Antemortem diagnosis of gastrointestinal involvement by non-Hodgkin's lymphoma occurs in approximately 10% of cases. Malabsorption secondary to small bowel involvement by lymphoma is distinctly uncommon and iron deficiency is rarely the sole manifestation of malabsorption. We report a patient with the unusual feature of iron deficiency anemia compounded by selective malabsorption of iron because of occult lymphomatous (diffuse large cell) involvement of the small intestine. Both upper gastrointestinal series with small bowel follow-through and CT scan demonstrated lymphomatous involvement of the duodenum and proximal jejunum by a retroperitoneal mass. An oral iron loading absorption test was consistent with malabsorption of iron. After two cycles of systemic chemotherapy, the retroperitoneal mass had resolved and the iron loading test normalized.
Iron Malabsorption in a Patient with Large Cell Lymphoma Involving the Duodenum

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Iron malabsorption compounded the anemia in a patient with diffuse large cell lymphoma involving the small intestine. Both upper gastrointestinal series with small bowel follow-through and computerized tomographic scan demonstrated lymphomatous involvement of the duodenum and proximal jejunum by a retroperitoneal mass. An oral iron-loading absorption test was consistent with malabsorption of iron. After two cycles of systemic chemotherapy, the retroperitoneal mass resolved and the iron loading test normalized.

INTRODUCTION

Antemortem diagnosis of gastrointestinal involvement by non-Hodgkin’s lymphoma occurs in approximately 10% of cases (1). The gastrointestinal tract is the most commonly involved extranodal organ. Gastrointestinal tract involvement occurs most often with diffuse large cell (DLCL) histology. Sites of involvement in decreasing order of frequency include: the stomach, small intestine, ileocecal area, and large intestine. Presenting complaints include abdominal pain, anorexia, weight loss malaise, nausea, vomiting, and weakness. Up to 15% of patients may have evidence of gastrointestinal hemorrhage. The incidence of anemia, usually attributable to gastrointestinal blood loss, is approximately 30% (2-4).

Malabsorption secondary to small bowel involvement by lymphoma is distinctly uncommon, but has been described in both Hodgkin’s and non-Hodgkin’s lymphomas (5-7). The presenting symptoms mimic those of celiac disease and include weight loss, usually with steatorrhea and variable peripheral edema. The diagnosis of malabsorption is made by the demonstration of increased fecal fat excretion and impaired D-xylose absorption.

Iron deficiency is rarely the sole manifestation of malabsorption. Documented cases of iron malabsorption in celiac disease were reversible by the institution of a gluten-free diet (8, 9). To our knowledge, malabsorption of iron due to lymphomatous involvement of the small bowel has not been previously reported. We report a case with the unusual feature of iron deficiency anemia due in part to selective malabsorption of iron because of occult lymphomatous involvement of the small intestine. Iron malabsorption and the normalization of iron absorption were documented before and after systemic chemotherapy, respectively.

CASE REPORT

In February 1989, a healthy 19-yr-old white male, with no previous medical problems, complained of weakness and several days of progressive dyspnea on exertion, at another hospital. One month later, a CBC showed a Hb of 5.3 g/dl; Hct, 18.3%; MCV, 61 fl; MCH, 24.1 pg; and reticulocyte count, 2.1%. The WBC and platelet count were normal. Iron studies revealed a serum iron of 1 µg/dl; TIBC, 71 µg/dl; saturation, 1%; and serum ferritin, 5 ng/ml. Stools were heme occult negative on several tests. He was placed on supplemental FeSO₄, 325 mg po qd. The following week, a CBC revealed a Hb of 6.1 g/dl; Hct, 21.3%; MCV, 63 fl; MCH, 24.7 pg; and reticulocyte count, 6.4%. A chest radiograph in March showed questionable left hilar adenopathy. In April, he received an RBC transfusion with the Hb improving to 7.9 g/dl; HCT, 27.4%; MCV, 79 fl; MCH, 29.1 pg; and reticulocyte count, 4%. There was no further improvement in the hemoglobin. The chest radiograph in May showed questionable left hilar adenopathy. In April, he received an RBC transfusion with the Hb improving to 7.9 g/dl; HCT, 27.4%; MCV, 79 fl; MCH, 29.1 pg; and reticulocyte count, 4%. There was no further improvement in the hemoglobin. The chest radiograph in May showed questionable left hilar adenopathy. In April, he received an RBC transfusion with the Hb improving to 7.9 g/dl; HCT, 27.4%; MCV, 79 fl; MCH, 29.1 pg; and reticulocyte count, 4%. There was no further improvement in the hemoglobin. The chest radiograph in May showed questionable left hilar adenopathy. In April, he received an RBC transfusion with the Hb improving to 7.9 g/dl; HCT, 27.4%; MCV, 79 fl; MCH, 29.1 pg; and reticulocyte count, 4%. There was no further improvement in the hemoglobin. The chest radiograph in May showed questionable left hilar adenopathy. In April, he received an RBC transfusion with the Hb improving to 7.9 g/dl; HCT, 27.4%; MCV, 79 fl; MCH, 29.1 pg; and reticulocyte count, 4%. There was no further improvement in the hemoglobin. The chest radiograph in May showed questionable left hilar adenopathy.
hematochezia, nausea, vomiting, diarrhea, symptoms of steatorrhea, or abdominal pain. Physical examination was remarkable only for conjunctival and mucosal pallor and a well-healed median sternotomy scar. The abdominal examination was normal. The tests revealed no masses. There was no adenopathy, and the stools were heme-occult negative on multiple examinations. The chest radiograph showed no residual mass. The WBC, differential, and platelet count were normal; the Hb was 6.4 g/dl; Hct, 21%; MCV, 60 fl; MCH 24.3 pg; and reticulocyte count, 0.7%. Erythrocytes were hypochromic and microcytic.

The serum iron was 37 μg/dl; TIBC, 311 μg/dl; saturation, 10%; and serum ferritin, 4 ng/ml—all unchanged in 2 months. Despite continued supplementation with 195 mg elemental iron per day (325 mg FeSO₄ tablets po tid), the anemia and reticulocyte counts failed to improve. The serum total protein and albumin were 6.7 and 4.0 g/dl, respectively. Serum electrolytes, BUN, creatinine, LDH, alkaline phosphatase, ALT, AST, bilirubin, calcium, and phosphate were normal. The Coombs test was negative. A bone marrow biopsy was normal except for absent iron stores; there was no evidence of lymphomatous involvement of the bone marrow. Esophagogastroduodenoscopy revealed mild esophagitis without evidence of bleeding. Biopsies showed normal villous architecture in the duodenum without evidence of submucosal infiltrates. Mild fibrosis with edema was noted in the gastric antrum. A small bowel follow-through (Fig. 1) showed a dilated fixed loop of duodenum and proximal jejunum with thickened irregular folds and displacement of adjacent bowel loops. A D-xylose absorption test was normal. A CT scan of the abdomen and pelvis revealed a large retroperitoneal mass (Fig. 2).

Because of the poor response to prolonged (4 months) oral iron therapy, an iron-loading test was performed on this patient, a patient with iron deficiency from chronic menstrual blood loss, and a patient with large cell lymphoma involving the small bowel before (unfilled circles) and after (filled circles) chemotherapy are included. (Fig. 3). The method is a modification of that previously reported (10-12). The patient and control subjects were fasted for 12 h. At time zero, a CBC, reticulocyte count, serum iron, TIBC, and ferritin were drawn. Two hundred milligrams of elemental iron were then ingested as 8 ml of a 125 mg/ml FeSO₄ solution containing 25 mg/ml elemental iron. (HI-TECH Pharmacal Co., Inc., Amityville, NY). At one, 3 and 7 h after ingestion of oral iron, blood was drawn for serum iron. The patient and control subjects resumed eating after the 3-h sample was obtained. Informed consent was obtained from the patient and both control subjects before initiation of the iron-loading test. A greater than

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Fig. 1. Barium study of the small bowel. The small bowel is displaced inferiorly. The arrows indicate involvement of the duodenum and proximal jejunum.

Fig. 2. CT scan of the abdomen. The retroperitoneal mass involving the small bowel is indicated by the arrow.

Fig. 3. Results of iron-loading test. Serum iron levels are plotted as a function of time after ingestion of 200 mg elemental iron. Two controls (unfilled squares, normal volunteer; filled squares, iron deficiency from chronic blood loss), and a patient with large cell lymphoma involving the small bowel before (unfilled circles) and after (filled circles) chemotherapy are included.
Iron deficiency anemia is a component of generalized malabsorption (18–20) from several potential etiologies (e.g., celiac disease, pancreatic insufficiency); however, the utilization of iron once incorporated is normal. Celiac disease has uncommonly been associated with the selective malabsorption of iron (19). In these cases, iron malabsorption was the sole indicator of celiac disease and reversed with a gluten-free diet (8, 9) or prednisone (21). Steatorrhea may be a manifestation of small bowel lymphoma (22), and has occasionally responded to a gluten-free diet (2) after an initial jejunal mucosal biopsy consistent with celiac disease, only to return in the presence of lymphoma, suggesting a relationship of celiac disease and the subsequent non-Hodgkin's lymphoma involving the gastrointestinal tract. Iron deficiency can impair iron absorption through an unknown mechanism (23), however, the malabsorption is generally not refractory to enteral iron supplementation (23, 24), and occurs in children rather than adults. Patient noncompliance is a consideration in the lack of response to iron therapy; however, this cannot explain the inability to absorb iron during an iron-loading test.

Selective malabsorption states likely reflect severe focal abnormalities in the mucosa normally responsible for the absorption. Generalized malabsorption is a consequence of diffuse mucosal involvement (25, 26). The enhanced response to iron loading in our patient after two courses of systemic chemotherapy strongly suggests that the initial malabsorption of iron was indeed a consequence of local or focal lymphomatous involvement of the gastrointestinal tract (Fig. 3), not secondary to iron deficiency. The association of near complete resolution of the retroperitoneal mass as documented by CT scan with improved iron absorption by an oral loading test supports this conclusion. If iron deficiency was the primary cause of the malabsorption, then the observed response to oral iron loading after chemotherapy would not be expected.

The case we report demonstrates iron deficiency anemia compounded by selective malabsorption from local proximal small bowel involvement of lymphoma. The observed malabsorption corrected after systemic chemotherapy. We suggest that in patients with iron deficiency anemia and malignancy who fail to respond to enteral iron supplementation, involvement of the duodenum and proximal jejunum should be suspected.

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