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CASE REPORT | COLON

Metastatic Cancer of Apparent Colon Origin With No Intraluminal Cancer After Resection of Colorectal Lateral Spreading Lesions

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ABSTRACT

We report a case of metastatic adenocarcinoma to the liver that presented 5 months after piecemeal endoscopic mucosal resection of 3 benign lateral spreading adenomas in the cecum. The pathologic features of the metastatic cancer indicated a probable colonic origin. However, when the cancer was identified, there was no endoscopic evidence of recurrent polyp or another primary lesion in the colon.

INTRODUCTION

Endoscopic mucosal resection (EMR) is the treatment of choice for benign colorectal lateral spreading lesions.[1,2] After completion of piecemeal EMR, lesions may recur, although the use of thermal ablation to the normal-appearing margin of EMR defects has dramatically reduced recurrence.[3] Rarely, follow-up at the EMR site shows cancer development, although pathologic assessment of the tissue obtained at the original resection did not show cancer.[4,5] In 2 large series of follow-up at EMR, the incidence of cancer at the resection site has been 0.17% and 0.25%.[4,5] We describe an even more rare occurrence, development of metastatic cancer to the liver considered to have a likely colon primary after EMR of benign colorectal lesions. There was no evidence of intracolonic cancer by repeat colonoscopy when the patient presented with metastatic cancer.

CASE REPORT

A 53-year-old man presented with intermittent loose stools for 3 years and underwent colonoscopy at an outside center. He had 42 mm, 18 mm, and 15 mm lateral spreading lesions in the cecum (Figure 1). Two months later, the more significant lesion was removed via EMR at our center. Pathology showed tubulovillous adenoma with low-grade dysplasia (Figure 2). Repeat colonoscopy 6 months later showed no recurrence (biopsies of the site were normal), and the other 2 cecal polyps were removed by EMR (both showed tubulovillous adenoma with low-grade dysplasia). Five months later, he developed epigastric discomfort and dysphagia. Ultrasound showed fatty liver, a 3.9 cm subcapsular anterior right lobe mass, and a 2.9 cm exophytic left kidney mass. Computed tomography showed 2 hepatic lesions with thick peripheral enhancing walls. There was no bile duct dilation. There were several 5–7 mm nodules with central cavitation in the lower lung lobes (subsequently shown to be squamous cell carcinoma).

The liver biopsy was positive for metastatic adenocarcinoma, suggesting primary colon cancer: caudal-type homeobox transcription factor 2 (CDX2), cytokeratin (CK) 20 positive, and negative for thyroid transcription factor and CK7 (Figure 1). Carcinoembryonic antigen was elevated at 91.37, and alpha-fetoprotein was normal. Microsatellite status was stable, no BRAF mutation, and KRAS G13D mutation present. Colonoscopy was repeated at our center using ENDOCUFF VISION (Olympus Corporation, Center Valley, PA). Bowel preparation was excellent. There was a 5 mm cecal adenoma. Three postmucosectomy cecal scars showed no endoscopic recurrence, and biopsy of each showed benign colonic mucosa. Esophagogastroduodenoscopy demonstrated a 2-cm hiatal hernia. The patient received 12 cycles of the folinic acid (leucovorin) fluorouracil (5-FU) irinotecan regimen and bevacizumab and then maintenance with capecitabine and bevacizumab. He currently remains in clinical remission. Our pathologists recut the blocks from the

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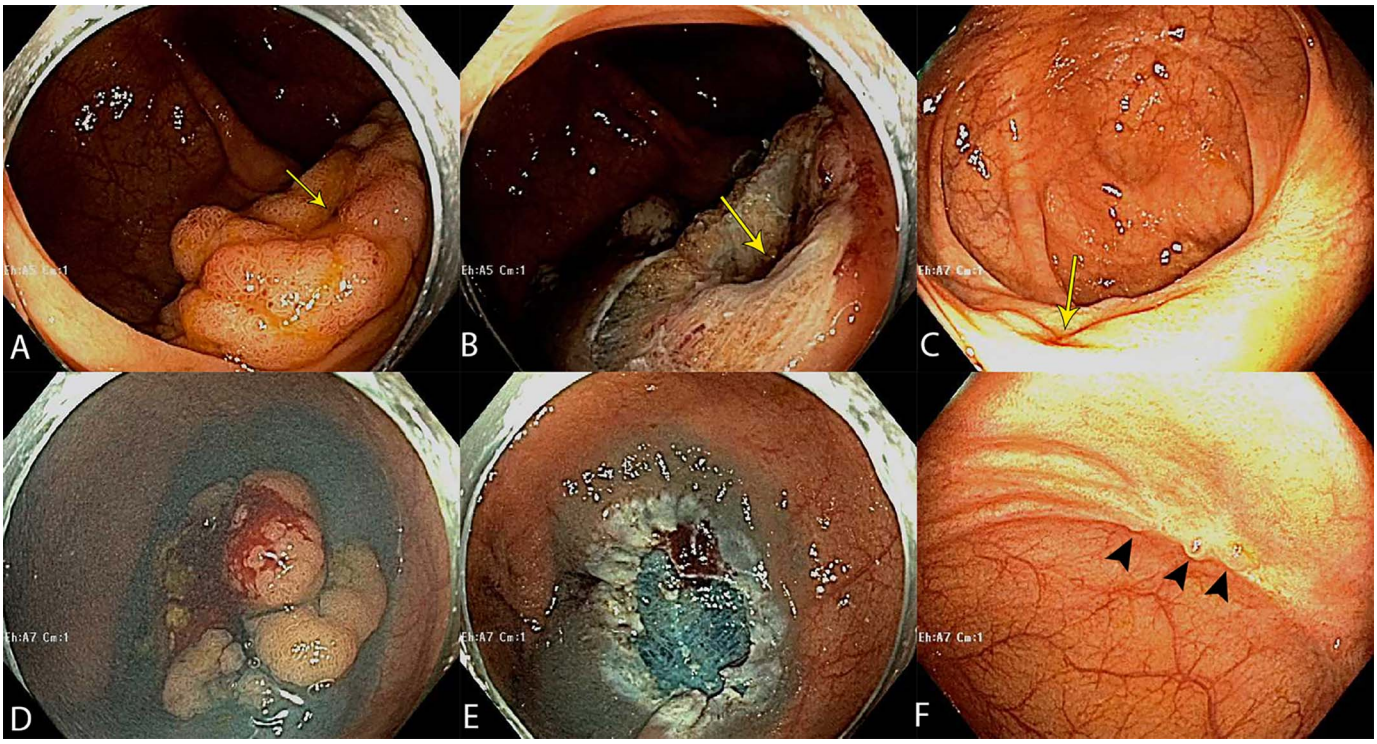

Figure 1. Endoscopic views of 2 resected lesions in the cecum. Yellow arrows point to the opening of ileocecal valve. (A) 45-mm adenoma surrounding the ileocecal valve orifice immediately before resection. (B) Lesion is seen in A after complete resection. (C) Scar at the follow-up of lesion seen in A. (D) 18 mm cecal adenoma after submucosal injection. (E) lesion seen in D immediately after endoscopic mucosal resection and snare tip soft coagulation treatment of the normal margin. (F) Scar at the follow-up of lesion seen in D. There is clip artifact (black arrowheads) but no residual lesion.

original EMRs. Additional sections demonstrated neither cancer nor high-grade dysplasia. Positron emission tomography scans obtained after the cancer diagnosis showed no evidence of cancer in the abdomen or pelvis other than the liver lesions.

DISCUSSION

We describe metastatic adenocarcinoma to the liver after EMR of 3 cecal adenomas negative for cancer and high-grade dysplasia. The pathologic features indicated the metastases were of probable colonic origin. Subsequently, there was no intraluminal evidence of cancer at the resection sites or any other location in the colon. In an experience that now includes 2,556 EMRs of lesions $\geq$ 20 mm, this is the only occurrence of this finding we have encountered. Furthermore, we did not identify reports of this occurrence in the medical literature.[4]

There are several potential explanations. First, although the histologic and molecular analyses favored colonic origin, possibly the tumor originated at another site.[6,7] CDX2 expression is an exquisitely sensitive and highly yet incompletely specific marker of intestinal adenocarcinomas. CDX2 expression can be seen in certain nongastrointestinal adenocarcinomas such as mucinous ovarian carcinomas, mucinous urinary bladder carcinomas, and the mucinous variant of cholangiocarcinoma.[8–12] The rare mucinous intrahepatic cholangiocarcinoma is CK7 positive in 83% of cases and CK20 positive in 17%.[8] A second possible explanation is that there was another primary colon cancer that we did not identify. Patients with large sessile or flat benign colorectal neoplasms have a high prevalence of additional neoplasia in the colon, including a nearly 1% prevalence of cancer in a lesion other than the 1 that the patient was referred for.[13]

However, the patient was examined in detail twice by a colonoscopist who is a known and proven high-level detector, both times with excellent bowel preparation, and the second time using an ENDOCUFF VISION and with full knowledge that the patient had developed metastatic cancer.[14,15] Despite that, no lesion was visible by colonoscopy, and the positron emission tomography scan was negative for the colon. A third possibility is that the pathologist failed to identify cancer in the materials submitted from the piecemeal resection of cecal lesions. Standard methodologies used by pathologists do not section through every millimeter of submitted tissue.[16] However, when blocks were recut, there was still no cancer or high-grade dysplasia identified. A fourth a priori possibility is that we failed to retrieve 1 or more pieces for pathologic assessment at the time of EMR and that those unretrieved pieces contained cancer.

Anecdotally, we systematically and carefully try to obtain all resected tissue during EMR, but we cannot exclude incomplete retrieval. If either the pathologist failed to identify cancer in the specimen or there was incomplete retrieval, the presumed mechanism of this occurrence would be cancer in the lesion

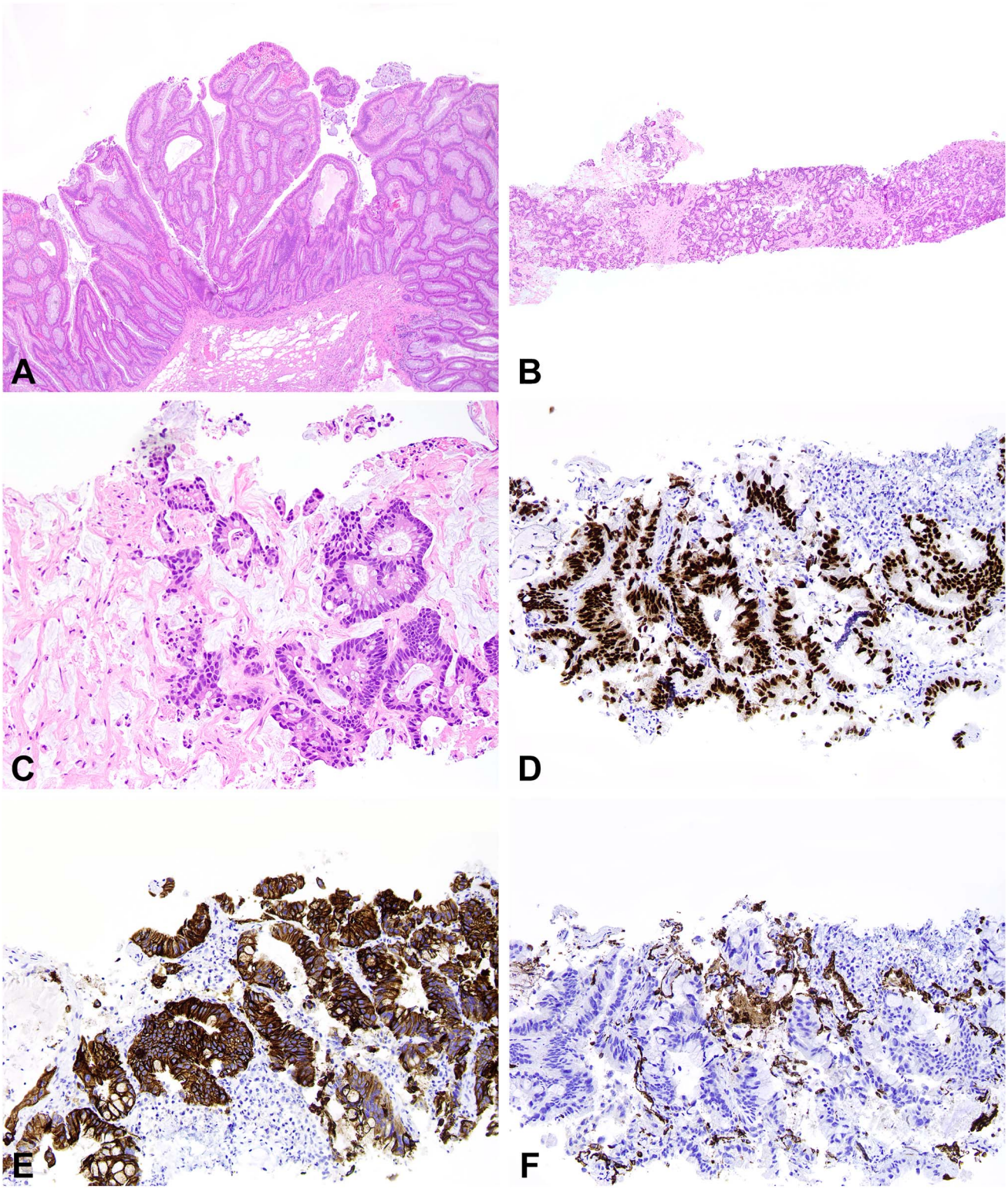

Figure 2. Histopathologic findings in cecal polyp and liver mass. (A) Intermediate-power magnification view showing a tubulovillous adenoma in the cecum (100X magnification). (B) Low-power magnification view showing a moderately differentiated adenocarcinoma infiltrating the liver (40X magnification). (C) High-power magnification view showing the mucinous differentiation of the tumor (400X magnification). (D) High-power magnification view showing that the tumor cells are positive for CDX2 with nuclear pattern (400X magnification). (E) High-power magnification view showing that the tumor cells are positive for CK20 (400X magnification). (F) High-power magnification view showing that the tumor cells are negative for CK7(400X magnification). CDX2, caudal-type homeobox transcription factor 2; CK, cytokeratin

with metastasis to an adjacent lymph node at the time of EMR. EMR would have eradicated all the intraluminal portion of the tumor, but the malignant lymph node was left in place to metastasize. Although the exact mechanism for this occurrence is unclear, our case is a reminder to collect all resected material after completing piecemeal EMR meticulously and that all submitted material should be sectioned for pathologic assessment. In summary, we describe an occurrence of metastatic adenocarcinoma to the liver after EMR of large cecal lesions. Pathologic assessment of the metastases suggested a colonic primary. However, there was no evidence of cancer or high-grade dysplasia in the EMR specimens and no intraluminal evidence of cancer in the colon at the follow-up colonoscopy.

DISCLOSURES

Author contributions: C.J. Lee wrote the manuscript and approved the final manuscript. K.C. Vemulapalli and J. Lin revised the manuscript for intellectual content and approved the final manuscript. D.K. Rex wrote the manuscript, revised the manuscript for intellectual content, approved the final manuscript, and is the article guarantor.

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