Letter to the Editor

Reply: Tissue IgG4-positive plasma cells in inflammatory bowel disease: a study of 88 treatment-naïve biopsies of inflammatory bowel disease

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To the editor: We read with interest the recent article by Virk *et al*¹ 'Tissue IgG4-positive plasma cells in inflammatory bowel disease: a study of 88 treatment-naïve biopsies of inflammatory bowel disease,' and have been investigating the role of IgG4 plasma cells in inflammatory bowel disease at our institution. Recently, we reported our findings from an adult patient cohort.² Our study supports the findings reported in Virk *et al*,¹ in that 24% of the overall inflammatory bowel disease patients had >10 IgG4 cells on mucosal biopsies compared with 0% of the normal and microscopic colitis patients. Specifically, 0/13(0%) biopsies from Crohn's patients and 13/41(31.7%) from ulcerative colitis patients demonstrated >10 IgG4 plasma cells per high-power field (hpf). Moreover, our study found a correlation between active inflammation in ulcerative colitis as well as the presence of primary sclerosing cholangitis with >10 IgG4 cells per hpf. Specifically, none of our inactive ulcerative colitis patients demonstrated >10 IgG4 plasma cells per hpf, whereas 30% of active ulcerative colitis, 25% of primary sclerosing cholangitis with inactive colitis, and 64% of primary sclerosing cholangitis with active colitis demonstrated >10 IgG4 plasma cells per hpf on rectal biopsies. Recent evidence suggests that IgG4 plasma cells can be seen in a subset of primary sclerosing cholangitis cases.^{3,4} In addition, we presume that Virk *et al*'s study examined actively inflamed mucosal biopsies because they were studying pretreatment biopsy material. To control for variability of inflammatory cells by anatomic site within the colon, we restricted our study to only rectal biopsies.

We would recommend that future studies examining IgG4 plasma cells in inflammatory bowel disease, specifically ulcerative colitis, report the presence of active inflammation, the anatomic sites of the biopsy material, and the presence or absence of primary sclerosing cholangitis. Quantifying inflammation (both active inflammation and IgG4 cells) in tissue can be difficult, and further studies

to evaluate the best and most reliable methods to quantify these inflammatory cells are needed, specifically in regards to IgG4 (ie, should we report only the number of IgG4 cells per hpf or the ratio of IgG4/IgG cells, or both?). Further studies are clearly indicated to explore the underlying mechanism for these findings and the clinical significance of the presence of IgG4 plasma cells.

Disclosure/conflict of interest

The author declares no conflict of interest.

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References

- 1 Virk R, Shinagare S, Lauwers GY, *et al*. Tissue IgG4-positive plasma cells in inflammatory bowel disease: a study of 88 treatment-naïve biopsies of inflammatory bowel disease. *Mod Pathol* 2013; epub ahead of print 9 August 2013.
- 2 Raina A, Yadav D, Regueiro M, *et al*. Mucosal IgG4 cell infiltration in ulcerative colitis is linked to disease activity and primary sclerosing cholangitis. *Inflamm Bowel Dis* 2013;19:1232–1237.
- 3 Ghazale A, Chari ST, Zhang L, *et al*. Immunoglobulin G4-associated cholangitis: clinical profile and response to therapy. *Gastroenterology* 2008;134:706–715.
- 4 Kawakami H, Zen Y, Kuwatani M, *et al*. IgG4-related sclerosing cholangitis and autoimmune pancreatitis: histological assessment of biopsies from Vater's ampulla and the bile duct. *J Gastroenterol Hepatol* 2010;25: 1648–1655.