

## Colonic Inflammation after Acute Diverticulitis-A Chronic Disease?

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### Editorial

Diverticular disease of the colon is a common condition in western societies; by the age of 85 two thirds of the population in developed countries will have developed colonic diverticula [1,2]. While most patients will remain asymptomatic, a sizable portion will suffer from complications associated with diverticulosis, the most common of which acute diverticulitis (AD) is occurring in 10-25% of the patients [2]. In most patients, the disease is mild, responds well to antibiotic therapy and does not recur [3].

However, in recent years, accumulating data suggests that the inflammatory response associated with AD is not always an isolated short-term event, but, in some cases, a prolonged inflammatory process with exacerbations and remissions.

In a prospective long term follow up of 261 patients after an attack of AD we have shown that patients' prognosis was influenced by the severity of the acute event [4]. The Odds ratio for sigmoidectomy due to recurrent symptoms after complicated AD was 16.2 (95% confidence interval, 13.4 to 19.6) compared to patients after non complicated AD. Reasons for sigmoidectomy were mostly recurrent attacks of AD and their complications (colonic perforation and fistula formation).

Trying to elucidate a possible mechanism for these observations, we postulated that following an attack of complicated AD, patients develop chronic colonic inflammation, and as a consequence a rise in long term complications risk. In order to prove our theory, a prospective study comparing inflammatory features as clinical parameters, histologic inflammation and cytokine expression in patient post complicated versus non complicated AD was conducted [5].

Our results showed that clinically, patients post complicated AD went on to experience continued abdominal pain consistent with the diagnosis of in symptomatic uncomplicated diverticular disease SUDD [5,6], whereas none of the non-complicated AD suffered from similar symptoms. Laboratory measures showed higher levels of C-reactive protein (CRP) and fecal calprotectin in these patients, as a marker of an on-going inflammatory process. These results are in line with previous data that show elevated calprotectin levels in patients with SUDD [7].

Immunologically, mucosal inflammatory cytokine expression was shown to be higher in patients suffering from SUDD and segmental colitis associated with diverticulosis (SCAD) [8]. Moreover, Tursi et al. showed that levels of TNF- $\alpha$  expression correlated to disease activity; TNF- $\alpha$  was significantly more expressed in SCAD than SUDD, and TNF- $\alpha$  levels in patients with asymptomatic diverticulosis did not differ than levels of healthy controls. Our results strengthen and extend these observations, showing elevated expression of TNF- $\alpha$  as well as

other inflammatory cytokines- IL-6 and IL-1 $\beta$  in patients post complicated AD [5].

Histologic evaluation showed corresponding results. Higher lymphocytic cell density as a marker of chronic inflammation was shown in diverticulosis patients compared to healthy controls [9,10]. Distribution of patients according to symptoms severity (asymptomatic diverticulosis, symptomatic uncomplicated diverticulosis and acute uncomplicated diverticulitis), showed correlation between the density of colonic inflammatory infiltrates and disease severity [9]. Furthermore, mucosal changes in patients suffering from uncomplicated diverticulosis consisted of increased lymphoid infiltrate, development of lymphoglandular complexes, mucin depletion, mild cryptitis, architectural distortion, Paneth cell metaplasia and ulceration [10]. Correlating to these results, our findings in patients post complicated AD showed significantly higher crypt distortion, increased number of lymphoid aggregates and increased number of lymphocytes in the lamina propria than in patients post uncomplicated AD.

These results are suggestive of persistent chronic inflammation in these patients, and further support the hypothesis that patients post complicated AD continue to suffer from prolonged chronic inflammation in the affected area. Notably, acute inflammation was absent histologically in most patients, highlighting the chronic nature of the inflammatory process.

In conclusion, accumulating data suggests chronicity of the inflammatory process in patients suffering from symptomatic diverticular disease. Evidence for prolonged inflammation is prevalent in multiple fields: clinically-recurrent abdominal pain, recurrent attacks and complications; laboratory results-elevated inflammatory markers; histologically- elevated chronic inflammatory infiltrate in the affected colonic tissue, and immunologically- elevated expression of inflammatory cytokines in the affected colonic tissue. Inflammation measures change according to disease severity. Therefore, the question now shifts from "is there a chronic disease?"-to which the answer is probably yes, to "what can we do about it?" Which is still open.

Several treatment options are currently practiced for the treatment of diverticular disease. The accepted treatments include fiber supplements, antibiotics, mesalazine and probiotics for both symptoms reduction [11-13] and prevention of recurrent attack [11,14,15]. Results so far are conflicting, and no treatment is currently the treatment of choice. The reason for these non-conclusive treatment outcomes is probably the large diversity in patients' selection and outcome measures. Future studies with better patients' stratification according to disease severity can help clarify and guide future therapeutic decisions in this chronic inflammatory disease.

## References

1. Hughes LE (1969) Postmortem survey of diverticular disease of the colon. *Gut* 10: 336-351.
2. Garcia G (2002) Diverticulitis. In: Blaser MT, Smith DD, Ravdin JI (eds.) *Infections of the gastrointestinal tract* (2nd ed.) Lippincott Williams & Wilkins, Philadelphia, pp: 306-316.
3. Kaiser AM, Jiang JK, Lake JP, Ault G, Artinyan A, et al. (2005) The management of complicated diverticulitis and the role of Computed Tomography. *Am J Gastroenterol* 100: 910-917.
4. Lahat A, Avidan B, Sakhnini E, Katz L, Fidder HH, et al. (2013) Acute diverticulitis: a decade of prospective follow-up. *J Clin Gastroenterol* 47: 415-419.
5. Lahat A, Necula D, Yavzori M, Picard O, Halperin S, et al. (2017) Prolonged recurrent abdominal pain is associated with on-going underlying mucosal inflammation in patients who had an episode of acute complicated diverticulitis. *J Clin Gastroenterol* (in press).
6. Cuomo R, Barbara G, Pace F, Annese V, Bassotti G, et al. (2014) Italian consensus conference for colonic diverticulosis and diverticular disease. *United European Gastroenterol J* 2: 413-442.
7. Tursi A, Brandimarte G, Elisei W, Giorgetti G, Inchingolo C, et al. (2009) Faecal calprotectin in colonic diverticular disease: a case-control study. *Int J Colorectal Dis* 24: 49-55.
8. Tursi A, Elisei W, Brandimarte G, Giorgetti GM, Inchingolo CD, et al. (2012) Mucosal tumor necrosis factor  $\alpha$  in diverticular disease of the colon is overexpressed with disease severity. *Colorectal Dis* 14: e258-263
9. Tursi A, Brandimarte G, Elisei W, Giorgetti GM, Inchingolo CD, et al. (2008) Assessment and grading of mucosal inflammation in colonic diverticular disease. *J Clin Gastroenterol* 42: 699-703
10. West AB, Losada M (2004) The pathology of diverticulosis coli. *J Clin Gastroenterol* 38: S11-16.
11. Elisei W, Tursi A (2016) Recent advances in the treatment of colonic diverticular disease and prevention of acute diverticulitis. *Ann Gastroenterol* 29: 24-32.
12. Ünlü C, Daniels L, Vrouenraets BC, Boermeester MA (2012) A systematic review of high-fiber dietary therapy in diverticular disease. *Int J Colorectal Dis* 27: 419-427.
13. Bianchi M, Festa V, Moretti A, Ciaco A, Mangone M, et al. (2011) Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease. *Aliment Pharmacol Ther* 33: 902-910.
14. Di Mario F, Aragona G, Leandro G, Comparato G, Fanigliulo L, et al. (2005) Efficacy of mesalazine in the treatment of symptomatic diverticular disease. *Dig Dis Sci* 50: 581-586.
15. Comparato G, Fanigliulo L, Cavallaro LG (2007) Prevention of complications and symptomatic recurrences in diverticular disease with mesalazine: a 12-month follow-up. *Dig Dis Sci* 52: 2934-2941.