Protein-Losing Enteropathy in a Case of Nodal Follicular Lymphoma without a Gastrointestinal Mucosal Lesion

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Abstract

Protein-losing enteropathy (PLE) is characterized by gastrointestinal loss of serum protein. It is usually caused by hypersecretion from a tumor, ulcer, or long standing lymphangiectasia. However, we report a 47-year-old man of peritoneal nodal follicular lymphoma who developed PLE with none of them. Oozing of whitish fluid from duodenal bulbar mucosa was endoscopically seen, resulting in continuous loss of protein. Chemotherapy was effective and PLE was rapidly diminished. Nodal lymphoma lesion was considered to disturb lymphatic flow and to regurgitate it to duodenal mucosa. To our knowledge, this is the second report of a lymphoma patient presenting PLE without a gastrointestinal mucosal lesion.

Key words: protein-losing enteropathy, follicular lymphoma

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Introduction

Protein-losing enteropathy (PLE) is a characteristic clinical condition caused by continuous protein leakage into the digestive tract, resulting in hypoproteinemia (1). It is usually associated with gastrointestinal tumorous or ulcerated lesions, i. e., carcinoma or malignant lymphoma and rarely intestinal lymphangiectasia. However, we encountered a patient with malignant lymphoma of abdominal paraaortic and perigastric lymph nodes who presented PLE without gastrointestinal tract lesions. It is generally considered that PLE arises in lymphoma patients only when the digestive tract is involved (2); only a single case report of PLE without mucosal lesions was found in the literature (3). Thus, we report the second case of this extremely rare clinical manifestation.

Case Report

A 47-year-old man was admitted to our department in January 2002, complaining of bilateral leg edema and gen-

eral fatigue that had continued for one month. On physical examination, a fist-sized tumor was palpated on his upper abdomen, but no surface lymph nodes were swollen. Pitting edema of his legs was also noted. Blood test showed markedly decreased serum protein at 4.4 g/dL with albumin at 2.7 g/dL, although they had been within normal limits on the routine medical check-up nine months previously. Laboratory data on admission is as follows: WBC 7,600/ μ L, RBC 451×10^4 / μ L, Hb 15.2 g/dL, Ht 43.0%, PLT 37.8×10^4 / μ L, LDH 205 IU/L, AST 23 IU/L, ALT 21 IU/L, ALP 180 IU/L, and CRP 0.06 mg/dL. Serum soluble interleukin-2 receptor was elevated at 3,380 U/mL. Since urinary protein was not detected, we considered PLE as a cause of hypoproteinemia. Gastroscopy was thus carried out and regurgitation of whitish mucous fluid from pyloric ring to the gastric antrum was found. When the scope was inserted into the duodenal bulb, continuous oozing of the fluid from whole bulbar mucosa was observed (Fig. 1). In the endoscopically biopsied duodenal specimen, dilation of submucosal lymphatic vessels or atypical cell was not pathologically found. The excretion rate of the fluid was about 3 mL per minute. It

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Figure 1. Endoscopic findings of duodenal bulb. Whitish mucous fluid continuously oozed from whole bulbar mucosa.

Figure 2. Abdominal CT. Swelling of paraaortic and perigastric lymph nodes was depicted. Duodenal wall of the second portion appeared to be thickened. No ascites was observed.

Figure 3. Microscopic view of the biopsied lymph node specimen ($\times 100$) (a). Proliferation of small and cleaved cells that are positive for bcl-2 was observed ($\times 400$) (b). Grade I follicular lymphoma was diagnosed.

was disclosed to contain 106 mg/dL of protein, resulting in daily loss of approximately 4.6 g. Only normal lymphocytes were cytologically seen. X-ray examination with contrast medium revealed no mucosal lesion on the second portion of duodenum and small intestines. Colonoscopy found no lesions in the colon and the terminal ileum. Abdominal CT revealed swollen paraaortic and perigastric lymph nodes corresponding to the palpated tumor (Fig. 2). Thickened duodenal wall of the second portion was also notable. Surgically biopsied specimen of the perigastric lymph node was histologically diagnosed as grade I follicular lymphoma (Fig. 3). The lymphoma cells were positive for CD10, 19, 20, and bcl-2. Karyotype was 46,XY. The specimen from duodenal mucosa was further examined. However, positivity for those surface markers was not detected and Southern blot hybridization detected no rearrangement of immunoglobulin heavy chain gene (data not shown), indicating that microinvasion of lymphoma cells to duodenal mucosa was appropriately excluded. Complete remission was acquired by eight cycles of combination chemotherapy consisting of cyclophosphamide, adriamycin, vincristin, and prednisolone. After the first cycle of the therapy, hypoproteinemia was

rapidly improved and oozing of the whitish fluid from duodenal mucosa endoscopically disappeared.

Discussion

Gastrointestinal lymphoma occasionally complicates PLE. In those cases, protein loss is usually due to hypersecretion of tumorous or ulcerated lesion. We could not find such lesions endoscopically in the stomach, duodenum, or colon. We also detected no jejunal or ileal macroscopic lesions radiographically, although it might be shown more clearly by using double balloon or capsular endoscope. On the other hand, intestinal lymphangiectasia, that often shows PLE, is also known to complicate malignant lymphoma during the long clinical course (4-6). Immunological disorder induced by continuous loss of lymphocytes or immunoglobulin is recognized as a predisposition to the development of malignant lymphoma (5). However, this is not consistent with the present patient since his history of PLE was too short to be considered as a result of intestinal lymphangiectasia that is long standing and no remarkable lymphangiectasia was detected in the biopsied duodenal mucosa. Moreover, chemo-

therapy markedly improved PLE. Thus, PLE was apparently caused by the nodal lymphoma lesion in our patient.

Lymphatic vessels of intestines meet and ascend along the bilateral sides of spine and flow into the thoracic duct. This lymphatic flow in our patient appeared to be disturbed by the peritoneal lymphoma lesions around the duodenum. We speculated that lymphatic fluid regurgitated to duodenal lymphatic vessels and oozed when the retention pressure was elevated. The thickened duodenal wall observed on CT might support this speculation. Konar et al reported the first case of malignant lymphoma presenting PLE without gastrointestinal lesions (3). It is notable that PLE in their case had

preceded the clinical manifestation of retroperitoneal tumors of diffuse large cell lymphoma. Retroperitoneal microscopic or subclinical lesion might disturb lymphatic flow. Serum albumin in both patients normalized after chemotherapy. The mechanisms of the pathogenesis of PLE in their case therefore appear to be similar to those in the present case. Although the frequency is low, PLE might indicate the underlying deep-seated lesions of malignant lymphoma. It should also be evaluated whether hyponutrition due to PLE affects the grade of side effects of chemotherapy or the long-term survival rate.

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