Anaemia in Waldmann’s disease: A rare presentation of a rare disease

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Abstract

A 32-year-old female presented with 5-year history of iron deficiency anemia, marked pallor and edema of both lower limbs. Laboratory investigations including complete blood count, blood film, iron studies, lipid profile, ascitic fluid analysis, test of stool for occult blood and alpha 1 anti-trypsin. Upper, lower gastrointestinal (GIT) endoscopies, and enteroscopy were performed. Imaging techniques as abdominal ultrasonography and computed tomography were done. Echocardiography, lymph node biopsy and bone marrow examination were normal. The case was diagnosed as Waldmann’ disease with protein losing enteropathy and recurrent GIT bleeding. Management started with low fat diet with medium chain triglyceride, octreotide 200 µg twice a day, tranexamic acid and blood transfusion. Then, exploratory laparotomy with pathological examination of resected segment was done when recurrent GIT bleeding occurred and to excluded malignant transformation.

Key words: Waldmann’s disease; Lymphangiectasia; Gastrointestinal bleeding; Iron deficiency anemia

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Core tip: To our knowledge, this is the first “Egyptian” case of primary intestinal lymphangiectasia. In addition, its presentation is rare with blood loss anemia in contrast to the more common presentation with hypo-proteinemia and edema. So, we are reporting a case with a rare clinical presentation of a rare disease. Double balloon enteroscopy was so beneficial in the diagnosis of the case superior to capsule endoscopy
because the advantage of biopsy and histopathologic examination. There is controversy about medical treatment options, surgical treatment may be preferred in localized lesions otherwise, has no role. Prognosis may be favorable.

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INTRODUCTION

Waldmann’s disease; also called primary intestinal lymphangiectasia (PIL) is a rare form of protein losing enteropathy caused by leakage of lymph inside the small intestinal lumen from dilated lacteals. The manifestations begin before the age of 30 years in 90% of cases, often in childhood. Whether bleeding into gastrointestinal tract a feature of PIL or not is still controversial. Here, we present a case of a young women with chronic blood loss anemia (iron deficiency and positive fecal occult blood test) caused by Waldmann’s disease.

CASE REPORT

A 32-year-old female with 5 year history of iron deficiency anemia was referred to our Gastroenterology Unit for further evaluation. History was irrelevant apart from easily fatigability and repeated blood transfusions as well as iron therapy. Examination revealed marked pallor and edema of both lower limbs.

Laboratory findings of a 32 years old female with Waldmann’s disease are shown in Table 1.

| Test                          | Result         | Normal reference       |
|-------------------------------|----------------|------------------------|
| Complete blood count          |                |                        |
| Hemoglobin                    | 5.2 g/dL       | 12-18 g/dL             |
| HCT                           | 18.30%         | 37%-51%                |
| MCV                           | 70.2 µg        | 80-97 µg               |
| MCHC                          | 28.4 g/dL      | 31-36 g/dL             |
| Platelets                     | 284            | 140-440 cell/cm³       |
| WBCs                          | 3.8            | 4.1-10.9 cell/cm³      |
| Lymphocytes                   | 500            | 600-1400               |
| Blood film                    |                |                        |
| Hypercellular bone marrow with no blast cells | | |
| Blood chemistry               |                |                        |
| s. Albumin                    | 2.1 g/dL       | 3.5-5.5 g/dL           |
| AST                           | 30 IU/L        | Up to 40 U/L           |
| ALT                           | 25 IU/L        | Up to 45 U/L           |
| s. Cholesterol                | 107 mg/dL      | Up to 200 mg/dL        |
| s. Triglyceride               | 54 mg/dL       | Up to 160 mg/dL        |
| s. Iron                       | 23 ng/dL       | 28-170 mg/dL           |
| s. Ferritin                   | 12 ng/mL       | 40-430 ng/mL           |
| TIBC                          | 750 ng/dL      | 261-478 ng/dL          |
| s. TSH                        | 1.2 mIU/L      | 0.3-3.04 mIU/L         |

Blood film

Hypercellular bone marrow with no blast cells

Blood chemistry

Table 1  Laboratory results for the patient

Management started with low fat diet with medium chain triglyceride, octreotide 200 µg/twice a day, tranexamic acid and blood transfusion till an acceptable level of hemoglobin was achieved (about 9 g/dL). She was discharged on diet regimen and regular follow up.

Nine months later during routine follow up, clinical examination showed marked pallor (Hb 6 g/dL) and abdominal ultrasonography revealed moderate ascites and mild right sided pleural effusion. Ascitic fluid was milky and turbid. Chemical analysis of ascitic fluid sample revealed glucose of 108 mg/dL, total protein of 1170 mg/dL, lactate dehydrogenase of 195 U/L, triglycerides of 1232 mg/dL (diagnostic of chylous ascites), WBCs of 250 cell/cm³ mainly lymphocytes.
and RBCs of $0.01 \times 10^6$. Cytological examination of ascitic fluid revealed no atypical or malignant cells. ZN stain and adenosine deaminase were negative. Triphasic CT scan was performed by 8 multi-slice G.E. CT scanner. It revealed right pleural effusion, mild ascites; both had uncomplicated fluid density: 0-20HU (Figure 2) and multiple splenic hemangiomas (Figure 3). Regarding small intestine, CT revealed dilated small intestinal loops with diffuse, nodular wall thickening (reaching up to 9 mm), mesenteric hypodense bands representing dilated lymphatic channels and mesenteric edema (Figure 4). Neither lymphadenopathy nor hepatomegaly was detected.

Surgical opinion was sought and malignant transformation was suspected. So, exploratory laparotomy was done through midline incision. Findings include minimal ascites, multiple cysts related to the small intestinal wall and its mesentry and a discolored segment of the proximal jejunum previously marked with India Ink by enteroscopy (Figure 5) but no masses were found. Resection anastomosis of the discolored segment was done. Histopathological examination revealed large gaping vascular spaces lined by flat endothelial cells and filled by lymph fluid, picture consistent with primary intestinal lymphangectasia (Figure 6).
anemia[^14], necrolytic migratory erythema[^15], recurrent hemolytic uremic syndrome[^16], and osteomalacia[^17].

Recurrent gastrointestinal bleeding was even more rare being reported in only 2 cases[^18,19].

Work up of diagnosis consist of laboratory, imaging studies and GIT endoscopy with confirmatory histopathological examination[^20].

The most common laboratory finding is hypoproteinemia. Hypo-albuminemia is most prominent and lymphopenia. Cholesterol levels are not usually elevated. PLE can be confirmed by presence of excess fecal α1-antitrypsin[^21,22].

Abdominal CT scan may show dilated thickened small intestinal loops, ascites, halo sign and edematous mesentery. It also helps rule out secondary causes[^23,24].

Diagnosis can only be confirmed by finding dilated lacteals both on endoscopic and histopathologic examination[^25,26]. Video capsule endoscopy imaging provides the same information and allow exploration of the whole small bowel but does not allow biopsies[^27].

PIL has to be differentiated from secondary causes of intestinal lymphangiectasia such as Crohn’s disease, intestinal tuberculosis, and Whipple’s disease as well as from causes of PLE without lymphangiectasia such as Menetrier’s disease and systemic lupus erythematosus (SLE)[^20].

Medical management relies on diet modification with low fat replaced by medium-chain triglycerides.
thus preventing fat overloading of intestinal lacteal.\[28,29\]
Response to other medications, such as octreotide\[30-31\] and steroids\[37\] is variable.
Small intestinal resection is indicated in localized forms of the disease\[38,39\].
Natural history of PIL is greatly variable; depending on involvement of intestine either generalized or localized with blockage of mesenteric lymphatic drainage. Prognosis may be favorable unless it is complicated by Mesenteric malformations of lymphatic Retropertitoneal fibrosis

| Table 2 Causes of protein losing enteropathy\[41\] |
|-----------------------------------------------|
| Erosive gastrointestinal disease            |
| Inflammatory bowel disease                 |
| Gut malignancy                             |
| Non steroid anti-inflammatory drug enteropathy |
| Erosive gastropathy                         |
| Acute graft vs host disease                 |
| Pseudomembranous enterocolitis              |
| Ulcerative jejunoenterocolitis              |
| Intestinal lymphoma                         |
| Sarcoïdosis                                 |
| Non erosive gastrointestinal disease        |
| Celiac disease                             |
| Hypertrophic gastropathies                  |
| Eosinophilic gastroenteritis                |
| Connective tissue disorders                 |
| Small intestinal bacterial overgrowth       |
| Amyloidosis                                 |
| Microscopic colitis                         |
| Tropical sprue                              |
| Whipple's disease                           |
| Parasitic diseases                          |
| Viral gastroenteritis                       |
| Increased intestinal pressure               |
| Intestinal lymphangiectasia                 |
| Congestive heart failure                    |
| Congstrictive pericarditis                  |
| Congential heart diseases                   |
| Fontan procedure for single ventricle       |
| Portal hypertensive gastroenteropathy       |
| Hepatic venous outflow obstruction          |
| Enteric lymphatic fistula                   |
| Mesenteric venous thrombosis                |
| Sclerosing mesenteritis                     |
| Mesenteric tuberculosis or sarcoïdosis       |
| Neoplasia involving mesenteric lymph nodes or lymphatics |
| Chronic pancreatitis with pseudocysts       |
| Chronic malformations of lymphatic          |

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**COMMENTS**

**Case characteristics**
A 32-year-old female presented with 5-year history of iron deficiency anemia, marked pallor and edema of both lower limbs.

**Clinical diagnosis**
Examination revealed marked pallor and edema of both lower limbs.

**Differential diagnosis**
Primary intestinal lymphangiectasia has to be differentiated from secondary causes of intestinal lymphangiectasia such as Crohn’s disease, intestinal tuberculosis, and Whipple’s disease as well as from causes of protein losing enteropathy without lymphangiectasia such as Mentrier’s disease and systemic lupus erythematosus.

**Laboratory diagnosis**
Patient hemoglobin level and serum albumin were 5.2 g/dL, 2.1 g/dL respectively.
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