False-Negative Endoscopic Biopsy of Colonic Adenocarcinoma in a Young Man

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A 26-year-old man presented with intermittent bright red blood per rectum. His physical examination was unremarkable; however, because microcytic anemia was noted, the patient underwent colonoscopy. A large ascending colonic lesion was noted, a biopsy of which was negative for cancer. Nevertheless, the patient underwent a radical hemicolectomy. Adenocarcinoma of the cecum was found. This case report is an example of a false-negative endoscopic-directed biopsy. A review of recorded video-endoscopy assisted the family physician in appropriate management.

KEY WORDS: Sigmoidoscopy; flexible sigmoidoscopy; biopsy; biopsy, false negative; colonoscopy; colorectal neoplasms. *(J Fam Pract 1996; 43:178-180)*

Since 1989, physicians performing flexible sigmoidoscopy in our family practice center have had both the equipment and the faculty support to convert a flexible sigmoidoscopy to a full colonoscopy contingent on endoscopic findings or new history, or both, encountered on the day of the examination. An extension to full colonoscopy in these circumstances has reduced the need for an additional appointment with a radiologist or gastroenterologist. This strategy has improved access for patients and reduced costs.

Minimal bright red blood per rectum is most commonly caused by perianal disease. The differential diagnosis, however, includes diverticulosis, angiodysplasia, carcinoma, ischemic colitis, and others.[1] Risk factors for colonic carcinoma include age greater than 50 years, inflammatory bowel disease, familial polyposis coli, family history, and personal history of colonic neoplasia.[2] Unexplained gastrointestinal symptoms of more than 2 weeks' duration also are associated with increased risk.

Perianal disease rarely produces anemia. Therefore, even in a low-risk patient, anemia from lower gastrointestinal bleeding requires further workup. Colonoscopy has many benefits in the evaluation of rectal bleeding,[3] and videocolonoscopy allows the family physician to subsequently share positive findings with a consultant.[4,5]

Flexible sigmoidoscopy and double-contrast barium enema are considered by some to be the diagnostic tools of choice for patients who present with rectal bleeding but are at low risk for neoplasm.[3] Colonoscopy, however, is the diagnostic study of choice for all patients who are classified as being at above-average risk for colorectal cancer.[6-9] Risk factors in the case described here included a combination of rectal bleeding and unexplained anemia. While flexible sigmoidoscopy has been recommended for screening in asymptomatic patients, "case finding" is defined by the investigation of signs and symptoms. Symptomatic patients at above-average risk require more extensive investigation than can be accomplished with flexible sigmoidoscopy.[10,11]

Case Report

A 26-year-old man presented to a family practice center complaining of intermittently bright red blood in his stool for more than 1 year. The patient noted that the frequency of bleeding had increased to once weekly during the previous month. He denied pain on defecation or blood on toilet tissue. The patient reported that his usual health was good, and he had no significant past medical history. The patient was a nonsmoker, occasionally used alcohol, and denied substance abuse. He was a high school graduate and was employed as an air-

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line baggage handler.

The family history was significant for a grandmother with cancer of an unknown location. The review of systems was negative for abdominal pain, nausea, vomiting, diarrhea, constipation, fever, palpitations, lightheadedness, or weakness. The remainder of the review of systems was unremarkable.

The patient was a well-developed, well-nourished man in no acute distress, and his physical examination was unremarkable except for the rectal examination, which showed scarring from previous anal fissures anterior in the midline. A small amount of stool in the rectal vault was negative for occult blood. The patient was discharged after screening blood tests were drawn and instructed to return if active bleeding recurred. Screening laboratory tests revealed a hematocrit (HCT) of 35.2%, mean corpuscular volume (MCV) of 70 fL (normal, 81 to 95), and total serum iron of 17 µg/dL (normal, 40 to 80).

The patient was contacted about these results. He was started on oral iron supplementation and an outpatient colonoscopy was scheduled. Additional blood tests were ordered at this time. Subsequent results included a carcinoembryonic antigen level of less than 0.5 g/mL and a negative finding on the human immunodeficiency virus (HIV) antibody test. The hematocrit was 40.2%, and MCV was 78 fL. The follow-up total iron was 36 µg/dL (normal, 75 to 175), iron saturation was 10% (normal, 20% to 45%), ferritin was 13 ng/mL (normal, 22 to 322), and reticulocyte count was 0.7% (normal, 0.5% to 2.5%). Liver function tests were within normal limits.

The patient underwent colonoscopy in the family practice center, and a large ulcerated circumferential lesion was found in the right colon (Figure). Four biopsies were taken from distinct nodular regions of the lesion.

The pathology report from the colon biopsy read, "histologically normal colonic mucosa with prominent submucosal lymphoid aggregates, no malignancy identified." On review of the photographs, the striking visual appearance was reaffirmed, and the lesion was considered to have a high probability of being neoplastic. A false-negative biopsy result was considered to be a valid working hypothesis, based on review of the photodocumentation. This "false negativity" was thought to be a sampling problem and not an inaccurate histologic interpretation. The patient was referred to a surgeon for a consultation.

FIGURE

View of lesion in the cecum. Note the asymmetry and nodularity. Despite negative biopsy results, the visual characteristics of the lesion (size, shape, and surface characteristics) suggest the need for a second opinion regarding possible neoplasia.

Independently, the surgeon obtained an abdominal computed tomographic (CT) scan and a barium enema. The radiology report describing the CT scan of the abdomen with contrast read, "abnormal appearing cecum with suggestion of a mass in this area. I am uncertain as to whether this is inflammatory or related to neoplastic process."

The barium enema test showed a large irregular mass in the cecum, highly suspect for a malignancy. The patient underwent right-sided hemicolectomy and terminal ileectomy 8 days after colonoscopy. After surgery, pathology specimens revealed moderately to poorly differentiated infiltrated carcinoma of the cecum with negative margins. Metastatic colonic carcinoma were found in 2 of 24 pericolic lymph nodes. Extranodal spread was present in one.

The patient tolerated the procedure well and had a routine postoperative recovery. Five weeks postoperatively, the patient was started on 5-fluorouracil 800 mg intravenously once weekly and levamisole hydrocholoride 50 mg three times daily for 3 days every 2 weeks. The patient is doing well and has returned to work.

DISCUSSION

Much has been written about false-negative biopsies of the gastrointestinal tract using endoscopic[12-15] and other biopsy methods.[16-20] Irvine et al[3] found sensitivity of colonoscopic biopsies to be 82% for adenoma and/or carcinoma. Reiser et al[14] presented three cases of missed adenocarcinoma in biopsies of colonic strictures during ulcerative colitis surveillance. Bardawil et al[15] found colonoscopic biopsy to have a sensitivity of 81% for neoplasm. They also advocated using a combination of biopsy by standard forceps and brushings of tissue with an endoscopic cytology brush to increase sensitivity.

False-negative findings can be the result of either sampling or interpretation error. When the slides from this biopsy were reviewed, no interpretation error was found. A sampling error can occur with nonrecognition of a lesion, sampling of adjacent normal tissue, or sampling of normal mucosa overlying carcinoma. This case could represent sampling of either adjacent mucosa or overlying normal mucosa. Additional biopsies might have reduced the likelihood of a false-negative biopsy. Brush cytologic testing has been recommended as another useful tool for decreasing the possibility of a false-negative biopsy.[13,15]

This case is interesting not only for the finding of adenocarcinoma in a low-risk patient but also for the assistance of photodocumentation by means of videoendoscopy.[10,11] When faced with a laboratory value or pathology report that may be falsely negative, clinicians need to rely on physical findings, patient history, and clinical judgment. The videocolonoscope was used as an extension of the physical examination. The visualization of a raised, nodular, irregular, and friable lesion increased the suspicion of carcinoma.[4,5]

Office endoscopy as a form of diagnostic imaging symbolizes the continued transfer of "user-friendly" tertiary care technology into the "high-touch arena" of primary care.[21] The continued growth of these diagnostic procedures has been predicted[22] and documented[23] as a part of the continued evolution of the medical specialty of family practice. This case report describes the early detection of colorectal cancer in a young man with subtle but undeniable risk factors. The availability of equipment, training, and expertise allowed early surgical excision with a likely prolongation of life.

REFERENCES

1. Tedesco FJ, Waye JD, Raskin JB, et al. Colonoscopic evaluation of rectal bleeding. Ann Intern Med 1978; 89:907-9.
2. Rodney WM. Gastroenterology. In: Rakel RE, ed. Textbook of family practice. Philadelphia, Pa: WB Saunders, 1995:1206-10.
3. Irvine EJ, O'Connor J, Frost RA, Shorvon P, Somers S, Stevenson GW, Hunt RH. Prospective comparison of double contrast barium enema plus flexible sigmoidoscopy vs colonoscopy in rectal bleeding: barium enema vs colonoscopy in rectal bleeding. Gut 1988; 29:1188-93.
4. Rodney WM, Ounanian LL, Werblun MN. Second-generation videosigmoidoscopy. Am Fam Physician 1985; 31:127-32.
5. Rodney WM. What does the scope show?—Detection of colorectal cancer. Prim Care Cancer 1985; 5(8):19-34.
6. Felmar E, Rodney WM. Who should do gastrointestinal endoscopy? [letter]. JAMA 1981; 246:1301.
7. Rex DK, Rodney WM. Colonoscopy [letter]. J Fam Pract 1994; 38:456-7.
8. Rex DK, Erickson RL, Rodney WM. Who should do colonoscopy? Fam Pract Res J 1994; 14:109-13.
9. Rodney WM, Dabov G, Orientale E, Reeves W. Sedation associated with a more complete colonoscopy. J Fam Pract 1993; 36:394-400.
10. Rodney WM, Felmar E. Why flexible sigmoidoscopy instead of rigid sigmoidoscopy? J Fam Pract 1984; 19:471-6.
11. Orientale E, Dabov G, Rodney WM. Colorectal cancer. In: Taylor RB, ed. Family medicine principles and practice. 4th ed. New York, NY: Springer-Verlag, 1993:709-16.
12. Milsom JW, Czyrko C, Hull TL, Strong SA, Fazio VW. Preoperative biopsy of perirectal lymph nodes in rectal cancer using endoluminal ultrasonography. Dis Colon Rectum 1994; 37:364-8.
13. Chen YL. The diagnosis of colorectal cancer with cytologic brushings under direct vision at fiberoptic colonoscopy. Dis Colon Rectum 1987; 30:342-4.
14. Reiser JR, Waye JD, Janowitz HD, Harpaz N. Adenocarcinoma and strictures of ulcerative colitis without antecedent dysplasia by colonoscopy. Am J Gastroenterol 1994; 89:119-22.
15. Bardawil RJ, D'Ambrosio FG, Hajdu SI. Colonic cytology, a retrospective study with histopathologic correlation. Acta Cytologica 1990; 34:620-6.
16. Zanetta G, Brenna A, Pittelli M, Lissoni A, Trio D, Riotta S. Transvaginal ultrasound guided fine needle sampling of deep cancer recurrences in the pelvis. Usefulness and limitations. Gynecol Oncol 1994; 54(1):59-63.
17. Dodd LJ, Sneige M, Villarrael Y, Fanning CV, Staerkel GA, Caraway NP, Silva EG, Katz RL. Quality assurance study of simultaneously sampled, noncorrelating cervical cytology and biopsies. Diagn Cytopathol 1993; 9:138-44.
18. Diezkmann KP, Kaup F, Loy V. False negative biopsy for testicular intraepithelial neoplasia. J Can Res Clin Oncol 1992; 119:1-4.
19. Derrick EK, Smith R, Melcher DH, Morrison EA, Kirkham N, Darley ER. The use of cytology in a diagnosis of basal cell carcinoma. Br J Dermatol 1994; 130:561-3.
20. Zitarelli J, Vurkhart LL, Weiss SM. False negative breast biopsy for palpable mass. J Surg Oncol Gynecol 1993; 52(1):61-3.
21. Rodney WM. High tech is most effective when blended with high touch and vice versa: office technology in the 21st century. Fam Pract Res J 1991; 11:235-8.
22. Harper MB, Mayeaux EJ, Pope JB. Procedural training in family practice residencies: current status and impact on resident recruitment. J Am Board Fam Pract 1995; 8:189-94.
23. Rodney WM. Flexible sigmoidoscopy and the despecialization of endoscopy: an environmental impact report. Cancer 1992; 70:1266-71.