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Visual Diagnosis Pearl

Metastatic Colorectal Cancer in the Setting of Uncontrolled Hypercholesterolemia

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CASE PRESENTATION

A 34-year-old woman with no past medical history presented to cardiology clinic for recurrent syncope. Despite losing 70-lbs in the past year from diet and exercise, the patient began to experience intermittent shortness of breath with substernal chest pressure and syncope with exertion in the past few months. She denied alcohol, smoking, or recreational drugs.

On presentation, BP was 166/121 mmHg, pulse 92 bpm, and oxygen saturation 98%. Cardiovascular examination revealed a grade II/VI systolic ejection murmur with clear lung fields. An electrocardiogram demonstrated normal sinus rhythm. Laboratory testing showed normal complete blood count, creatinine, TSH, total bilirubin, and albumin. Complete metabolic panel was notable for hypokalemia (3.4 mEq/L); and elevated ALT (40 U/L), AST (114 U/L), and alkaline phosphatase (222 U/L). Lipid panel demonstrated marked hypercholesterolemia with total cholesterol 416 mg/dL, LDL 354 mg/dL, low HDL 27 mg/dL, and triglycerides 141 mg/dL. Transthoracic echocardiogram and exercise stress testing revealed normal ejection fraction and excellent functional capacity without ischemic changes. Ambulatory cardiac monitoring did not show any arrhythmia.

Secondary hypertension workup including renin, aldosterone, cortisol, and metanephrines was unrevealing. Renal artery ultrasound incidentally showed large calcified hepatic masses and a pancreatic body lesion. CT abdomen/pelvis confirmed extensive live metastases, retroperitoneal lymphadenopathy and a partially calcified mass invading the descending colon; CT chest revealed a left breast mass and supraclavicular lymphadenopathy. Liver biopsy confirmed metastatic colorectal adenocarcinoma, and outpatient FOLFOX chemotherapy was initiated.

DISCUSSION

Colorectal cancer (CRC) is the third leading cause of death in the United States.¹ Even though the incidence and mortality of CRC have declined in adults aged 65 years and older, the incidence of CRC in adults under 55 years old has increased by 2% annually in the past 30 years.² The American Cancer Society (ACS) reported that 20% of CRC cases were discovered in adults who were 54 years old and younger in 2019 compared to 11% in 1995.² Furthermore,

younger people are more likely to be diagnosed with more advanced disease.² CRC is now the leading and second leading cause of cancer deaths in men and in women under the age of 50, respectively.³ The U.S. Preventative Service Task Force (USPSTF) lowered the age of screening for colorectal cancer to the age of 45 in 2021.

The biggest risk factor for colorectal cancer is family history, having an affected first-degree relative increases the risk 2-4 fold.² However, more than half of the CRC cases in the United States are related to lifestyle, such as heavy alcohol, smoking, sedentary lifestyle, obesity, and a diet of processed, low-fiber, and high-fat foods.²

The most common site of metastasis for CRC is the liver. Notably, metastasis to the liver can be associated with cholesterol dysregulation. One study showed that metastatic CRC cells in the liver activate the cholesterol biosynthesis pathway, which increases cholesterol production in the tumor tissue.³ Higher LDL-c was associated with earlier disease progression and more aggressive metastatic types of colorectal cancer.⁴ A clinical study suggests that statin therapy with chemotherapy can be associated with improved overall survival in patients with metastatic CRC.⁵

In conclusion, CRC is one of the leading causes of cancer deaths amongst adults who are younger than 50 years old. Increased LDL-C is associated with more aggressive forms of metastatic CRC with worse outcomes. More research is needed to elucidate this relationship between cholesterol metabolism and metastatic CRC as a potential therapeutic target.

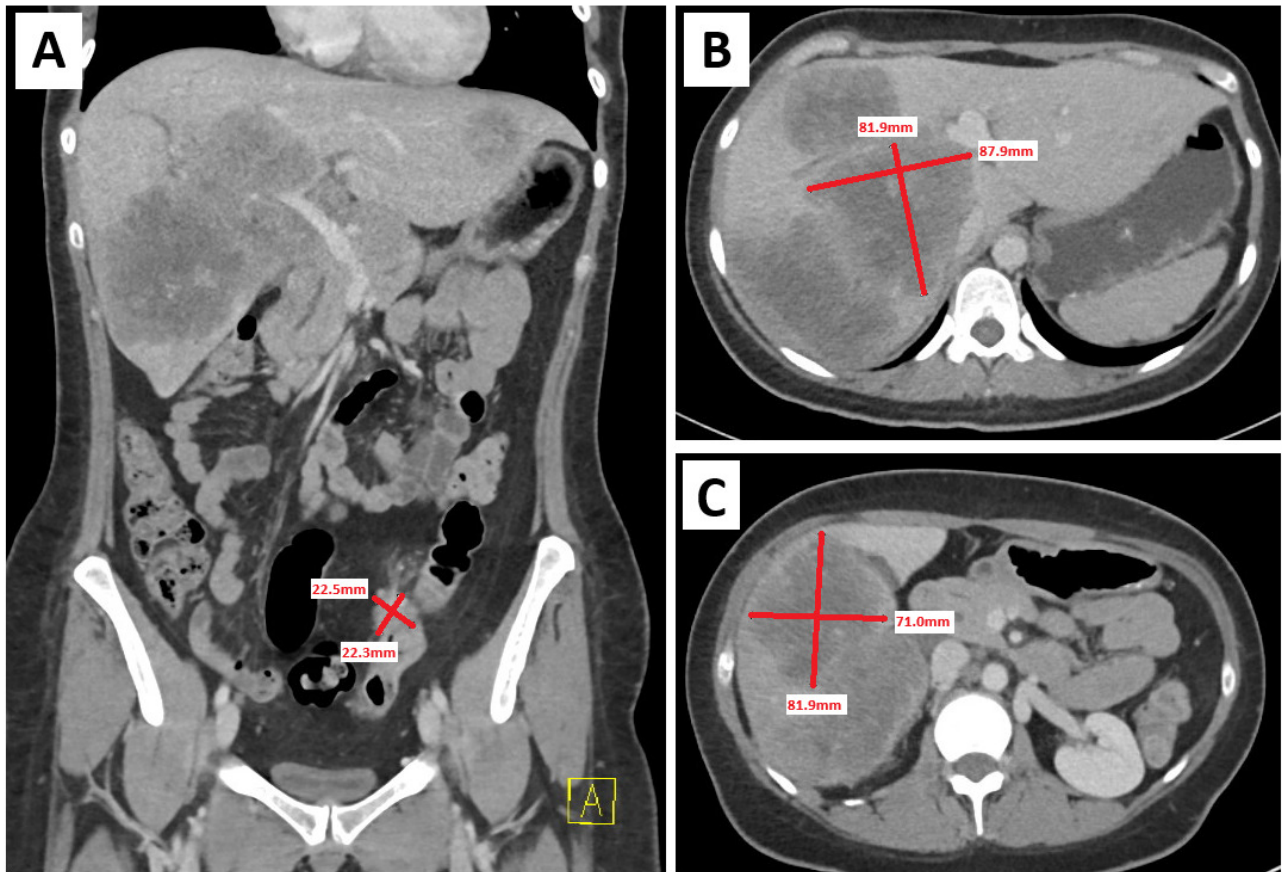


Figure 1. A. Partially calcified mass in the descending colon. B, C. Large metastatic lesions in the liver.



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