A 79-year-old woman complained of increasing fatigue with a few episodes of dizziness. Past medical history included hypertension, total hysterectomy at the age of 37 years for a fibroid uterus, and appendectomy at the age of 16 years. The patient reported she was taking the combination product hydrochlorothiazide and triamterene (Dyazide), propranolol, vitamins, and iron. She had smoked since the age of 20 years, 2 packs per day for 50 years. She said she drank one cocktail of vodka and a glass of wine daily. Physical examination revealed pallor and a right abdominal mass. On colonoscopy, she had a large, black, ulcerated cecal mass. Computed tomography scan revealed no metastases. Three guaiac test results were negative for heme. Her white blood cell count was 12,600 cells/mm³ with a differential of 84% neutrophils, 9% lymphocytes, and 7% monocytes. Other laboratory values included the following: hemoglobin, 8.8 g/dL; hematocrit, 27%; mean corpuscular volume, 67.5 fl³; red blood cell distribution width, 18.1%; platelet count, 0.533 × 10³/μL; protein, 5.8 g/dL; and albumin, 2.9 g/dL. The carcinoembryonic antigen level was 13.9 ng/mL before surgery. Right hemicolectomy was performed. A 9.0 × 8.5 × 8.0-cm, tar-black tumor mass with extensive ulceration was present in the cecum (Figure 1). The mucosal surface surrounding the base of the large mass was thickened and ragged. Histopathologic sections of the ulcer showed syncytial solid sheets of tumor with rare lumen formation, punctuated by extensive areas of necrosis (Figure 2, original magnification ×40) and covered by numerous gram-positive and gram-negative bacilli. Sections revealed medium-to-large neoplastic cells with round-to-oval nuclei having clumped to vesicular chromatin and 1 to 3 variably prominent nucleoli with moderate amounts of eosinophilic cytoplasm (Figure 3, original magnification ×400). Ten mitotic figures per 10 high-power fields were identified. The malignant cells were strongly positive for cytokeratin (CK) 20 (Figure 4) and negative for CK7, S100, Melan-A, and vimentin. A minimal desmoplastic stromal reaction heavily infiltrated by lymphocytes and plasma cells surrounded the tumor. One of 25 lymph nodes contained a 0.2-cm focus of carcinoma; this node was located immediately adjacent to the main tumor mass.

What is your diagnosis?
Pathologic Diagnosis: Medullary Adenocarcinoma of the Colon, Poorly Differentiated

Medullary adenocarcinoma (MAC) of the colon is a subtype of poorly differentiated colon adenocarcinoma. Often patients with this type of tumor are elderly women with mainly right-sided tumors, either in the cecum or proximal colon, composed of predominantly solid sheets of malignant cells, minimal or no glandular differentiation, little cellular pleomorphism, and peritumoral lymphocytic infiltrate.1-5 Early in 1977, Gibbs4 described an undifferentiated carcinoma that tended to grow large before symptoms were produced but that patients with this carcinoma nevertheless had a good prognosis when it was locally resectable. Appleman7 described these tumors as lymphoepithelioma-like carcinomas, invariably poorly differentiated, and often huge, with no or very few nodal metastases, considering the size of the tumor. The significantly different clinicopathologic features of MAC of the colon are proximal location, large size, invasive into adjacent organs, expanding pattern of growth, low incidence of distant metastases, conspicuous peritumoral lymphocytic involvement, and Crohn-like lymphoid reaction.5 Microscopically, the tumor consists of nests, trabeculae, and sheets of small- to medium-sized cells with scant-to-abundant eosinophilic cytoplasm. Some cells contain mucin vacuoles. The nuclei have an open chromatin pattern and exhibit prominent nucleoli and frequent mitotic figures. Lymphatic permeation in the stroma is present in most cases. Dolcetti et al6 found that the lymphocytes in the epithelial compartment of the tumors were predominantly CD8+ T-cell receptor β cells and express perforin, a molecule that participates in one mechanism of cell killing. Immunohistochemical findings are positive cytokeratin, carcinoembryonic antigen, and epithelial membrane antigen but negative p53.3,5 Most MACs are DNA diploid by flow cytometric analysis. In addition, young patients with MACs often have a family history highly suggestive of a hereditary background. Most MACs are strongly associated with widespread microsatellite instability (MSI-H).2,3 Medullary adenocarcinomas show high specificity for MSI-H status (99%; P < .001) but low sensitivity (only 14%) due to the low frequency of this tumor type (4%).6

In this case, the large, black, ulcerated cecal tumor (9.0 × 8.5 × 8.0 cm) showed syncytial solid sheets of malignant cells with minimal gland formation and extensive necrosis. The neoplastic cells were medium to large with round or oval nuclei having clumped to vesicular chromatin and 1 to 3 variably prominent nucleoli with a moderate amount of eosinophilic cytoplasm. Mitotic figures were increased to approximately 10 per 10 high-power fields. The malignant cells are strongly positive for CK20 and carcinoembryonic antigen but negative for CK7, S100, Melan-A, p53, CD117 (c-Kit), epidermal growth factor receptor, and vimentin. The tumor cells did not express p53. Numerous lymphocytes and plasma cells permeated the minimal desmoplastic stroma and expressed mostly CD3 with some of them having CD8 positivity (Table).

<table>
<thead>
<tr>
<th>Antibody Panel Studies*</th>
<th>Expression by Antibody</th>
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<tbody>
<tr>
<td>CEA, CK20, CK7, S100, Melan-A, c-Kit, EGFR, p53, CD3, CD8</td>
<td>+ + - - - - - + +</td>
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* CEA indicates carcinoembryonic antigen; CK, cytokeratin; EGFR, epidermal growth factor receptor; plus sign, positive; and minus sign, negative.

References
3. Appleman H. Surgical pathology of the gastrointestinal tract. ASCP Educational Course presented at the Newport Marriott; June 2-6, 1998; Newport, RI.