## Letters to the Editor

### Carcinoma of the Colon in a Patient Presenting With Thrombotic Thrombocytopenic Purpura-Hemolytic Uremic Syndrome

*To the Editor*: Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS) as the initial presentation of cancer is extremely rare.[1-3] We describe a patient presenting with TTP-HUS who was found to have previously undiagnosed adenocarcinoma of the colon. The TTP-HUS improved with standard therapy and resolved after tumor resection. To our knowledge, this is the first reported case of carcinoma of the colon in a patient presenting with TTP-HUS.

**Report of a Case.—**A 66-year-old woman presented with a 1-month history of intermittent fever, generalized headache, bloody diarrhea, progressive shortness of breath, and lower extremity edema. Physical examination findings were remarkable for fever, bilateral basilar crackles on auscultation of the lungs, and bilateral pitting pedal edema. Bilateral minimal pleural effusions and interstitial edema were seen on chest x-ray film, and transthoracic echocardiography revealed normal biventricular size and function with normal valve anatomy. The laboratory test results on admission suggested acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia (blood urea nitrogen [BUN], 51 mg/dL; creatinine, 3.6 mg/dL; hemoglobin, 5.9 g/dL; hematocrit, 18.4%; platelet count, $46 \times 10^9$/L; and lactate dehydrogenase [LDH], 630 U/L). Coombs test results were negative, the coagulation profile was normal, and the peripheral blood film showed numerous schistocytes. The patient was diagnosed as having TTP-HUS.

Further evaluation included serologic tests for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus, all of which were negative. Stool cultures for *Escherichia coli* O157:H7, *Shigella* species, *Salmonella* species, and *Campylobacter* species remained sterile. Antinuclear antibody levels were elevated, but levels of antineutrophil cytoplasmic antibodies (cytoplasmic and perinuclear), anti–double-stranded DNA antibody, and cryoglobulins were normal. A single irregular mass (3-cm diameter) was seen at 30 cm from the anus on flexible sigmoidoscopic examination. Biopsy of the mass revealed invasive, well-differentiated adenocarcinoma of the colon. Staging work-up showed no locoregional or distant metastases.

Oral prednisone ($1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$) and daily plasma exchange were initiated. Five weeks later, laboratory tests showed the following: hemoglobin, 12.7 g/dL; hematocrit, 39.4%; platelet count, $162 \times 10^9$/L; BUN, 16 mg/dL; creatinine, 1.0 mg/dL; and LDH, 234 U/L. Left hemicolectomy with colorectal anastomosis was then performed. Pathologic examination of the resected tumor confirmed the diagnosis of invasive moderately differentiated adenocarcinoma of the colon that was limited to the submucosa. The surgical margins were clear of disease, and no lymph node metastases were found. Platelet count and creatinine and LDH levels remained stable postoperatively. No adjuvant therapy was offered because the tumor was American Joint Committee on Cancer stage I (T1 N0 M0). Plasma exchange and prednisone were gradually tapered over the 6 weeks following surgery. The patient remains disease free 9 months after initial presentation with normal renal function and platelet count (BUN, 22 mg/dL; creatinine, 0.9 mg/dL; platelet count, $243 \times 10^9$/L; and LDH, 163 U/L).

Cancer-associated TTP-HUS has been reported primarily as a manifestation of metastatic cancer or as a complication of cancer chemotherapy[4]; TTP-HUS as the initial presentation of cancer is extremely rare. Although the chance occurrence of 2 disease processes in this patient cannot be excluded, search for occult malignancy should be considered in the work-up of patients presenting with TTP-HUS, especially if no other causative factor is identified.

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### Toward Safer Warfarin Therapy: Does Precise Daily Dosing Improve International Normalized Ratio Control?

*To the Editor*: Warfarin therapy is prescribed for the prevention of stroke and embolism, not only for patients who have a prosthetic valve but also for a growing number of elderly patients with atrial fibrillation. Control of the international normalized ratio (INR), by which warfarin therapy is monitored, is a daunting challenge. As stated by Gage, "Variation in the INR is unavoidable…."[1] The annual risk of major hemorrhage can approach 3% to 4% and is proportional to the percentage of patient-days of INR at 5.0 or higher.[1]

In my prescribing experience, a key factor is the dosing schedule, about which little has been published. Warfarin is available in several strengths (1, 2, 2.5, 3, 4, and 5 mg) of scored tablets. Patients often require a daily dose that is neither a precise multiple of a single tablet nor a multiple of its half-strength. For example, a weekly requirement of 30 mg (4.28 mg/d) is customarily prescribed in some alternating-day fashion (that is, one 5-mg tablet on Sunday, Tuesday, Wednesday, Friday, and Saturday and one-half tablet on Monday and Thursday).[1,2] The term "customary" is used advisedly. This

 