Letter to the Editor

Paolo Declich[1], Barbara Omazzi[2], Enrico Tavani[1], Stefano Bellone[1], Claudio Gozzini[2], Aurora Bortoli[2], Alberto Prada[2]

Fundic Gland Polyps and PPI: the Mozart Effect of Gastrointestinal Pathology?

[1]Service of Pathology,
[2]Division of Gastroenterology and Gastrointestinal Endoscopy, Rho Hospital, Italy

Dear Sir,

We have read with interest the article by Kuipers [1]. The paper is mainly focused on the development of corpus atrophic gastritis in *H. pylori* positive patients on long term PPI therapy. As such, it was not devoted to discuss exhaustively on other aspects.

Nonetheless the author find room for a brief comment about the (possible) link between PPI and fundic gland polyps (FGPs). We feel that this point deserve some more comment.

First of all we would like to deal with the histopathologic diagnosis of FGPs. We certainly agree that FGPs are characterized by "distorted glandular cysts lined with fundic-type epithelial cells", but… it is not enough! They are also characterized by foveolar-type cysts. One should be very strict on this criterium, otherwise the distinction between FGPs and parietal cell hyperplasia (PCH) (or protrusion) is blurred [2, 3]. We published a case of PCH with deep cystic dilations stressing the subtle differences with the FGPs [4].

A second point is the debate about PPI and FGPs. There have been reports favouring [5, 6] and others denying any influence [2, 7, 8]. Kuipers seems to favour a positive influence, but in fact, the cited paper does not support this view [9]. Cats et al, in their reply, agreed with us that their findings had demonstrated a link between omeprazole-gastrin and parietal cell protrusions, and "that at this time one can only speculate about causal link between omeprazole-fundic gland cysts-fundic gland polyps" [10].

Moreover, a year later Klinkenberg-Knoll et al. [11], in a very large prospective study from the same institution, could not find any de-novo case of FGPs developing under omeprazole therapy [12].

Possibly, Vieth and Stolte [13] have definitely demonstrated that *H. pylori* negative patients, with and without PPI therapy show an almost identical prevalence of FGPs. As FGPs do not develop, or disappear with an infection by *H. pylori* [4, 15], one should compare patients in therapy with PPI with *H. pylori* negative controls. Bearing these facts in mind, *H. pylori* eradication and not omeprazole per se produces "de-novo" FGPs appearance. Recently, even an authoritative text of gastrointestinal pathology seems to have incorporated this view [16].

In conclusion, we can not exclude, as suggested by Burt, "that a small subset of patients is susceptible to forming fundic gland polyps when placed on acid suppression" [17], but we would like not to propagate a sort of "Mozart effect" of gastrointestinal pathology [18].

References

1. *Kuipers EJ:* Proton pump inhibitors and gastric neoplasia. Gut 2006, 55, 1217–1221.
2. *Stolte M, Bethke B, Seifert E et al:* Observation of gastric glandular cysts in the corpus mucosa of the stomach under omeprazole treatment. Z Gastroenterol 1995, 33, 146–149.
3. *Riddell RH:* The biopsy diagnosis of gastroesophageal reflux disease, "carditis," and Barrett's esophagus, and sequelae of therapy. Am J Surg Pathol 1996, 20, 31–50.
4. *Declich P, Ambrosiani L, Bellone S et al:* Parietal cell hyperplasia with deep cystic dilations: a lesion closely mimicking fundic gland polyps. Am J Gastroenterol 2000, 95**,** 566–568**.**
5. *Graham JR:* Gastric polyposis: onset during long-term therapy with omeprazole. Med J Aust 1992, 157, 287–288.
6. *Choudhry U, Boyce HW Jr, Coppola D:* Proton pump inhibitor-associated gastric polyps: a retrospective analysis of their frequency, and endoscopic, histologic and ultrastructural characteristics. Am J Clin Pathol 1998, 110, 615–621.
7. *Declich P, Ferrara A, Galati F et al:* Do fundic gland polyps develop under long term omeprazole therapy? Am J Gastroenterol 1998, 93, 1393.
8. *Declich P, Ambrosiani L, Grassini R et al:* Fundic gland polyps: a still elusive entity on the eve of the year 2000. Pol J Pathol 2000, 51, 3–8.

9. *Cats A, Schenk BE, Bloemena E et al:* Parietal cell protrusions and fundic gland cysts during omeprazole maintenance treatment. Hum Pathol 2000, 31, 684–690.
10. *Declich P, Bellone S, Porcellati M et al:* Parietal cell protrusions with fundic gland cysts and fundic gland polyps: are they related or simply similar but distinguishable? Hum Pathol 2000, 31, 1536-1537 (with authors' reply).
11. *Klinkenberg-Knol EC, Nelis F, Dent J et al:* Long-term omeprazole treatment in resistant gastroesophageal reflux disease: efficacy, safety, and influence on gastric mucosa. Gastroenterology 2000, 118, 661–669.
12. *Declich P, Tavani E, Porcellati M et al:* Long-term omeprazole treatment and fundic gland polyps: a very authoritative proof against a link? Am J Gastroenterol 2001, 96, 1650.
13. *Vieth M, Stolte M:* Fundic gland polyps are not induced by proton pump inhibitor therapy. Am J Clin Pathol 2001, 116, 716–720.
14. *Watanabe N, Seno H, Nakajima T et al:* Regression of fundic gland polyps following acquisition of Helicobacter pylori. Gut 2002, 51, 742–745.
15. *Declich P, Tavani E, Bellone S et al:* Sporadic fundic gland polyps: what happened before? Gut 2004, 53, 1721.
16. *Bhattacharya B:* Non-neoplastic disorders of the stomach. In: Gastrointestinal and liver pathology. Iacobuzio-Donahue CA, Montgomery EA (eds). Churchill Livingstone Elsevier, Philadelphia 2005, 102–103.
17. *Burt RW:* Gastric fundic gland polyps. Gastroenterology 2003, 125, 1462–1469.
18. *Bangerter A, Heath C:* The Mozart effect: tracking the evolution of a scientific legend. Br J Soc Psychol 2004, 43, 605-623.

Address for correspondence and reprint requests to:
Paolo Declich,
Service of Pathology,
Rho Hospital,
Corso Europa n. 250,
I-20017 Rho, ITALY
E-mail: paolo.declich@libero.itl