COMMENTARY
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What Is Different between Postpolypectomy Fever and Postpolypectomy Coagulation Syndrome?

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See "Postpolypectomy Fever, a Rare Adverse Event of Polypectomy: Nested Case-Control Study" by Seung-Hoon Lee, Kyung-Jo Kim, Dong-Hoon Yang, et al., on page 236-241

Colorectal cancer (CRC) is a major cause of cancer deaths in developed countries and the basis for its development is the adenoma-carcinoma sequence. Screening colonoscopies and polypectomies are widely used for the prevention of CRC around the world. Although up to 33% of patients report at least 1 minor, transient gastrointestinal symptom after colonoscopy,[1] serious complications such as bleeding, perforation, and postpolypectomy coagulation syndrome (PPCS) are uncommon.[2,3] However, with recent increases in the frequency of colonoscopic polypectomy, the incidence of complications will likely rise because complications are inherent to the procedure.

PPCS, which is one of the serious complications of colonoscopic polypectomy, is the result of an electrocoagulation injury to the colonic wall that induces a transmural burn and localized peritoneal inflammation without evidence of perforation on radiographic studies. PPCS has typical symptoms such as abdominal pain, fever, leukocytosis, peritoneal tenderness, and guarding.[4,5] PPCS is therefore called postpolypectomy syndrome or transmural burn syndrome. Typically, patients with PPCS present 1 to 5 days after colonoscopy with fever, localized abdominal pain, localized peritoneal signs, and leukocytosis.[6] The incidence of PPCS varies widely from 0.003% to 0.1%.[1,5] Most of these patients do not require surgical treatment and are usually managed by intravenous hydration, broad-spectrum parenteral antibiotics, and avoiding oral ingestion until the symptoms subside.[7]

After conducting a long-term study, Cha et al.[5] recently published their large, multicenter study on the clinical characteristics, clinical outcomes, and risk factors associated with PPCS. Among 47,083 consecutive patients who underwent colonoscopic polypectomies, 34 patients with PPCS (0.07%) were treated following hospitalization for their symptoms. Abdominal pain and fever were found in 88.2% and 64.7% of these patients, respectively. In a multivariate analysis, hypertension (odds ratio [OR], 3.023; 95% confidence interval [CI], 1.034 to 8.832), larger lesion size (OR, 2.855; 95% CI, 1.027 to 7.937), and nonpolypoid configuration (OR, 3.332; 95% CI, 1.029 to 10.791) were found to be independent risk factors related to PPCS. The most remarkable finding in this study was that hypertension, large lesion size (≥10 mm), and nonpolypoid configuration of the lesion were independently associated with PPCS. PPCS is known to develop when the electrical current applied during colonoscopic polypectomy extends past the mucosa into the muscularis propria and serosa, resulting in a transmural burn without perforation.[4,8,9] Therefore, larger lesions and a nonpolypoid configuration are logical risk factors, as they usually require the application of a large amount of thermal energy for a longer duration. The mechanism of hypertension in promoting PPCS is unclear. Patients with hypertension are more likely to have endothelial dysfunction and atherosclerosis,[10,11] which may be contributing factors.

Recently, in this issue of *Clinical Endoscopy*, Lee et al.[12] reported a nested case-control study of postpolypectomy fever (PPF). PPF in this study was defined as: 1) no fever at admission; 2) no symptoms or signs of infection before polypectomy; 3) development of fever with a temperature over 37.2°C (98.9°F) following polypectomy during the index hospitalization period; and 4) no evidence of other explainable fever foci. Patients with colon perforation, hemorrhage, or signs or

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symptoms of infection associated with conditions other than colonoscopic polypectomy were excluded. PPF developed in seven of the 3,444 patients (0.2%). The median interval from polypectomy to the occurrence of fever was 7 hours, and the median duration of fever was 9 hours. A polyp size larger than 2 cm (adjusted OR, 1.08; 95% CI, 1.01 to 1.15; p=0.02) and hypertension (adjusted OR, 14.40; 95% CI, 1.23 to 180.87; p=0.03) were associated with a significantly increased risk of PPF. The authors discussed possible mechanisms underlying PPF. The first hypothesis is that PPF is a manifestation of PPCS because one of the seven patients in this study had localized tenderness, although no patient had signs of peritoneal irritation. The second hypothesis is that bacteria translocate from the gut to the bloodstream through a mucosal break during the colonoscopic procedure. However, blood culturing was only performed in three of the seven patients and all cultures were negative. The third hypothesis is that PPF may be caused by an inflammatory mechanism other than infection because a large size polyp is associated with higher levels of proinflammatory cytokines,[13] and some hypertensive patients have increased plasma levels of proinflammatory cytokines such as interleukin-6 and tumor necrosis factor-α.[14,15]

As I read this article, two questions came to mind. First, are PPCS and PPF really different entities? With the exception of the presence of abdominal tenderness, PPCS and PPF are very similar in several respects. Especially, the fact that risk factors such as a large size lesion and hypertension were significant in the development of both entities suggests that they develop by the same mechanism. If so, it is highly probable that PPF is a mild form of PPCS that develops by transmural burn.

Second, are there other factors that lead to the development of PPF except colonoscopic polypectomy itself? Fever after colonoscopy or colonoscopic polypectomy may be associated with bacteremia. Transient bacteremia after colonoscopy, with or without polypectomy, occurs in approximately 4% of procedures, with a range of 0% to 25%.[16,17] However, signs or symptoms of infection are rare. Furthermore, bacteremia may result from contamination of the injection needle catheter during submucosal injection. Because the suction channel is always contaminated by enteric bacteria during colonoscopy, contamination of the injection needle catheter that was passed through the suction channel of the colonoscope is inevitable. Bacteremia can develop if the contaminated needle tip punctures the submucosal blood vessels or penetrates the colon wall. Accordingly, contamination during submucosal injection-assisted polypectomy cannot be avoided by using a disinfected colonoscope, sterile needles, and sterile injection fluid. Bacteremia may also develop due to conditions unrelated to colonoscopy, since the incidence of PPF in this study was relatively high compared with that of PPCS (0.2% vs. 0.003% to 0.1%). These possibilities therefore suggest that numerous factors can be involved in the development of PPF.

In conclusion, PPF is a rare condition with a good prognosis without surgical treatment. Because PPF is similar in symptoms and risk factors to PPCS, it is appropriate to consider that PPF is a mild form of PPCS rather than a new disease entity. However, a large prospective study is required to elucidate this suggestion and the precise mechanism of PPF.

Conflicts of Interest

The author has no financial conflicts of interest.

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