H, Stoppa A, Archimbaud E, Harousseau JL, Bauters F, Fenaux P: Therapy-related acute myeloid leukemia with t (8;21), inv (16), and t (8;16): A report on 25 cases and review of the literature. J Clin Oncol 11:2370–2379, 1993.
3. Smith MA, Rubinstein L, Cazenave L, Ungerleider RS, Maurer HM, Heyn R, Khan FM, Gehan E: Report of the cancer therapy evaluation program monitoring plan for secondary acute myeloid leukemia following treatment with epipodophyllotoxins. JNCI 85:554–558, 1993.
4. Grunberg SM, Burris III, H, Livingston R: The price of success. J Clin Oncol, 13:797–798, 1995.
5. Le Beau MM, Albain KS, Larson RA, Vardiman JW, Davis EM, Blough RR, Golomb HM, Rowley JD: Clinical and cytogenetic correlations in 63 patients with therapy-related myelodysplastic syndromes and acute non-lymphocytic leukemia: Further evidence for characteristic abnormalities of chromosomes no. 5 and 7. J Clin Oncol 4:325–345, 1986.

Severe Vitamin K Deficiency Induced by Occult Celiac Disease BR96-026

To the Editor: This report describes the clinical course of an elderly woman in whom celiac disease was diagnosed, in the absence of gastrointestinal symptoms, after she developed ecchymoses due to vitamin K deficiency. After 1 year of receiving a gluten-free diet, she continued to have subclinical malabsorption, based on a warfarin requirement of <1.3 mg daily for anticoagulation following a cardiac valve replacement. This report and other studies [1,2] suggest that occult malabsorption may be a likely etiology for vitamin K deficiency or low warfarin requirements in elderly patients.

Case Report

A 68-year-old woman was admitted for evaluation of diffuse ecchymoses, which developed after outpatient therapy for sinusitis consisting of ampicillin (10 days) followed by trimethoprim-sulfamethoxazole (2 days). The patient had no history of liver disease or unusual diet, and was not receiving warfarin. She noted a 4-lb weight loss in the previous 2 months, but denied diarrhea or abdominal pain. A gastrointestinal evaluation performed 1 year earlier for iron-deficiency anemia was normal, and the anemia resolved with iron supplementation.

Other medical problems included: idiopathic hypoparathyroidism, hypocalcemia, low-normal vitamin D levels, and osteoporosis treated with calcitriol and calcium; hypothyroidism treated with levothyroxine; rheumatic heart disease and chronic atrial fibrillation, treated with triamterene/hydrochlorothiazide and digoxin; and a seizure disorder treated with phenytoin.

The patient, who was 58 inches tall and weighed 40 kg (88 lb), had ecchymotic lesions on her extremities but did not have mucosal bleeding, lymphadenopathy, or hepatosplenomegaly. The stool tested guaiac-negative. Initial laboratory data (Table I) revealed anemia and deficiency of vitamin K-dependent factors. The deficiency of vitamin K-dependent factors was rapidly corrected with subcutaneous vitamin K (10 mg). Small-bowel biopsy revealed villous atrophy with chronic inflammation, consistent with celiac disease. A gluten-free diet was initiated and the patient gradually gained 9 kg (20 lb). Her coagulation studies remained normal, her bone density improved, and she no longer required calcium or calcitriol. One year later, after undergoing cardiac valve replacement, the patient's warfarin requirement was 9 mg/week (<1.3 mg/day), which suggested residual occult malabsorption.

TABLE I. Summary of Laboratory Data at Presentation (Time 0), and 18 Hr After Vitamin K Administration*

Test	Time 0 hr	After 18 hr	Normal
Platelets/μl	173,000		150–450,000
Hematocrit (%)	24		37–47
MCV (μ^3)	99		81–99
PT (sec)[a]	45.5	14.5	11–14
aPTT (sec)[a]	102.6	32.9	22–34
Fibrinogen (mg/dl)	530		200–400
Factor II (%)	45	55	50–150
Factor VII (%)	5	97	50–150
Factor IX (%)	4	61	50–150
Factor X (%)	2	34	50–150
Factor V (%)	148		50–150
Thrombin time (sec)	12.2		11–14
Reptilase time (sec)	12.0		10–13

*MCV, mean cell volume; PT, prothrombin time; aPTT, activated partial thromboplastin time.
[a]Studies corrected when patient plasma was mixed with normal plasma in 1:1 ratio.

Discussion

Hematologic manifestations of celiac disease (or malabsorption in general) are usually limited to iron or folic acid deficiency [3]. Subclinical vitamin K deficiency is common in malabsorption but rarely results in an overt coagulopathy [2,4].

Although the patient improved clinically on a gluten-free diet, her warfarin requirement was extremely low, suggesting that the gastrointestinal tract may not have undergone complete healing. The prevalence of occult malabsorption in elderly patients who require minimal doses of warfarin to achieve anticoagulation may be higher than currently recognized.

Immunofluorescence assays for endomysial and antireticulin antibodies, and an enzyme-linked immunosorbent assay for antigliadin antibodies, can now be used to exclude celiac disease as a cause for malabsorption [5]. If these tests are positive, small-bowel biopsy should still be performed, since there is an increased risk of intestinal lymphoma associated with celiac disease [3].

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References

1. Swinson CM, Levi AJ: Is coeliac disease underdiagnosed? Br Med J 281:1258–1260, 1980.
2. Krasinski SD, Russell RM, Furie BC, Kruger SF, Jacques PF, Furie B: The prevalence of vitamin K deficiency in chronic gastrointestinal disorders. Am J Clin Nutr 41:639–643, 1985.
3. Michalski JP, McCombs CC: Celiac disease: Clinical features and pathogenesis. Am J Med Sci 307:204–211, 1994.
4. Kark R, Souter AW, Hayward JC: A haemorrhagic diathesis in idiopathic steatorrhoea: Observations on its association with vitamin K deficiency. Q J Med 9:247–261, 1940.
5. Ferreira M, Davies SL, Butler M, Scott D, Clark M, Kumar P: Endomysial antibody: Is it the best screening test for coeliac disease? Gut 33:1633–1637, 1992.