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## CLINICAL VIGNETTE

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# Malignant Common Bile Duct Stricture due to Metastatic Colon Cancer

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### *Introduction*

Colon cancer with metastatic disease to the bile duct is not common but has been described in the literature.<sup>1-3</sup> This is a case study of a patient with colon cancer and subsequent metastatic disease to the bile duct. Immunohistochemistry helped distinguish that the patient had metastatic colon CA to the bile duct rather than colon cancer with a 2<sup>nd</sup> primary tumor to the bile duct.

### *Case Study*

A 54-year-old female was admitted to a community hospital for 3 weeks of diffuse abdominal pain and 8-pound unintentional weight loss.

On physical exam, she is a thin female with a BMI 24.

Vitals showed a blood pressure of 114/71, temperature 98.1, pulse 87, and respiration 17. Her abdomen was soft with good bowel sounds and she had mild lower abdominal tenderness. There was no rebound tenderness. There was no hepatosplenomegaly.

The rest of her physical exam was within normal limits.

She was anemic on admission with Hgb 12.4. Iron studies showed a iron 12, TIBC 297, and saturation of 4%, consistent with iron deficiency anemia. CT scan of the abdomen and pelvis showed a 6.5 cm proximal transverse colon mass with circumferential wall thickening. There was distention of the ascending colon with her distal colon being collapsed. There was extensive periaortic and mesenteric adenopathy. Colonoscopy showed an obstructing proximal transverse colon mass with inability to pass the colonoscope beyond the lesion. She had an exploratory laparotomy with right hemicolectomy with primary anastomosis. The surgical pathology showed poorly differentiated adenocarcinoma. The tumor invaded into the colonic wall and into peri-colonic fat. Twenty out of 31 lymph nodes were positive for metastatic adenocarcinoma. Patient recovered from her surgery and consulted with an oncologist as an outpatient for chemotherapy.

Five weeks later, she was readmitted to the hospital for diffuse abdominal pain and found to have elevated liver tests. Her bilirubin was 3.7 with AST 360, ALT 562, and Alkaline phosphatase 339. Her WBC was 4.4 with Hgb 12.2. Acute hepatitis panel was negative. CT scan of abdomen and pelvis done

showed previous resected right colon, retroperitoneal adenopathy, high density material within the gallbladder. RUQ ultrasound showed hepatomegaly with numerous gallstones within gallbladder. The CBD was dilated to 9 mm.

Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed. It showed a 5.5 cm CBD stricture in the proximal common bile duct. The common bile duct stricture was dilated using a 6 and 8 mm dilating Hurricane balloons. Biliary sphincterotomy was performed and a 10 Fr x 9 cm plastic stent was placed across the common bile duct stricture. Brushings of the common bile duct showed atypical ductal epithelial cells suspicious for adenocarcinoma. Initial immunohistochemistry studies raised the possibility that the origins of the cells may be a primary biliary malignancy. Immunohistochemistry stains showed positive CK-7 and negative CK-20 and negative CDX-2. Typically, biliary duct malignancies are positive for CK-7 and negative for CK-20 and CDX-2, and colorectal cancers, immunostain is negative for CK-7 but positive for CK20 and CDX 2.<sup>4,5</sup> The cytology specimen was sent to tertiary care center for a second opinion. The 2<sup>nd</sup> pathologist noted considerable crush artifact making interpretation difficult. Nevertheless, repeat immunostain revealed CK-7 was positive but immunostain for CK-20 and CDX-2 was equivocal.

Despite the cytology and tenuous immunohistochemistry results, oncology consultants started patient on FOLFOX chemotherapy with Avastin as an outpatient. They presumed she had metastatic colon cancer to her bile duct.

Six weeks after her initial ERCP, patient was readmitted for symptoms of nausea and vomiting with fevers. She was diagnosed with ascending cholangitis with bilirubin elevated to 2.3 and WBC 28.1. She was treated with appropriate antibiotics. Her plastic biliary stent was replaced with a permanent metal stent.

Subsequent Endoscopic ultrasound (EUS) was done at a tertiary care center. EUS was done to try to get more tissue to try to distinguish whether she has colon cancer with metastatic disease to the bile duct or she had colon cancer with a separate 2<sup>nd</sup> primary malignancy of the bile duct. EUS showed an ill-defined 3 cm x 2.5 cm irregular hypoechoic area near the head of pancreas and adjacent to the stent. FNA was done and adequate tissue sample was obtained. The pathology returned as adenocarcinoma. Immunohistochemistry studies showed

CK-7 negative, and CK-20 and CDX-2 positive. These findings indicate that the bile duct tumor is metastatic disease coming from the colon. A confirmatory immunochemical study done was SATB-2. The SATB-2 was positive which further supports bile duct tumor coming from the colon.<sup>6</sup> The positive SATB-2 further refutes the early bile duct cytology immunohistochemistry study results that the bile duct malignancy may be a 2<sup>nd</sup> primary.

## Discussion

Colorectal cancer (CRC) is the second most common cancer death in the United States with 50,000 deaths per year and 140,000 new cases per year.<sup>7</sup> In contrast, cholangiocarcinoma is extremely uncommon, 3000 cases per year.<sup>8</sup>

It is important to rule out metastasis colon cancer to the bile duct as opposed to primary bile duct cancer since treatment and chemotherapy for these diseases are different.

Biliary metastasis from colon cancer is a very rare manifestation of colon CA. It was first described in 1946 by Herbut and Watson.<sup>9</sup> Two different clinical presentations of biliary metastasis has been described, malignant biliary stricture (such as in our case) and the other is a endoluminal lesion.<sup>10,11</sup>

There are two hypotheses to explain the metastatic pattern of CRC, the first is the mechanical/hemodynamic theory and the second is the seed and soil theory.<sup>12</sup> The mechanical/ hemodynamic theory presents anatomic delivery via vascular invasion through lymphatics, blood stream, or implantation of malignant cells through bile.<sup>13</sup>

The seed and soil theory is due to metastasizing tumor cells that find a tissue bed that is congenial for it growth and deposit.<sup>14</sup>

Primary tumors of the bile duct are indistinguishable from metastatic CRC both clinically and when tissue is examined on routine H & E sections. Immunohistochemistry was not widely used until the late 1990s.<sup>5</sup> Typically, CRC is negative for CK-7 but positive for CK-20 and CDX-2. In contrast, bile duct cancer is positive for CK-7 and negative for CK-20 and CDX-2.

Seog-Yun Park, et al evaluated the immunohistochemistry of 314 primary adenocarcinomas with 50 cases each of CRC, gastric, lung, pancreatic, bile duct, breast and 14 cases of ovarian origin.<sup>15</sup> He reported sensitivity of markers individually for CRC as follows: CK-7 positive (14.3%), CK-20 positive (87.8%), and CDX-2 positive 93.9%. However, if you combine the 3 markers as a panel, the specificity is very high, CRC is 97.1% for panel of CK-7 negative/CK-20 positive/CDX-2 positive, and for bile duct cancer is 98% for panel CK-7 positive/CK-20 negative/CDX-2 negative.

An additional immunohistochemistry stain, SATB-2 was obtained from EUS tissue further confirmed the bile duct tissue is coming from CRC metastatic disease. Special AT-rich sequence-binding protein 2 (SATB-2) are DNA binding pro-

teins that are nuclear matrix-associated proteins involved in chromatin remodeling and regulation of gene expression. Magnusson K, et al analyzed the tissue expression of SATB-2 from 9 independent cohorts of 1882 specimens with primary and metastatic CRC.<sup>6</sup> In this study, SATB-2 protein was found in cancer cells in 85% of all primary CRC and 81% of all CRC metastases. When SATB-2 positive is combined with CK-20 positive, the sensitivity of these 2 combined test identifies 95% of all colorectal cancer. In our case, the EUS FNA specimen was SATB-2 positive and CK-20 positive confirming that she had metastatic colon cancer to the bile duct.

In summary, colon cancer with metastatic disease to the bile duct is rare. Immunohistochemistry marker studies were invaluable in our case to confirm she had colon cancer that was metastatic to the bile duct.

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