

CASE REPORT

Protein Losing Enteropathy as a Sole Manifestation of Intestinal Non-Hodgkin's Lymphoma; A Case Report and Review of the Literature

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ABSTRACT

Protein losing enteropathy (PLE) as an initial finding of lymphoma, is extremely rare in childhood. We describe clinical and pathological features of an unusual case of gastrointestinal lymphoma presented with PLE as a sole manifestation. Differential diagnosis in children presenting with PLE is critical because early diagnosis and treatment are important for survival in patients with lymphoma.

Keywords: Protein losing enteropathy, Pediatric lymphoma, Malignant lymphoma

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BACKGROUND

Lymphoma is the third most common malignant neoplasm of children.(1-2), Unlike adults in whom the stomach is most often involved, the most common sites in affected children are the distal ileum, secum and appendix.(3), Primary gastric lymphoma of the stomach is extremely rare in childhood.(4), Children with abdominal lymphoma frequently have presenting symptoms of abdominal pain, distention, change of bowel habits, and nausea or vomiting.(5), Protein losing enteropathy (PLE) is an uncommon presentation in children with lymphoma. Edema or hypop-

roteinemia has not been reported as the initial feature of gastric lymphoma.(6), PLE is a rare presenting sign in non- Hodgkin's lymphoma (NHL). Differential diagnosis in patients presenting with PLE is critical because early diagnosis and treatment are important for survival in patients with lymphoma. We report an unusual case of PLE, which highlights the matter.

CASE REPORT

A previously healthy 4-year-old boy was referred to our medical center two weeks after the onset of progressive pitting edema. There was no history of fever, diarrhea or vomiting. On physical examination he looked unwell and pitting edema, extended from his ankles to the chest and dorsum of the hands were notable findings. There were

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bilateral pleural effusions and tense ascites but no features of chronic liver disease or cardiac and renal failure. Hepatosplenomegaly and superficial lymphadenopathy were not detected. Laboratory investigations included: Hemoglobin (Hb) 8.7 g/dl (normal range, 11.5-15 g/dl), mean corpuscular volume 72 μm^3 (normal, 77-95 μm^3), hematocrit 27% (normal range, 35-45%), serum iron 20 $\mu\text{g}/\text{dl}$ (normal range, 22-184 $\mu\text{g}/\text{dl}$), iron binding capacity 440 $\mu\text{g}/\text{dl}$ /dl (normal range 250-400 $\mu\text{g}/\text{dl}/\text{dl}$), ferritin 10 ng/ml (normal range 7-140 ng/ml), White Blood Cell (WBC) 13000/ mm^3 (normal range 4000-10000/ mm^3), platelet 360,000/ mm^3 (normal range 150-450,000/ mm^3), erythrocyte sedimentation rate (ESR) 8 mm/h (normal range 0-15 mm/h). Total serum proteins was 2.6 g/dl (normal range, 6.1-7.9 g/dl), albumin 1.05 g/dl (normal range, 3.5-5 g/dl), but results of liver function tests, coagulation profile, along with electrolyte level, urea and creatinin levels were normal. Urinalysis did not show proteinuria and the stool α -1-antitrypsin was high. A diagnosis of PLE was made. A chest x-ray confirmed normal mediastinum, bilateral pleural effusions and abdominal sonography demonstrated several large para-aortic lymph nodes, profuse ascites, prominent gastric mucosal folds and thickening of the intestinal loops. Examination of ascites disclosed degenerative and inflammatory cells. The patient was treated with intravenous albumin for 4 days and a low sodium, high protein diet was imposed. After 1 week, ascites and edema were remarkably decreased. On the 7th hospital day, upper gastrointestinal endoscopy performed and revealed hypertrophy of gastric rugae, diffuse large volcano like nodules in the fundus and body of the stomach, leafy like mucosal protrusions in the first, second and third parts of duodenum. The fourth part of the duodenum appeared normal.

Microscopic examination of both gastric and duodenal lesions showed sheets of neoplastic cells infiltrate widely in lamina propria and forming rare foci of lymphoepithelial lesions. The neoplastic cells were non cohesive with no gland or cord formation. The cells had high nuclear

/cytoplasm (N/C) ratio, vesicular nuclei and relatively prominent nucleoli and nuclear membranes. The neoplastic cells were positive for LCA* and CD20; they were negative for CD3 and neuron specific enolase (NSE).

There was no evidence of Menetrier's disease, no *helicobacter pylori* was identified in Geimsa staining.

The patient was diagnosed as a case of malignant gastroduodenal B-cell lymphoma according to histopathologic and immunohistochemistry findings. On the 12th hospital day he was referred to oncology department for further investigation and management.

DISCUSSION

Lymphoma is the most common malignancy of the pediatric intestinal tract, with non-Hodgkin's lymphoma, occurring much more frequently than Hodgkin's disease. Extranodal involvement of NHL in children is more frequent than in adults.(7), The intestinal tract is the most common site of extranodal NHL.(8), Malignant lymphomas of the small intestine are relatively common in developing countries, particularly in the Middle East.(9), In the Iraqi tumor registry (1986-1988), for example, small intestinal lymphoma constituted about 19% of all non-Hodgkin's lymphoma and 78% of all small intestinal malignant tumors. Generally these lymphomas can be divided into three subtypes.(10), Burkitt's lymphoma, which is most common in children, usually involves the terminal ileum. The second relatively common, is similar to the "Western" type involving various parts of the small intestine. The third type is the so-called Mediterranean lymphoma affecting mainly young adults and involves predominantly the proximal small intestine and is usually associated with chronic diarrhea and abdominal pain.(11)

A total of 935 patients with extranodal non-Hodgkin's lymphomas diagnosed in the period between January 1985 and December 2000 in Kuwait cancer center.

* Leukocyte common antigen

Extra nodal lymphomas accounted for 45% of all NHLs observed during this period. According to the latest WHO* classification (2000), the most common lymphoma observed was diffuse large cell lymphoma. The most common site of extra nodal site was stomach (19%) in the adults group, large intestine (29.8%) and small intestine (19.7%) in the pediatric group.(12), High occurrence of malignant lymphomas has been reported in studies conducted in Iran; Hashemi and Parvaresh in their study showed that the high-grade non-Hodgkin's lymphomas were more prevalent than low-grade lymphomas compared to western countries.(13)

Primary gastric lymphoma of the stomach is extremely rare in childhood; most reported cases have been in children older than 9 years. Only 17 cases gastric carcinoma occurring in patients less than 21 years old have been reported since 1990, with only one patient less than 10 years old. In no case of lymphoma was edema or hypoproteinemia an initial feature.(4), PLE, though sometimes associated with common gastrointestinal disorders, and representing a small part of the clinical picture, can be a sole manifestation of an underlying disease and may cause a difficult diagnostic problem. PLE is occasionally found in malignant lymphoma. Proposed mechanism for occurrence of PLE in lymphoma include direct tumor infiltration and lymphatic obstruction.(14), Although a few cases of lymphomas (Hodgkin and non-Hodgkin), presenting with PLE have been reported in children and adults(15-19), according to our knowledge this unique case with a sole manifestation of PLE is the first report of gastrointestinal B-cell lymphoma of childhood in Iran.

It would be highly recommended to consider malignant gastrointestinal lymphoma as the secondary cause of PLE in very young children's therefore early diagnosis and treatment are important for survival in patients with lymphoma.

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* World Health Organization