Letter to the Editor

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

Fundic Gland Polyps: Sporadic or Not Sporadic, That Is the Question

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

Dear Sir:

We read with great interest the article by Burt [1] and the related letter by Sebastian et al. [2]. This letter raised some issues that prompted us to write some comments.

First of all, we strongly agree with the conclusions by Burt: we have stated time and again that sporadic FGPs are, by themselves an "innocuous curiosity" [3]. What is really relevant is their possible relationship with FAP, attenuated FAP, and Zollinger-Ellison syndrome that certainly warrants a careful evaluation of every patient [4]. After the review article by Burt, Jalving et al. published the first report of high grade dysplasia in a sporadic FGP patient [5], a possible but obviously an extremely rare possibility. So, we think that particularly sporadic FGPs are by themselves largely "innocuous" or "trivial", but in our mind this statement it is not at all dismissive of the FGPs: every new patient with FGPs deserve a careful study to rule out the above mentioned clinical associations.

Sebastian et al., addressing the problem of a higher risk of colonic adenomas in patients with sporadic FGPs, reported a conclusion from a previous paper by Jung et al. [6], that "in the group with sporadic FGPs colorectal adenomas were found in 28.1%". We too found in our retrospective study a similar figure (29.4%) [4]. Nonetheless, reading carefully again the paper by Jung, we could not find any reference to familiar anamnesis for colon carcinoma, and even the word sporadic never appears in that paper. Jung et al. simply speak of "80 patients with FGPs" and in the discussion section they state that "this study reveals a statistically significant increase in the incidence of colorectal tumours in patients with Elster glandular cysts of the corpus mucosa". Even if on the whole we agree with Jung et al., we would read about a prospective study of sporadic FGPs and colon adenoma risk, with strict selection criteria (negative family history for colon carcinoma and possibly genetic testing to rule out attenuated variants of FAP).

When Sebastian et al. argue that hypergastrinemia may act as a promoter for colonic epithelial cells (and hence a higher frequency of colonic adenomas), they seem to take for granted the pathogenetic role of PPI on FGPs. This issue, after years of discussion, both for [7-9] and against [10, 11], it is all but settled. Probably, the elegant paper by Vieth et al. [12] has put an authoritative end to this vexed problem.

Ethiopatogenetic problems apart, we were puzzled by the ensuing statement by Sebastian et al "In addition there are data to suggest that PPI therapy may be involved in inducing beta-catenin mutation, which has a role in colon carcinogenesis", citing a previous work by Abraham et al. [13]. Again, reading through that paper, we found a statement regarding the promoting role of gastrin in colon carcinogenesis, but nothing regarding a role of PPI on beta-catenin mutation. After an immediate literature search, we only found a brief statement of this topic in another paper by the Abraham group [14], but only as a hypothesis dismissed by the Authors themselves: "One possibility is that PPI may cause beta-catenin mutations. However, in one of the cases, we used oxyntic mucosa with parietal cell protrusions (typically seen in PPI treatment) as control tissue, and no mutations were detected, suggesting that this early histological change of PPI therapy is not associated with detectable beta-catenin mutations".

We would like to finish our letter with a half-joky, half-serious statement. We obviously agree with the final line by Sebastian that "it is probably premature to dismiss the finding of FGPs at endoscopy as 'trivial' ", and how we could not? We wrote some years ago of a letter with a near identical title [15], and similar conclusions. Possibly a citation would have been an elegant act.

In conclusion, we strongly would like to recommend a careful study of every new patient with FGPs, bearing in mind that they may be sporadic (and hence probably harmless), but they may associated with FAP, attenuated FAP and Zollinger-Ellison syndrome. So, the ultimate problem may be really to define the FGPs as "sporadic or not sporadic" [16].

References

1. *Burt RW:* Gastric fundic gland polyps. Gastroenterology. 2003, 125, 1462-1469.
2. *Sebastian S, Qasim A, McLoughlin R, O'Morain CA, O'Connor HJ:* Fundic gland polyps: not so trivial entity and worth evaluation. Gastroenterology 2004, 126, 1497-1498.
3. *Declich P, Sironi M:* Sporadic fundic gland polyps: an innocuous curiosity possibly with important pathological associations. Hum Pathol 1997, 28, 1328-1329.
4. *Declich P, Ambrosiani L, Grassini R, Tavani E, Bellone S, Bortoli A, Gozzini C, Prada A:* Fundic gland polyps: a still elusive entity on the eve of the year 2000. Pol J Pathol 2000, 51, 3-8.
5. *Jalving M, Koornstra JJ, Gotz JM, Van Der Waaij LA, De Jong S, Zwart N, Karrenbeld A, Kleibeuker JH:* High-grade dysplasia in sporadic fundic gland polyps: a case report and review of the literature. Eur J Gastroenterol Hepatol 2003, 15, 1229-1233.
6. *Jung A, Vieth M, Maier O, Stolte M:* Fundic gland polyps (Elster's cysts) of the gastric mucosa. A marker for colorectal epithelial neoplasia? Pathol Res Pract 2002, 198, 731-734.
7. *Graham JR:* Omeprazole and gastric polyposis in humans. Gastroenterology 1993, 104, 1584.
8. *el-Zimaity HM, Jackson FW, Graham DY:* Fundic gland polyps developing during omeprazole therapy. Am J Gastroenterol 1997, 92, 1858-1860.
9. *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.
10. *Dickey W, Kenny BD, McConnell JB:* Prevalence of fundic gland polyps in a western European population. J Clin Gastroenterol 1996, 23, 73-75.
11. *Declich P, Ferrara A, Galati F, Caruso S, Baldacci MP, Ambrosiani L:* Do fundic gland polyps develop under long term omeprazole therapy? Am J Gastroenterol 1998, 93, 1393.
12. *Vieth M, Stolte M:* Fundic gland polyps are not induced by proton pump inhibitor therapy. Am J Clin Pathol 2001, 116, 716-720.
13. *Abraham SC, Park SJ, Mugartegui L, Hamilton SR, Wu TT:* Sporadic fundic gland polyps with epithelial dysplasia: evidence for preferential targeting for mutations in the adenomatous polyposis coli gene. Am J Pathol 2002, 161, 1735-1742.
14. *Torbenson M, Lee JH, Cruz-Correa M, Ravich W, Rastgar K, Abraham SC, Wu TT:* Sporadic fundic gland polyposis: a clinical, histological, and molecular analysis. Mod Pathol 2002, 15, 718-723.
15. *Declich P, Ferrara A, Galati F, Ambrosiani A, Caruso S, Baldacci MP, Bellone S, Tavani E:* Fundic gland polyps: a not so innocuous entity worth a careful evaluation. Am J Gastroenterol 1998, 93, 2641.
16. *Shakespeare W:* Hamlet, Act 3, Scene 1. ca 1600.

Address for correspondence and reprint requests to:
Paolo Declich
Service of Pathology
Rho Hospital
Corso Europa n. 250
I-20017 Rho
ITALY