Celiac Sprue Presenting as Severe Hemorrhagic Diathesis due to Vitamin K Deficiency

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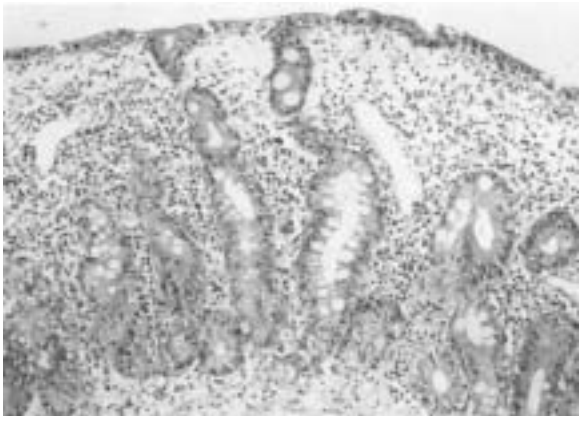
Celiac sprue results from loss of the normal small bowel architecture secondary to intolerance to gluten, and more specifically, to gliadin, a water-insoluble protein of gluten that is present in wheat, barley, rice and – in smaller amounts – oats [1]. Low serum levels of albumin, calcium, magnesium, phosphorus, potassium, cholesterol and carotene are some of the laboratory abnormalities that can be present in this disorder. Bleeding diathesis secondary to vitamin K deficiency has been infrequently noted in children presenting with celiac disease [2], and has exceptionally been reported as the presenting



Low power view of the duodenal mucosa showing total villous athrophy, crypt hyperplasia and increased number of inflammatory cells within the lamina propria (Hematoxylin-eosin x 100)

syndrome in adults with this disorder [3]. A patient presenting with severe bleeding secondary to vitamin K deficiency is presented.

Patient Description

A 41 year old patient was admitted with severe anemia and a 3 week history of multiple hematomas and easy bruising following minimal trauma. No previous history of a hemorrhagic tendency was present. He also noted some decrease in appetite over the previous 3 months, fatigue and loss of 3–4 kg weight. He recently had light-colored fatty stools two to three times daily. His history included hepatitis B infection 23 years earlier, but no alcoholism, acute or chronic pancreatitis, diarrhea or malabsorption. He had not taken any medication regularly. He worked as an electrician in a normal environment and there was no history of contact with toxic materials.

On physical examination he was thin and pale but not jaundiced. His pulse was 92, and blood pressure 130/80. Multiple hematomas were present over the upper and lower extremities. There was no lymphadenopathy or organomegaly on abdominal palpation. The rest of the physical examination was within normal limits. Hemoglobin was 6.4 g/dl, mean cell volume 68 m^3 and mean cell hemoglobin concentration 20 g/dl, white blood cell count 6,000/mm^3, platelets 122,000/mm^3, creatinine 1.0 mg/dl, total protein 6.9 g/dl, albumin 3.5 g/dl, cholesterol 85 mg/dl, triglycerides 89 mg/dl, aspartate aminotransferase 34 U, alanine aminotransferase 26 U, gamma-glutamyltransferase 20 U, lactate dehydrogenase 222 U, bilirubin total 0.7 mg/dl, bilirubin direct 0.4 mg/dl, iron 18 μg/dl, folic acid 4.9 ng/ml, vitamin B12 200 pg/ml, B carotene 24 μg/dl, fibrinogen 285 mg/dl; prothrombin time was unclottable (no coagulation), activated partial thromboplastin time was 106 seconds, thrombin time 19.5 sec (control 15–20 sec); factor X 2.0% (normal 70–130), factor VII 7.0% (normal 70–130), factor V 74% (normal 70–130), factor II 4.0% (normal 70–130), factor VIII 100% (normal 70–130), factor IX 22% (normal 70–100). Xylose test was 0.2 g/5 hours (normal >5) and fecal fat loss 24 ng/24 hours (normal <16). HLA typing showed 88, DR3 positive.

On admission 10 mg of vitamin K were administered. The PT and aPTT returned to normal values and remained normal for the rest of his hospitalization. Ultrasound of the upper abdomen showed edema of the small bowel. A small bowel film was not informative. An upper endoscopy and an abdominal CT were normal. A biopsy of the duodenum showed villous atrophy, crypt hyperplasia, numerous inflammatory cells and other changes compatible with the diagnosis of celiac sprue [Figure]. A gluten free-diet was instituted, and during the following 3 months the patient gained 8–10 kg in weight. Stools became less frequent and of normal aspect and color. No recurrent bleeding or hematomas were detected. The PT and aPTT remained normal, without additional vitamin K administration, and the hemoglobin increased to 13.8 g/dl. A small bowel biopsy performed 3 months after discharge showed marked improvement in the intestinal architecture.

Comment

Celiac sprue, first described more than a century ago, is characterized by villous atrophy associated with intolerance to gluten, a high molecular weight protein found especially in wheat and wheat products [1]. Gliadin, an alcohol-soluble component of gluten, is responsible for the toxic effect of this protein and the changes in the intestinal mucosa in patients with celiac sprue. The disease characteristically affects children, resulting in malabsorption and steathorrea-celiac disease, although a similar condition may be present also in adults. Both states represent a single disease, or celiac sprue.

The diagnosis of celiac sprue requires three conditions: a) presence of malabsorption, b) a typical histologic picture, and c) resolution of most symptoms after a diet without gluten [1]. Biopsy of the mucosa of the proximal small intestine with the sample preferably taken from the region of the duodenojejunal junction remains the essential step in the diagnosis of celiac sprue [1]. Although characteristic, the histologic appearance of the mucosa is not specific, and demonstration of a clear clinical improvement after gluten withdrawal is required to establish the diagnosis [1]. Our patient had both steatorrhea and malabsorption. Intestinal biopsy showed findings typical of celiac sprue, and a gluten-free diet resulted in marked clinical improvement.

Our patient presented with multiple hematomas and severe vitamin K deficiency. This was evidently a consequence of malabsorption, as the blood levels of many other compounds, such as cholesterol, triglycerides, albumin and ferrum, were low. Furthermore, a xylose test was positive and steatorrhea was present.

Occult gastrointestinal bleeding has been detected in a high proportion of patients with active or refractory celiac sprue [4], but this finding was not associated with significant anemia and the prothrombin time was not prolonged in patients with occult bleeding [4]. Even though an association between celiac sprue and vitamin K deficiency is not infrequent, it is usually not severe and does not lead to a bleeding diathesis in most cases. Hemorrhage secondary to vitamin K deficiency has been uncommonly described in children with this disorder [2], and seems to be even more rare in adults with this disease [3].

Why is bleeding secondary to vitamin K deficiency associated with celiac sprue so

infrequent? It is possible that in most patients with this disorder diarrhea and malabsorption are of such a degree that the diagnosis is made long before a severe hypovitaminosis K develops. Nevertheless, and despite its rarity, we must keep in mind the possibility of celiac sprue when confronted with a patient presenting with bleeding and vitamin K deficiency, as this disease can be completely reversed with the appropriate gluten-free diet.

References

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Errata

In two articles in the November issue, the legends of some figures were inadvertently transposed. The correct figures and legends appear below.

Brunner's Gland Hamartoma of the Duodenum (Brunneroma),
by S.A. Becker and N. Ziv-Sokolovskya (page 702)

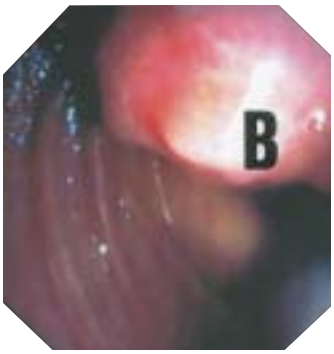

Figure 1. Endoscopic view of Brunneroma in the second portion of duodenum. B = Brunneroma.

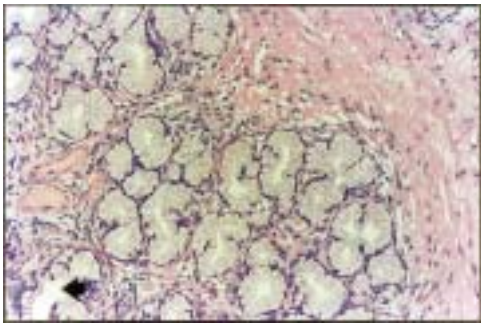

Figure 2. Histology: Brunner's gland hamartoma: lobules of Brunner's glands surrounded by bands of muscles. Arrow in dilated gland.

Simple Imaging Technique for Fitting a Below the Knee First-Time Prosthesis,
by A. Tsur, N. Loberant and G. Volpin (page 714)

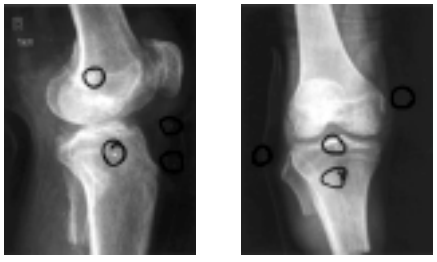

Figure 1. Good alignment of prosthesis; the weight-bearing points in the socket correspond to those of the stump.

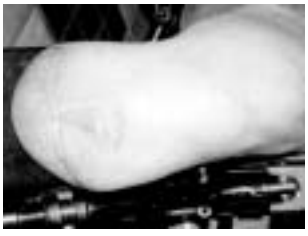

Figure 2. Skin breakdown in the stump several days after fitting of prosthesis and gait training.

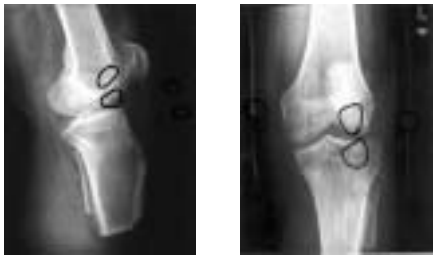

Figure 3. Malalignment of prosthesis; the weight-bearing points in the socket do not correspond to those of the stump.