* colonization decreased in the corpus, the medium-grade chronic active gastritis persisted. In June 1991, additional lymphocytic infiltration of the entire lamina propria of the corpus mucosa, partially associated with infiltration into the glandular epithelium and focal destruction of individual glands, was seen for the first time (see Fig. 1). These signs of autoaggressive gastritis progressed until the middle of 1994, when both the length and the number of corpus glands were moderately reduced and micronodular hyperplasia of the ECL cells was present (see Fig. 2). On the basis of the histological picture, a presumptive diagnosis of active

**Table 1** Natural history of gastritis September 1988–Sept.1996 (*HP* Helicobacter pylori, – normal, + low-grade, ++ medium-grade, +++ high-grade; *Auto-aggr. inf.* auto-aggressive infiltrates, *ECL* ECL cell hyperplasia, *PC hyperpl.* parietal-cell hypertrophy)

| | *Antrum* | | | | *Corpus* | | | | | | *Gastrin* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HP Density | Degree | Activity | Atrophy | HP Density | Degree | Activity | Atrophy | Auto-aggr. inf.[a] | ECL[b] | PC hyperpl.[c] | (pg/ml) |
| Sept. 1988 | +++ | ++ | ++ | – | +++ | ++ | ++ | – | – | – | ++ | 59 |
| 1989 | + | ++ | + | – | +++ | +++ | ++ | – | – | – | +++ | |
| 1990 | – | ++ | + | – | + | +++ | ++ | – | – | – | +++ | 126 |
| 1991 | – | + | – | – | + | ++ | ++ | – | ++ | + | +++ | 680 |
| June 1992 | – | + | – | – | + | +++ | + | – | ++ | + | +++ | 450 |
| Dec. 1992 | – | + | – | – | – | ++ | – | + | ++ | + | +++ | 426 |
| June 1993 | – | + | – | – | – | ++ | + | + | ++ | + | +++ | |
| June 1994 | – | + | – | – | + | +++ | + | ++ | +++ | +++ | +++ | 650 |
| Dec. 1994 | – | + | – | – | + | ++ | ++ | ++ | +++ | ++ | +++ | 490 |
| Cure of *Helicobacter pylori* infection | | | | | | | | | | | | |
| Mar. 1995 | – | + | – | – | – | + | – | + | + | + | + | 95 |
| Sept. 1995 | – | + | – | – | – | + | – | – | – | + | + | |
| Mar. 1996 | – | + | – | – | – | + | – | – | – | – | +++ | 75 |
| Sept.1996 | – | + | – | – | – | + | – | – | – | – | +++ | |

[a] Grading of auto-aggressive infiltrates and parietal-cell hypertrophy was done as previously reported elsewhere [16, 17]

autoimmune gastritis was made, and omeprazole was discontinued. When 24-h pH-metry was carried out 2 weeks after discontinuation of treatment a pH of 7 was revealed. The search for antibodies to parietal cells and intrinsic factor in the serum proved negative. On the assumption that antigastric autoantibodies might well be responsible for triggering and maintaining autoaggressive gastritis in *H. pylori* infection [3, 4], *H. pylori* eradication treatment (40 mg omeprazole and 1000 mg amoxicillin b.i.d. for 14 days) was administered. While this treatment initially eliminated the patient's symptoms, 3 months after eradication therapy he again experienced heartburn, and endoscopic examination revealed stage I reflux oesophagitis. Repeat 24-h pH-metry revealed a mean pH of 2.5, and acid reflux present for 78% of the time. After successful *H. pylori* eradication treatment the histological work-up now revealed only low-grade inactive gastritis in the antrum and corpus. The density of lymphocytic infiltrates in the lamina propria had greatly diminished, and only low-grade atrophy was now seen. Ten months after *H. pylori* eradication, autoaggressive lymphocytic infiltrates were no longer present and the glands appeared normal (see Fig. 3). These normal findings persisted until September 1996 with the patient continuing to take omeprazole.

The concentration of gastrin in the serum (see Table 1) during omeprazole treatment was initially 59 pg/ml (1988); it increased to 126 pg/ml in 1990 and to 680 pg/ml in 1991, and finally decreased to 426 pg/ml in 1992. Three months after *H. pylori* eradication and before renewed treatment with omeprazole, the gastrin serum level was 95 pg/ml.

## Discussion

This case report shows that chronic autoaggressive gastritis with partial atrophy of the corpus glands, developing in *H. pylori* gastritis during long-term treatment with a proton pump inhibitor (PPI), can be reversed by eradicating *H. pylori*.

This moderate atrophy in association with autoaggressive gastritis, characterized by lymphocytic infiltration and partial destruction of the corpus glands, is a rare finding that may also occur in patients with *H. pylori* gastritis who are not receiving PPI treatment. The histological picture is identical with that of active autoimmune gastritis without severe atrophy of the corpus glands but with parietal cell antibodies in the serum, as we described previously [17]. In our patient, however, no antibodies to either parietal cells or intrinsic factors were detected in the serum. The mechanisms triggering the autoaggressive inflammatory process were very probably antigastric, anticanalicular autoantibodies induced by *H. pylori* gastritis [3, 11]. It is known that these antigastric autoantibodies decrease after *H. pylori* infection has been cured [4]. Hence, the success of *H. pylori* eradication treatment, resulting in the disappearance of autoaggressive lymphocytic infiltrates and normalisation of the glands, supports the hypothesis that an autoimmune process may be triggered by autoantibodies in *H. pylori* gastritis. Unfortunately, it was not possible to detect *H. pylori*-associated anticanalicular autoantibodies when *H. pylori* treatment was initiated in our patient. Consequently, we are unable to provide direct confirmation of this hypothesis. An alternative mechanism may be *H. pylori*-triggered autoreactive T lymphocytes causing *H. pylori*-dependent, atrophy-associated, active corpus gastritis. However, no data in support of this hypothesis are currently available.

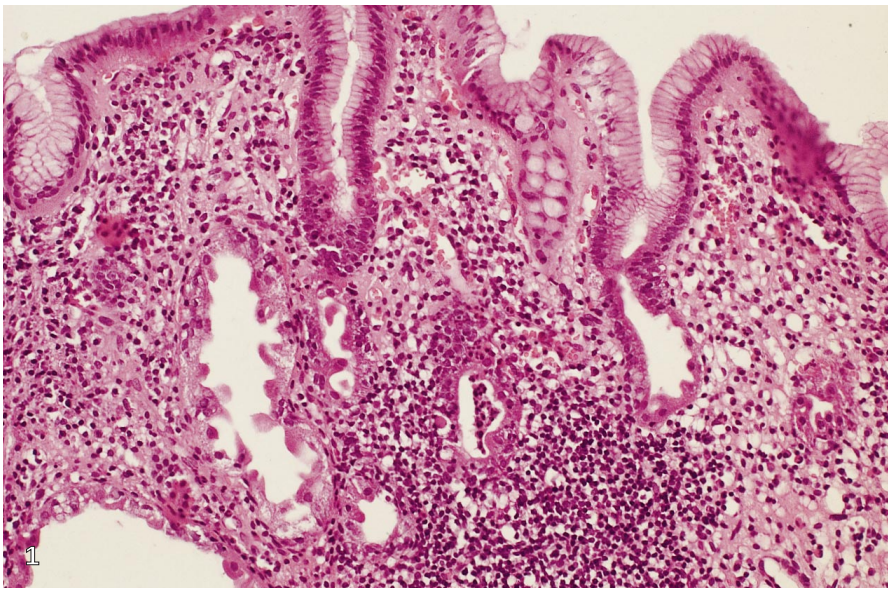


**Fig. 1** June 1991: Medium-grade, chronic active *H. pylori* gastritis in the corpus with autoaggressive infiltrates (i.e. lymphocytic infiltration of the entire lamina propria and focal destruction of individual glands)

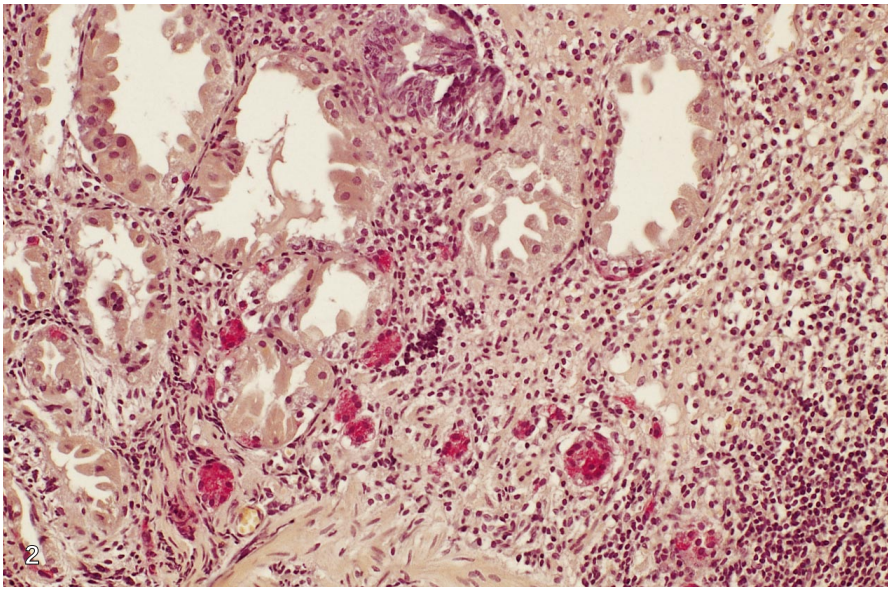


**Fig. 2** June 1994: high-grade active autoimmune gastritis with medium grade atrophy and micronodular hyperplasia of the ECL cells. Chromogranin A

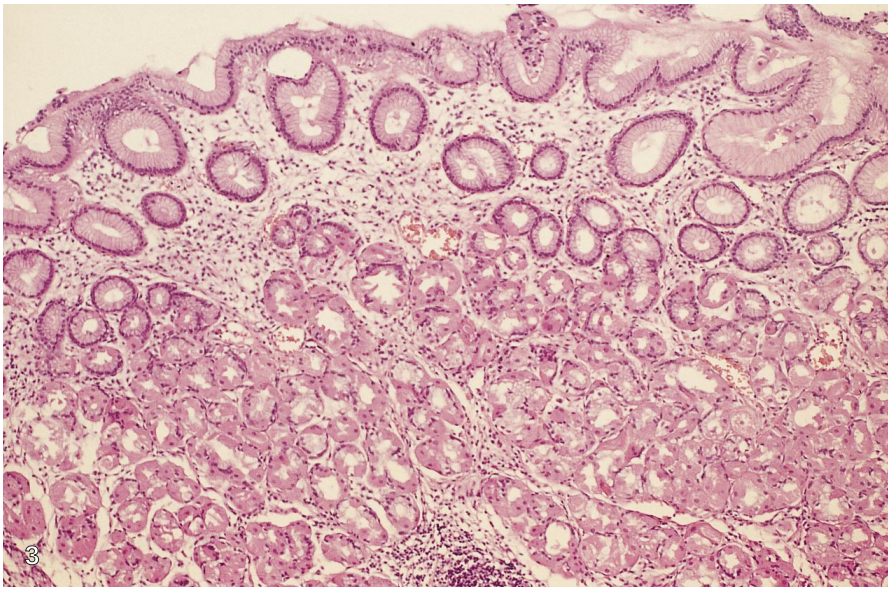


**Fig. 3** September 1995: 10 months after *H. pylori* Eradication, normalization of gastric glands with few infiltrating lymphocytes/plasma cells

The results of our investigations show that in future, atrophic gastritis in patients on long-term PPI treatment [7] must be considered more criticaly than has hitherto been the case. Although the therapeutic suppression or blockade of gastric secretion by vagotomy [5, 13], antacids or H2 blockers [9, 10] and PPI [6–8, 14, 15], regularly aggravates *H. pylori* gastritis in the corpus, atrophy of the corpus glands is rare [8, 14, 15].

Inhibition of acid secretion leads to reduced buffering of the ammonia produced by *H. pylori* [9], and probably also to a reduced washout of all cytotoxic and inflammation-activating products of *H. pylori* present in the foveolae [12]. As a result, greater damage is done to the surface epithelium, with depletion of mucus and increased infiltration of the interfoveolar lamina propria by lymphocytes, plasma cells and neutrophils [1]. While 12 months of PPI treatment in *H. pylori*-infected patients has not been reported to induce atrophy of the corpus glands or intestinal metaplasia of the corpus mucosa [19], long-term (5 years) treatment with omeprazole has been shown to induce subatrophic changes in the corpus mucosa, but not intestinal metaplasia [7].

However, on the basis of our present case, it may be assumed that even atrophic corpus gastritis developing during long-term PPI treatment can be cured by eradicating *H. pylori*. It is already known that this is the case in severe active *H. pylori* corpus gastritis with very dense mixed inflammatory infiltrates. Even unusually severe *H. pylori* gastritis in the corpus with hypertrophic rugae can heal following eradication of the bacteria [18].

At first glance, the regression of atrophy observed in our case might appear surprising. A sampling error during the histological work-up can be excluded, however, since three biopsy specimens from the antrum mucosa and five specimens from the corpus were obtained at every examination. All specimens revealed similar changes. In addition, no intestinal metaplasia was found, which means that the foveolae, including the stem cells of the neck of the gland, were all well preserved. It is not surprising that once autoaggressive destruction of the corpus glands has stopped regeneration may follow. However, this might not be the case when there is complete atrophy with burned-out mucosa, leaving no stem cells.

In view of our experience with this case, we have since used *H. pylori* eradication treatment in some similar cases of autoaggressive corpus gastritis, both with and without long-term PPI treatment, and the results have confirmed those described here [20]. For a definitive clarification of the positive effect of such treatment in *H. pylori*-induced autoaggressive corpus gastritis, however, controlled prospective studies will be necessary.

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