An Unexpected Recurrence After Endoscopic Resection of Low-Risk T1 Colorectal Cancer

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An Unexpected Recurrence After Endoscopic Resection of Low-Risk T1 Colorectal Cancer

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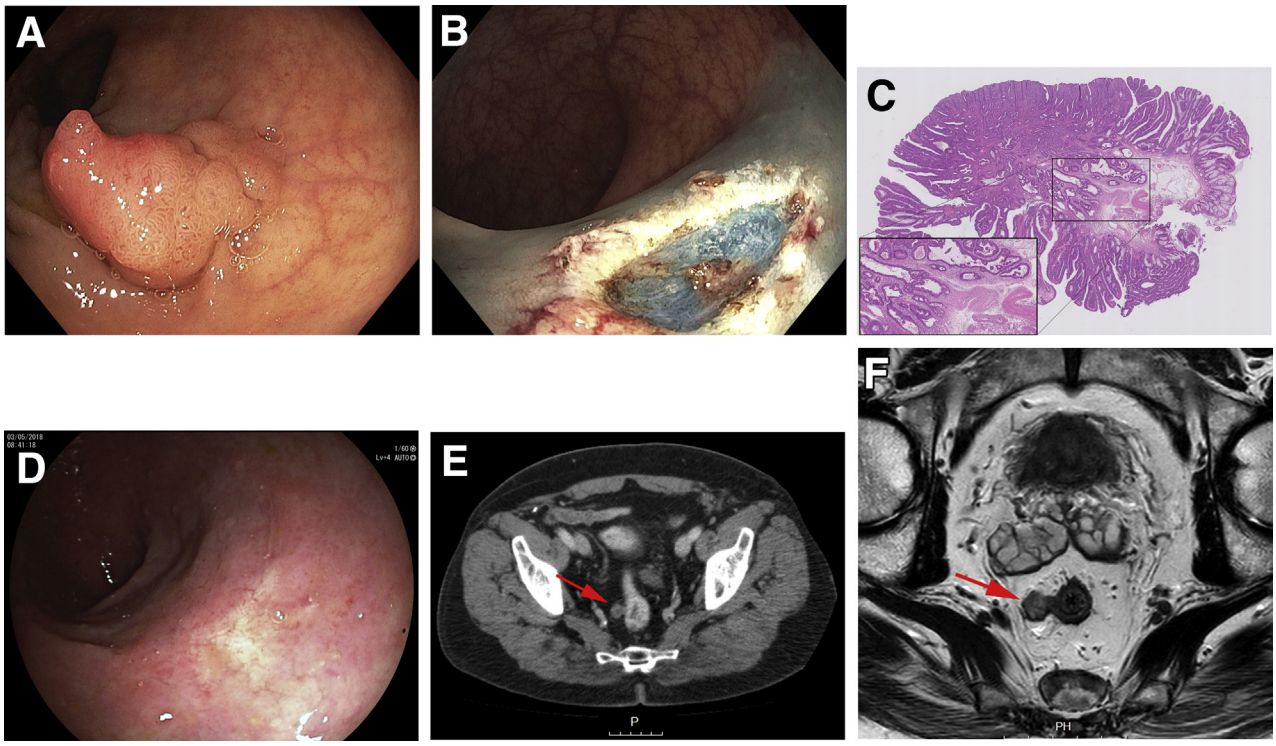

Question: A 71-year-old man was referred to the gastroenterology department for colonoscopy because of a positive fecal immunochemical test as a part of the Dutch Bowel Cancer Screening Programme. His past medical history was uneventful; he had no complaints and his physical examination was unremarkable. During colonoscopy, a 15-mm sessile polyp located in the rectum (Figure *A*) was removed by en bloc endoscopic mucosal resection (EMR). Hemostasis after EMR was obtained with snare tip coagulation (Figure *B*) and the placement of 2 hemoclips. Pathologic examination showed a tubulovillous adenoma, radically resected with a 2-mm margin, containing a 0.3-cm well-differentiated adenocarcinoma that invaded into the submucosa (Figure *C*). Neither lymphangioinvasion nor tumor budding was seen. Owing to the elongated shape of the polyp, an exact invasion depth could not be determined. The Kikuchi level was at first classified as Sm1-2; after reexamination by a second pathologist the Kikuchi level was reported most likely to be Sm1.

Because the polyp was regarded as a low-risk case of T1 colorectal cancer (ie, without high-risk features such as poor differentiation, lymphangioinvasion, deep submucosal invasion (Kikuchi level $\geq$ Sm2), positive resection margins, or tumor budding,[1] a wait-and-see policy with close follow-up was decided together with the patient. During multiple surveillance endoscopies (at 1, 3, 6, 12, and 24 months after en bloc EMR), no abnormalities were seen: in particular, the post-EMR scar repeatedly did not show any signs of local recurrence (see Figure *D* for a photo of the scar taken during the most recent endoscopy). Moreover, multiple scar biopsies showed normal mucosa without any dysplasia. Magnetic resonance imaging at 3 months after EMR showed no abnormalities, and the patient did not experience any complaints during follow-up. The carcinoembryonic antigen level was measured 4 times (at 1 months after EMR, 3.4 ng/L; at 13 months, 4.1 ng/L; at 15 months, 4.1 ng/L; and at 24 months, 5.2 ng/L). Based on the second increase in the carcinoembryonic antigen level, further

imaging of the abdomen was performed. Both computed tomography scanning (Figure *E*) and magnetic resonance imaging (Figure *F*) showed no significant abnormalities, except for a 12-mm convex lesion adjacent to the mid-rectum.

What is your diagnosis?

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Conflicts of interest
The authors have made the following disclosures.

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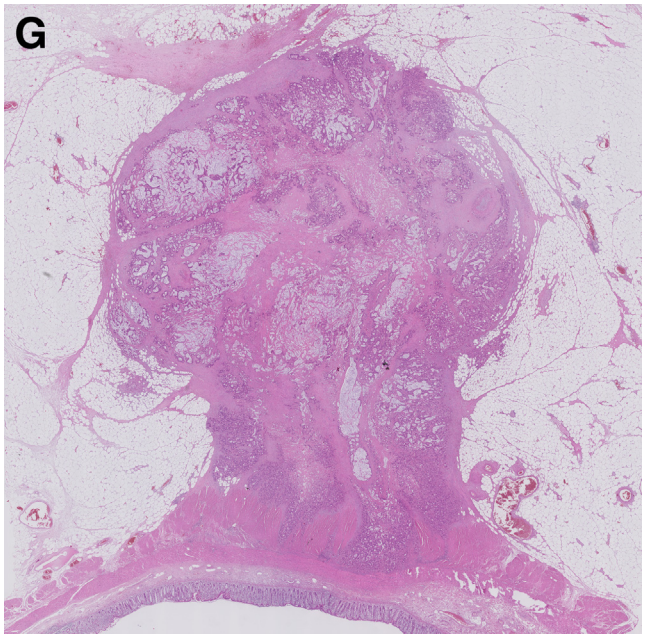
Answer to: Image 1: Locally Recurrent Cancer (pT3N0) after en bloc Endoscopic Mucosal Resection for a Low-Risk T1 Rectum Carcinoma



Initially, the lesion was suspected to be a perirectal lymph node metastasis (cT0N1) of the previously removed T1 rectum carcinoma. Hence, it was decided in the multidisciplinary team meeting to treat this patient with neoadjuvant radiotherapy (5 × 5 Gray) followed by a laparoscopic low-anterior resection. Surprisingly, pathologic examination of the resected specimen showed a 15-mm rectal adenocarcinoma without any evident lymphatic background, extending from the muscularis propria to the perirectal adipose tissue (Figure *G*). The moderately differentiated tumor had not responded to the neoadjuvant radiotherapy. Interestingly, the overlying (sub)mucosal layer showed no dysplasia or other abnormalities, which is consistent with the normal intraluminal appearance of the rectum and earlier biopsies. Thirteen lymph nodes were retrieved; none of these turned out to be positive. Therefore, the tumor was classified as pT3N0.

In the absence of obvious reasons such as tumor budding in the primary tumor or underestimation of the invasion depth owing to tangential cut artefacts, we hypothesize that this unusual form of local recurrence may be explained by the theory of exfoliated cells [2]. Under normal conditions, cell exfoliation from colonic epithelium appears to be a relatively rare event; however, the rate of exfoliation increases with the degree of cell dysplasia and with the amount of mechanical force on the intestinal wall [3]. The theory of exfoliated cells states that cancer cells that escape resection ('exfoliated cells') are subject to perioperative physiological changes and might disseminate and colonize distant organs, thus contributing to postoperative cancer recurrence. Applying this theory to our case, we propose that exfoliated tumor cells were already present at the site of resection, either owing to malignant transformation or mechanical stress on the tumor. During and/or after *en bloc* EMR, some malignant cells may have spread into the deep submucosal tissue or the muscularis propria. Dissemination of these cells may have been facilitated by the damage to the (sub)mucosal microvasculature caused by the *en bloc* EMR, the release of local pro-inflammatory factors or further manipulation of the wound bed. Apparently, these disseminated cells were able to home in the muscular microenvironment and to even further invade the rectal wall, without leaving any traces in the overlying (sub)mucosal layer.

Strikingly, this type of "extra-luminal" recurrence occurred in a patient with a low-risk T1 colorectal carcinoma. In general, extra-luminal surveillance is not part of standard follow-up of low-risk cases because the estimated risk of metachronous lymph node metastasis during follow-up is very low [1]. However, follow-up after endoscopic resection of T1 colorectal cancer is yet quite heterogeneous, because guidelines are often not evidence-based and no expert consensus has been reached on the most optimal frequency and method of surveillance. Currently, our research team is making efforts to determine the most appropriate follow-up scheme, according to the incidence and pattern of cancer recurrence.

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