ACG CASE REPORTS JOURNAL

IMAGE | SMALL BOWEL

Targeted BRAF Inhibitor Therapy Induces Remission of Unresectable Ampullary Adenocarcinoma

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CASE REPORT

A 66-year-old man with a history of stage 3 colon cancer s/p right hemicolectomy in 2018 and completed 5-fluorouracil and oxaliplatin (FOLFOX) chemotherapy in 2019 was noted to have a rising carcinoembryonic antigen level. An F-fluorodeoxyglucose positron emission tomographic computed tomography revealed marked hypermetabolism in the mid-duodenum, and a magnetic resonance imaging (MRI) of the abdomen revealed an oval mass effect in the second portion of the duodenum in the ampullary region measuring 2 × 2 × 1.5 cm (Figure 1). On esophagogastroduodenoscopy, a large, polypoid, and friable ampullary mass was seen (Figure 2). It occupied half the circumference of the duodenum. Biopsies revealed an infiltrating tumor with vaguely papillary architecture underlying the duodenal mucosa. Immunohistochemical stains showed the tumor cells strongly positive for CK7 (Figure 3).[1] The cells were negative for CK20 and CDX-2. The overall morphologic and immunohistochemical findings were suggestive of a pancreatobiliary origin. The tumor was unlikely to be of a colonic origin. He was referred to surgery but was deemed high risk given his poor functional status, prior surgeries, and significant comorbidities. After discussing with the patient, targeted therapy was considered the best option, and the tissue was sent for multipanel gene testing. It came back positive for v-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600 E mutation, and vemurafenib, a selective inhibitor of his driver mutation, was started. His carcinoembryonic antigen levels normalized. A computed tomography performed 6 months after treatment showed no thickening of the small bowel. An esophagogastroduodenoscopy performed 10 months into the treatment failed to reveal a mass in the duodenum (Figure 4), and biopsies of the ampullary region were negative for malignancy.

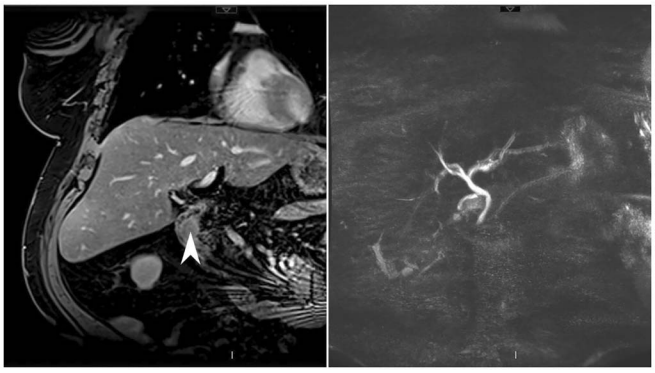

Figure 1. Magnetic resonance imaging of the abdomen showing tumor in the second portion of the duodenum (white arrow) and normal magnetic resonance cholangiopancreatography (MRCP).

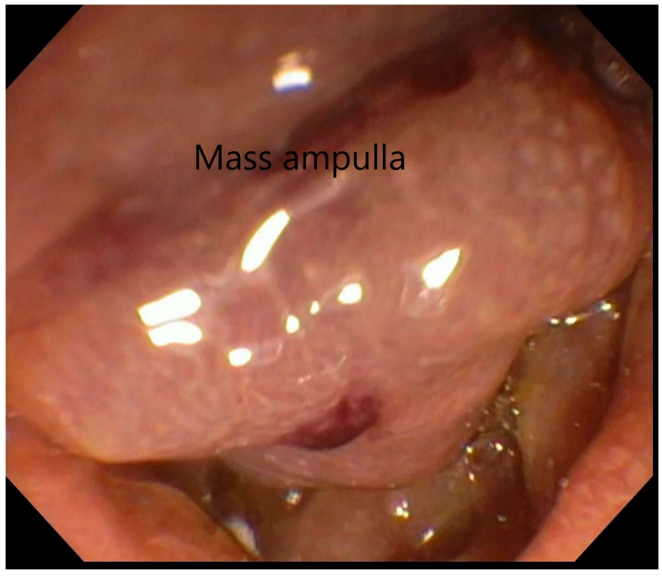

Figure 2. Ampullary mass.

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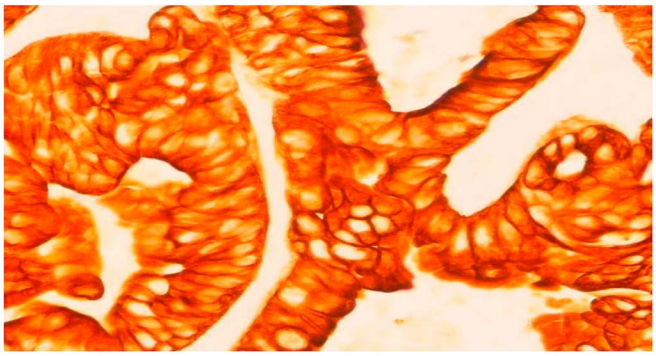

Figure 3. Immunohistochemistry with tumor cells positive for CK7.

The incidence of ampullary carcinoma is less than 1% of all digestive cancers.[2] There are 2 subgroups: intestinal and pancreatobiliary. The intestinal type contains columnar cells with pseudostratified oval nuclei. The pancreatobiliary type contains a single layer of cuboidal cells without pseudostratification. Activation of the RAS-RAF-MAPK pathway is believed to play a role in the development of ampullary carcinomas. BRAF mutations are seen in 0%–10% based on previous studies.[3–5] Of BRAF mutations, V600 accounts for 90%.[5] In colon cancer, vemurafenib monotherapy is ineffective unless coupled with epidermal growth factor receptor (EGFR) inhibition, a combination that may be difficult to tolerate given overlapping skin toxicities. The decision in this case to use BRAF targeting was made with the intent to add a subsequent EGFR inhibitor if needed to minimize toxicity. This case raises the question of altered cellular pathways in ampullary adenocarcinoma where EGFR may not be expressed or possibly a genomic loss of EGFR as in this case.

DISCLOSURES

Author contributions: R. Rego wrote, edited, and reviewed the literature; approved the manuscript; and is the article guarantor. A. Safar advised in the writing of the manuscript.

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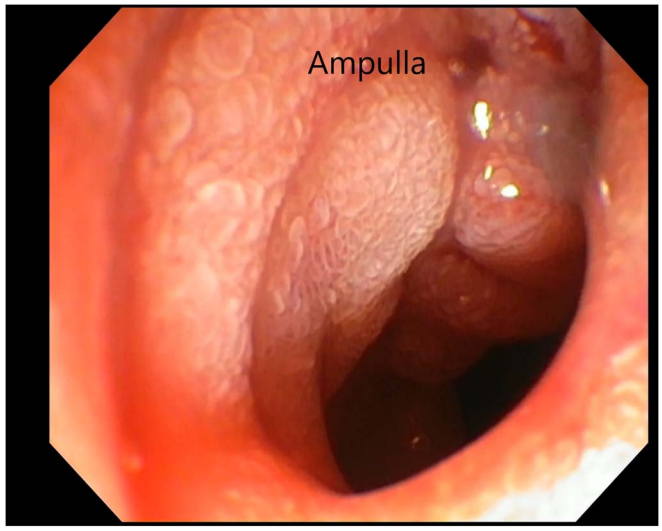

Figure 4. Absence of the ampullary mass on subsequent esophagogastroduodenoscopy.

Informed consent was obtained for this case report.

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