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Rapidly growing colon adenocarcinoma and its differential

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Among cancers in the United States, colorectal cancer is the third most commonly diagnosed, and the second leading cause of death. Most colon cancers are thought to develop from adenomatous polyps through the adenoma-carcinoma sequence, which emphasizes the importance of screening colonoscopies for early detection and obliteration of precancerous polyps. As the adenoma-carcinoma sequence is estimated to take 10-15 years to occur, current guidelines recommend screening colonoscopies every 10 years, beginning at the age of 50, for average-risk individuals. For those that have adhered to screening guidelines and experienced a consistently negative detection of polyps, screening is no longer recommended after the age of 75 and recommended against after the age of 85. Currently, there are no guidelines on the management of patients with inadequate bowel preparation for colonoscopy, which has been associated with a significant adenoma miss rate. This report illustrates the management of a high-grade invasive adenocarcinoma of the right colon that was identified in an 88-year-old patient who had received a colonoscopy 7 years earlier with no evidence of polyp growth. This was either an unusual case of rapid growth or an unfortunate case of a previously missed adenoma (carcinoma). It invites an evaluation of the current guidelines and their implications.

Case presentation and physical findings

An 88-year-old female presented to the emergency department with severe epigastric pain, nausea, and vomiting. She reported having had periods of intermittent epigastric pain over the past few months, but not to the extent she had experienced that day. An abdominal computed tomography scan without contrast was performed, and it identified a possible obstructive mass in the right colon (Figure 1). She was subsequently admitted.

Her medical history was significant for chronic kidney disease, dementia, and atrial fibrillation, for which she was taking warfarin. Her surgical history was significant for total abdominal hysterectomy and bilateral salpingo-oophorectomy, appendectomy, and cholecystectomy. The patient's last colonoscopy was done 7 years earlier and was significant only for diverticulosis.

Following her admittance, it was noted that her stools were tarry black in appearance, and a mass-like effect was identified on palpation of the right hypochondrium of the abdomen. The physical examination was otherwise unremarkable. Her vital signs were normal. Plain radiographs of the chest and abdomen were also unremarkable. Laboratory studies showed decreased hemoglobin level and hematocrit of 8.2 and 28.4, respectively, with microcytic indices. Biochemical studies showed elevated levels of blood urea nitrogen and creatinine of 30 and 1.5, respectively. Her coagulation profile showed the current level of administration of warfarin to be therapeutic with an international normalized ratio of 2.9.

An upper and a lower endoscopy were performed to evaluate the patient's anemia and gastrointestinal symptoms. The upper endoscopy showed no pathology. The lower

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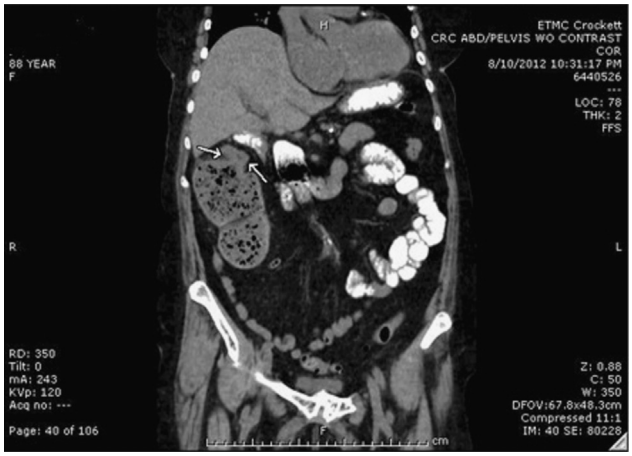

Figure 1 Computed tomography scan showing obstructive lesion in right upper abdominal quadrant (arrows).

endoscopy showed sigmoid diverticulosis and an infiltrating, ulcerative mass lesion obstructing any further passage of the colonoscope at the level of the ascending colon. The lesion encompassed the circumference of the bowel lumen and was highly vascularized. Biopsies were taken and the colonoscope was then withdrawn.

A right hemicolectomy was planned to excise the lesion and prevent any further bleeding or impending obstruction. The patient was given time for bowel preparation, international normalized ratio and laboratory values to be brought to nominal value, and anemia correction before the operation.

On the day of the operation, a 1-stage procedure of colectomy and anastomosis was performed. The tumor was identified at the hepatic flexure and resected with adequate margins. After the procedure, the patient was taken to the intensive care unit in a satisfactory condition.

Laboratory and imaging reports

Figure 1 shows computed tomography scan showing obstructive lesion in right upper abdominal quadrant (arrows).

Pathology

On gross examination, the specimen consisted of a portion of ileum measuring 2.5 cm in length and 3 cm in diameter attached to a portion of colon including the cecum measuring 15 cm in length and ranging from 3.8-5 cm in diameter. The appendix was present despite the patient's reported appendectomy, measuring at 4 cm in length and 0.9 cm in diameter, and contained fibrovascular adhesions. The bowel was opened to reveal an ulcerated circumferential mass measuring 4 × 2.5 × 1.4 cm located 3.5 cm from the distal resection margin. The tumor extended through the bowel wall. The surrounding bowel showed 2 0.5-cm polyps distal to the tumor.

On microscopic examination, the specimen showed moderately to poorly differentiated adenocarcinoma. It extended through the muscular wall and into the surrounding adipose tissue. The tumor was composed of irregular glandular structures lined by cells with very pleomorphic nuclei and increased mitotic figures. Tumor was seen within the lymphovascular spaces. The tumor was not seen extending to the proximal, distal, or radial margins. Eleven lymph nodes were examined, and 1 was positive for metastatic adenocarcinoma.

Discussion

An introduction to colorectal cancer burden and its treatment

In the United States, among cancers, colorectal cancer is the third most commonly diagnosed and the second leading cause of death. The American Cancer Society estimates that in 2012 over 143,000 Americans would be diagnosed, and 51,960 people would die of the disease.[1] It is most commonly diagnosed in the sixth and seventh decades of life, and is influenced by dietary, hereditary, and environmental factors.[2] Most colon cancers are thought to develop from adenomatous polyps through the adenoma-carcinoma sequence, which emphasizes the importance of screening colonoscopies for early detection and obliteration of precancerous polyps.[3] The current United States Preventive Services Task Force (USPSTF) guidelines for average-risk patients recommend screening colonoscopies every 10 years from the age of 50, with more frequent colonoscopies (at intervals of 2 months to 5 years, depending on the type and number of polyps) for those who have a history of polyp detection on previous screening colonoscopy.[4] Acceptable screening alternatives to colonoscopy include fecal occult blood test (FOBT) every year or flexible sigmoidoscopy every 5 years with FOBT every 3 years. Barium enema is no longer considered an acceptable screening alternative because of its inferior sensitivity and decreasing use rates for this purpose, which have precluded screening trials of its efficacy.[5] For patients who have adhered to screening guidelines and experienced a consistently negative detection of polyps, screening is no longer recommended after the age of 75. Furthermore, screening is recommended against after the age of 85 for patients who fit this profile.[5]

Those who have a family history of colorectal cancer before the age of 60 should undergo an initial screening 10 years prior to the principal case and subsequent screening at an interval of 5 years.[4] Those with inflammatory bowel disease are also at increased risk and are advised to begin screening 8 years after diagnosis and continue every 1-3 years.[6] Approximately 5%-10% of colon cancers occur in the context of genetic predisposition, most commonly following from familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer syndrome.[7] Patients with familial adenomatous polyposis should initiate screening by colonoscopy at the age of 10-12, with eventual prophylactic colectomy. Patients with hereditary nonpolyposis colorectal cancer syndrome syndrome should initiate

screening by colonoscopy at the age of 20-25 and continue screening at 1-2-year intervals.[4]

The primary treatment for colon cancer is surgical resection. A margin of at least 5 cm is removed on either side of the tumor, along with the lymphatics draining the involved segment.[8] The goals of colectomy are both curative and palliative. Resection of the diseased segment of bowel removes a site that is vulnerable to inflammation, infection, and metastatic disease. Palliative effects include the removal of a bowel obstruction, which presents with the inability to pass feces or flatus, melena, nausea, vomiting, and abdominal distention.

Postoperative complications include bleeding, ileus, infection at the surgical site, and cancer recurrence. Adjuvant chemotherapy after colon cancer resection is indicated for patients with nodal disease or local invasion.

The significance of colorectal cancer screening

Colorectal cancer screening by way of colonoscopy is unique in its ability to capitalize on the most common cause of cancer development in the colon, the adenoma-carcinoma sequence. It has the potential to prevent the adenoma-carcinoma sequence from progressing to completion with the obliteration of polyps that may be cancerous precursors. An estimated 50% reduction in mortality is attributed to the adherence of screening colonoscopy guidelines.[9] The significance of screening colonoscopies in preventing overall mortality in the United States is more than that of wearing a seat belt while riding in a motor vehicle.[9,10]

An evaluation of colorectal cancer screening guidelines and considerations

The American College of Physicians recommends colorectal cancer screening in the form of annual high-sensitivity FOBT, sigmoidoscopy every 5 years with FOBT every 3 years, or colonoscopy every 10 years for average-risk patients over the age of 50, and for high-risk patients (ie, family history or inflammatory bowel disease) over the age of 40. Furthermore, they recommend that clinicians stop screening for colorectal cancer in patients over the age of 75 or with a life expectancy of less than 10 years.[11] The USPSTF, from which the American College of Physicians guidelines are in keeping with, asserts that the adenoma-carcinoma sequence takes place over a period of 10-15 years, and follows with the guideline for colorectal cancer screening to be conducted at 10-year intervals.[5]

This case poses an exception to this growth hypothesis, as our 88-year-old patient had undergone a screening colonoscopy 7 years prior to her diagnosis, and it showed no indication of polyp growth. The patient was diagnosed with diverticular disease at the time of previous colonoscopy, but this has not been shown to increase the risk of colon cancer in the long term or affect colon cancer mortality.[12] This case suggests that severe dysplastic growth can occur in less than 10 years. However, recent studies[13] suggest that this patient's progression was a rare exception to the rule, rather than an indication that screening guidelines need to be reevaluated. There is currently no evidence to suggest that more frequent screening measures reduce cancer-related deaths or improve patient outcomes on a population-wide scale. Furthermore, there are significant risks associated with screening colonoscopies, especially in older patients, including bowel perforation and major hemorrhage. A study conducted in 2011 by Goodwin et al. found that colonoscopies were being overused in geriatric patients, with screenings at less than 10-year intervals and in those over the age of 80, with no significance in improved patient outcomes.[13] It is also a procedure for which healthcare costs must be managed responsibly. Therefore, although increasing screening colonoscopy frequency and duration could potentiate a slight reduction in mortality and possibly even the incidence of colorectal cancer, the most recent evidence suggests that this benefit would not be significant enough to outweigh the risks and costs.

A "middle-ground" modality might be found in annual high-sensitivity guaiac or immunochemical FOBT, which could be used as an initial noninvasive screening alternative for patients over the age of 75. Although this screening measure does not have the benefit of simultaneously obtaining a tissue sample or obliterating polyps (as with colonoscopy), it has a low-risk profile, is inexpensive, and can be highly sensitive and specific in the detection of colorectal cancer.

Guaiac tests detect trace blood by capitalizing on the peroxidase-like effect of heme using absorbent paper, which changes color in the presence of hydrogen peroxide. They are inexpensive (costing around $5) and ideal for home or office use; however, patients must be cautioned that certain foods (red meat, radishes, and grapefruit) and medications (nonsteroidal anti-inflammatory drugs and excess vitamin C) can produce false-positive results. Immunochemical tests use antibodies against globin to detect occult bleeds. These cost around $20 and are ideal for the office or inpatient setting. A systematic review of 59 studies on FOBT efficacy reported Haemoccult Sensa to be the most sensitive guaiac test (62%-78.6%) and Immudia HemSp to be the most sensitive immunochemical test (43.3%-97.7%) with regard to colorectal cancer detection. In measures of diagnostic accuracy, specificity was greater than 79% for all guaiac tests and greater than 88% for all immunochemical tests.[14]

A newer modality, stool DNA tests, function to identify dysplastic changes in the cells lining the colon. A study conducted in 2009 found the sensitivity in detection of cancer to be 87%-91% (specificity 85%-96%).[15] The cost ranges from $350-$850 and is not covered by Medicare. As a gold standard clinical trial is yet to be performed comparing FOBT and stool DNA tests, the USPSTF does not advise the use of stool DNA tests for the screening of average-risk patients.[5]

Therefore, FOBT could serve as a valuable precursor study for older individuals, particularly in those with cognitive

impairments who would be less able to communicate the experience of symptoms indicative of colorectal cancer. However, in keeping with the USPSTF recommendations, on a population-wide scale, a patient is more likely to die from another cause when colorectal cancer occurs after the age of 75.[5] With the availability of multiple screening modalities, each having its own costs and benefits, each patient must be managed individually, with concerns for comorbidities, life expectancy, and palliative care. To actualize the intent to "first do no harm" it is essential that the modern-day physician balances screening recommendations with clinical judgment.

The differential for rapid growth: Inadequate bowel preparation

An alternative explanation for this seemingly rapid growth is inadequate bowel preparation for the colonoscopy that was conducted 7 years earlier. Bowel preparation allows for visualization of the colon during colonoscopy. One common regimen includes 2 days of clear liquids and the consumption of 4 L of polyethylene glycol (PEG) electrolyte lavage solution, beginning on the eve of the colonoscopy. An estimated 5%-15% of individuals do not complete this preparation because of its large volume and disagreeable taste.[16] Alternatives to the PEG regimen have been shown to be equally effective, and include sulfate-free electrolyte lavage, low-volume electrolyte lavage with bisacodyl or magnesium citrate, and sodium phosphate regimens (Table 1). Pulse irrigation can be employed to improve visualization during the procedure, and a barium enema can be used as an alternative method to visualize the distal colon afterwards.[16]

Although patient motivation is essential for proper preparation, a recent study found that over 80% of patients with inadequate preparation claimed adherence to the preparation instructions.[16] Factors that have been associated with poor preparations include a later colonoscopy starting time, inpatient status, delayed colon transit times, tricyclic antidepressant use, and a history of stroke or dementia. The incidence of polyp identification with adequate preparation in the average-risk individual is around 33%.[18] With inadequate preparation, the incidence drops to 22%-25%.[18,19] It is possible, with this patient's comorbidities and concurrent dementia, that the preparation was inadequate 7 years ago.

There are currently no formal guidelines that address inadequate bowel preparation. If no adenomas were identified, many physicians opt to schedule the next colonoscopy at an interval of less than 10 years.[18] The American Society of

Table 1 Comparison of commonly used bowel preparations[16,17]

	Dosing volume	Comparability to PEG regimen	Considerations
PEG electrolyte lavage solution (Colyte, GoLYTELY,)	4 L; can be divided into 3 L the evening before and 1 L the morning of procedure	Standard of comparison; 5%-15% do not complete due to intolerance (poor palatability, large volume)	Relatively safe for patients with electrolyte imbalances and vulnerabilities to fluid overload (renal failure, congestive heart failure, liver disease with ascites)
Sulfate-free PEG (NuLYTELY, TriLyte)	4 L; can be divided into 3 L the evening before and 1 L the morning of the procedure	Comparable in safety, effectiveness, and tolerance	Improved palatability; equal volume
Low-volume PEG/PEG-3350 with bisacodyl delayed-release tablets (Halflytely)	2 L; 8 oz every 10 min, beginning 6 h after ingestion of 4 bisacodyl tablets	Equal efficacy, improved tolerance	Magnesium citrate may be used as an alternative to bisacodyl
Low-volume PEG-3350 without electrolytes with bisacodyl relayed-release tablets (Miralax)	2 L; 8 oz every 10 mins, beginning 6 h after ingestion of 4 bisacodyl tablets	Equal efficacy, improved tolerance	
Aqueous NaP (Fleet)	48 oz; given in 2 doses of 8 oz oral solution followed by 16 oz of liquid, taken at least 10 h apart	More or equally effective, better tolerated	Significant fluid and electrolyte shifts can occur; risk of phosphate nephropathy in patients taking ACE inhibitor or ARB; consider additional carbohydrate electrolyte rehydration solution to prevent excess volume retraction
Tablet NaP (Visicol)	32-40 tablets, taken as 4 tablets at a time with 8 oz of water	Equal efficacy, fewer side effects, improved palatability, better tolerated	Bisacodyl can be used as an adjunct

PEG: polyethylene glycol; NaP: sodium phosphate; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker.

Colon and Rectal Surgeons recommend ascertaining from the patient if the preparation protocol was followed, and modifying the preparation as needed for the next procedure. Augmenting the preparation can be done by prolonging the standard 2-day interval for clear liquids, alternating or combining preparation solutions (PEG or sodium sulfate or both), doubling the amount of PEG, or adding additional purgative agents (magnesium citrate, bisacodyl, or senna) to the standard preparation.[18]

The need to repeat a colonoscopy and its preparation is an understandable inconvenience as it prolongs patient discomfort and creates a financial burden. However, the inability to conduct an adequate colonoscopy precludes the benefits of its employment, and the absence of a standard guideline for inadequate preparation may leave many patients vulnerable to progression of the adenoma-carcinoma sequence. The importance of patient-physician communication becomes ever more essential in managing this situation, with collaborative informed consent for the time frame between repeat procedures and modifications in the preparation protocol.

Patient course

The patient was transferred to the hospital floor from the intensive care unit 2 days later to complete the postoperative recovery process. She was discharged to a nursing home with an oncology referral.

References

1. American Cancer Society. "Colorectal Cancer Facts and Figures 2011-2013." 〈http://www.cancer.org/Research/CancerFactsFigures/ColorectalCancerFactsFigures/colorectal-cancer-facts-figures-2011-2013-page〉. Accessed August 10, 2012.
2. Levine JS, Ahnen DJ. Clinical practice. Adenomatous polyps of the colon. *N Engl J Med*. 2006;355(24):2551–2557
3. Bond JH. Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps. Practice Parameters Committee of the American College of Gastroenterology. *Am J Gastroenterol*. 2000; 95(11):3053–3063
4. Levin B, Lieberman D, McFarland B, et al: Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology*. 2008;134(5):1570–1595
5. U.S. Preventive Services Task Force. Screening for colorectal cancer: USPSTF recommendation statement. *Ann Intern Med*. 2008;149(9): 627–637.
6. Leighton JA, Shen B, Baron TH, et al: ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease. *Gastrointest Endosc*. 2006;63(4):558
7. Labianca R, Nordlinger B, Beretta GD, et al: Primary colon cancer: ESMO clinical practice guidelines for diagnosis, adjuvant treatment and follow-up. *Ann Oncol*. 2010;21(5):70–77
8. Hewett PJ, Allardyce RA, Bagshaw PF, et al: Short-term outcomes of the Australasian randomized clinical study comparing laparoscopic and conventional open surgical treatments for colon cancer: the ALCCaS trial. *Ann Surg*. 2008;248:728–738
9. Division of Cancer Prevention and Control (DCPC), United States. Centers for Disease Control and Prevention. Vital signs: colorectal cancer. 〈http://www.cdc.gov/vitalsigns/cancerscreening/〉; 2011.
10. Office of Surveillance, Epidemiology and Laboratory Services (OSELS), United States. Centers for Disease Control and Prevention. Vital signs: adult seat belt use in the US. 〈http://www.cdc.gov/vitalsigns/SeatBeltUse/LatestFindings.html〉; 2011.
11. Qaseem A, Denberg TD, Hopkins RH Jr, et al: Screening for colorectal cancer: a guidance statement from the American College of Physicians. *Ann Intern Med*. 2012;156(5):378–386
12. Granlund J. Diverticular disease and the risk of colon cancer–a population based case-control study. *Aliment Pharmacol Ther*. 2011; 34(6):675–681
13. Goodwin JS, Singh A, Reddy N, et al: Overuse of screening colonoscopy in the Medicare population. *Arch Intern Med*. 2011;17(11): 335–343
14. Burch JA, Soares-Weiser K, St John DJ, et al: Diagnostic accuracy of faecal occult blood tests used in screening for colorectal cancer: a systematic review. *J Med Screen*. 2007:14132–14137
15. Ahlquist D. Next-generation stool DNA testing: expanding the scope. *Gastroenterology*. 2009;136(7):2068–2073
16. Wexner SD, Beck DE, Baron TH, et al: A consensus document on bowel preparation before colonoscopy: prepared by a task force from American Society of Colon and Rectal Surgeons, American Society for Gastrointestinal Endoscopy, and Society of American Gastrointestinal and Endoscopic Surgeons. *Gastrointest Endosc*. 2006;63(7):894–909
17. Lichtenstein G. Bowel preparations for colonoscopy: a review. *Am J Health Syst Pharm*. 2009;66(1):27–37
18. Chokshi R, Hovis C. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. *Gastrointest Endosc*. 2012;75:1197–1203
19. van Rijn JC, Reitsma JB, Stoker J, et al: Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am J Gastroenterol*. 2006; 101:343–350