Intestinal lymphangiomatosis presenting with protein-losing enteropathy

Protein kaybettiren enteropati ile presente olan intestinal lenfanjiomatozis

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Lymphangioma is a benign tumor characterized by proliferation and dilatation of lymph vessels. Lymphangiomas are submucosal tumors consisting of an endothelial lining with lymphatic spaces, lymphoid tissue, and smooth muscle. They can affect all the organs except the brain, because the brain does not contain a lymphatic system. Although this disease can be seen in any organ, intestinal presentation in an adult is very rare. In this case report, we present a 44-year-old woman with pretibial edema and hypoalbuminemia. Abdominal ultrasonography showed minimal free fluid, and a computed tomography scan showed segmental wall thickening of the ileum. The patient was diagnosed with intestinal lymphangiomatosis by capsule endoscopy.

Key words: *Protein-losing enteropathy, lymphangioma*

Lenfanjioma lenfatik sistemde proliferasyon ve genişleme ile karakterize bir benign tümördür. Lenfanjiomalar submukozal tümörlerdir, endotel ile kaplı lenfatik alan, lenfatik doku ve düz kas içerirler. Beyin dokusu lenfatik sistem içermediği için beyinde görülmez, bunun dışında bütün organları etkileyebilmektedir. Her organda görülebilmesine karşın yetişkin hastalarda ve intestinal tutulum çok nadirdir. Bu vakada pretibial ödem ve hipoalbuminemisi olan 44 yaşında bayan hasta anlatılmıştır. Batın ultrasonografisinde minimal serbest sıvı görüldü. Tomografide ileumda segmental duvar kalınlaşması bulundu. Hastaya kapsül endoskopi ile intestinal lenfanjiomatozis tanısı konuldu.

Anahtar kelimeler: *Protein kaybettirici enteropati, lenfanjioma*

INTRODUCTION

Lymphangioma is a benign tumor characterized by proliferation and dilatation of lymph vessels (1,2). Lymphangiomas are submucosal tumors consisting of an endothelial lining with lymphatic spaces, lymphoid tissue, and smooth muscle (3,4). They can affect all the organs except the brain, because the brain does not contain a lymphatic system (5,6). Although this disease can be seen in any organ, intestinal presentation in an adult is very rare (7). In this case report, we present a 44-year-old woman with hypoalbuminemia, pretibial edema, and diagnosed intestinal lymphangiomatosis.

CASE

A 44-year-old female patient who had complaints of swelling in both legs and weight loss for 1 year was admitted to hospital. She had a history of hypertension and was using metoprolol 50 mg. The patient's physical examination was normal, except bilateral pretibial edema. Her laboratory findings were as follows: white blood cells 4.100 mm^3 (4000–10500 mm^3), hemoglobin 12.3 g/dl (normal: 12–16 g/dl), urea 19 mg/dl, creatinine 0.49 mg/dl, total protein 3.4 mg/dl, albumin 2.07 mg/dl, glucose 64 mg/dl, aspartate aminotransferase (AST) 14 U/L, and alanine aminotransferase (ALT) 10 U/L. The patient did not have urinary protein loss nor a history of chronic hepatic insufficiency. Anti-endomysium, cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA), perinuclear anti-neutrophil cytoplasmic antibodies, (pANCA), anti-gliadin immunoglobuline (Ig)A and IgG, and anti-transglutaminase IgA and IgG were all negative. She did not have tuberculosis. The patient was referred to the cardiology department. Echocardiographic and cardiologic evaluation were normal. Abdominal ultrasonography showed minimal free fluid, which reached a maximum of 10 mm at the Douglas pouch and between the intestinal loops. An abdominal computed tomography (CT) scan revealed paraaortic, aortocaval, and paraceliac conglomerate lymph nodes, the largest of which was 23 mm in diameter. At the ileum, there was a 35-cm-long segmental wall thickening (Figure 1,2). The patient underwent colonoscopy and gastroscopy. Gastroscopy found gastritis, and colonoscopy was normal. On positron emission tomography

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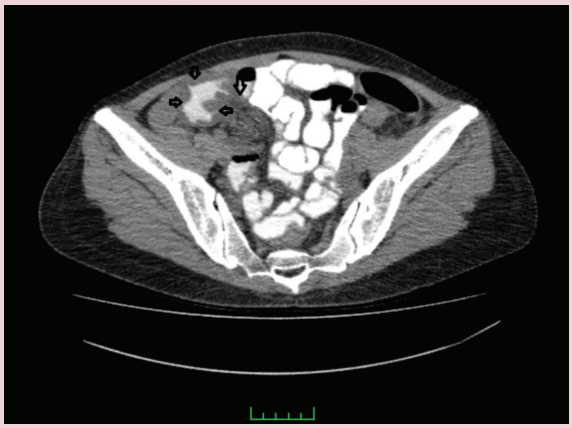

Figure 1. Segmental wall thickening at the ileum.

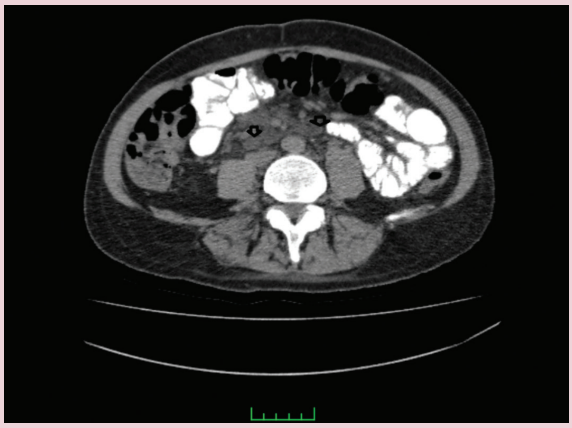

Figure 2. Lymph nodes in the abdomen.

(PET)-CT, there was fluorodeoxyglucose (FDG) uptake at the sites of intestinal wall thickening. Bone marrow biopsy results were normocellular to mild hypercellular and immunophenotype analysis gave no pathologic results. Neck CT scan did not reveal any suspicious findings. Double balloon enteroscopy was performed and showed edema and lymphangiectasis at the ileum. After that, the patient underwent capsule endoscopy, and the results showed a polypoid formation bulging into the lumen of the jejunum, and the mucosa was viewed as dense lymphangiectasia (Figure 3,4). This view continued for a 40-cm segment of middle and distal jejunum. Lymphangiectasia was also present at the ileum. The patient was given a diet rich in protein and underwent laparoscopic excision. Macroscopy of the removed intestinal segment revealed, at the serosal surface, 2-cm grey-yellow spots and small, white, fluid-filled spaces. Microscopic observations were cystic, dilated lymphovascular formations of the intestinal mesentery and subserosa, which sometimes extended to the mucosa. The endothelium lining the lesions was D240, CD31, and ERG positive and CD34 negative. At the excision border, cystic, dilated lymphovascular formations at the submucosa were observed. These findings were compatible with a diagnosis of mesenteric and subserosal intestinal lymphangiomatosis.

The patient's post-surgical follow-up showed significant improvement, albumin reached normal levels, and her complaints resolved. At 1-year follow-up, her albumin was 4.24 g/dl, and she had no weight loss and no pretibial edema.

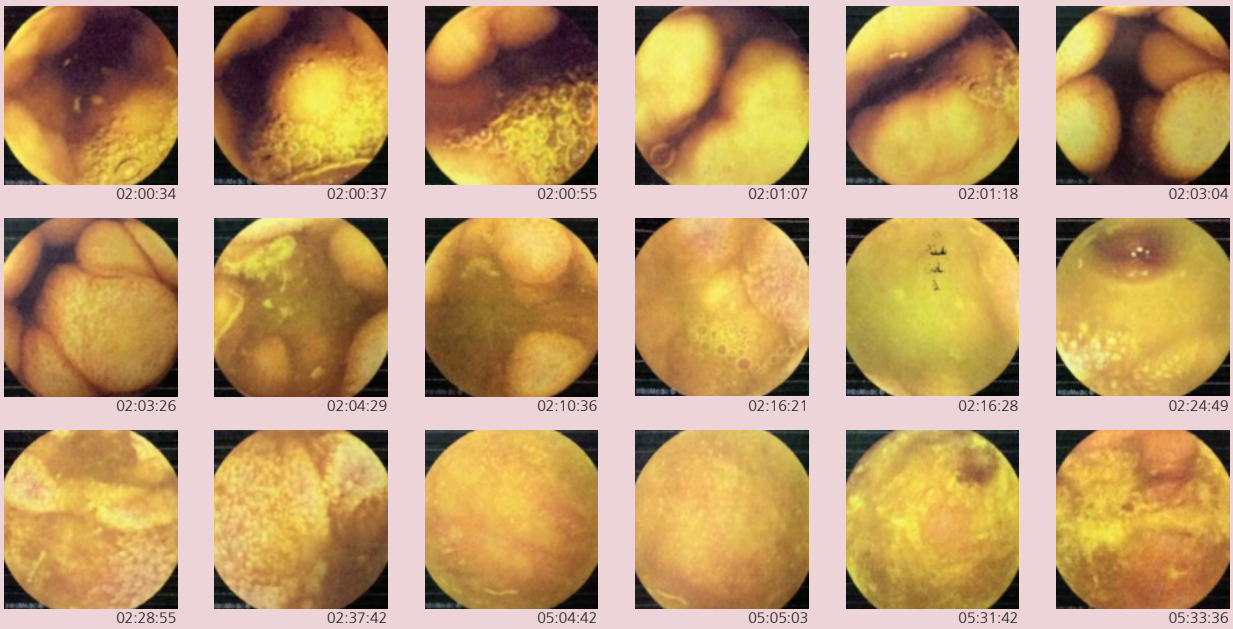

Figure 3,4. Capsule endoscopy with lymphangiectasia in the jejunum and ileum

DISCUSSION

Lymphangioma is a congenital lymphatic system malformation, which generally affects infants and children rather than adults. Its primary locations are the head and neck regions, which constitute 95% of cases (8), whereas other localized presentations, such as the retroperitoneum or abdomen, are very rare. Lymphangiomas can occur in all organs. The brain is the one exception, as it lacks lymphatic channels (9-11). Lymphangioma classification is divided into four categories: capillary lymphangioma, cavernous lymphangioma, cystic lymphangioma, and hemolymphangioma (12). Diffuse lymphangiomas involving the skin occasionally occur in children, and this condition is called generalized lymphangiomatosis (11,12).

There are several theories about the pathogenesis of lymphangiomas. These theories include sequestration of lymphatic tissue during embryonic development, abnormal budding of lymphatic vessels from the primitive lymphatic system, connection failure between the lymphatic and venous systems, and obstruction of the efferent lymphatic vessels. Trauma, infections, chronic inflammation, and obstructions during embryonic development can cause lymphangiomas. The association of several growth factors with lymphangiomas has been suggested; these include vascular endothelial growth factor C (VEGF-C), VEGFR-3, and the transcription factor Prox-1 (13). Abdominal and mesenteric presentations of lymphangiomas are uncommon, their growth pattern is generally slow, and they manifest themselves in early adulthood (14).

Abdominal lymphangiomas are very rarely seen in adult populations: their incidence is reported between 1 in 20,000 and 1 in 250,000 in the literature (15-17). In children, lymphangiomas are reported at the same frequency in males and females (18). Ninety percent of lymphangiomas occur in children before 2 years of age (19). However, Allen et al. suggested a female predominance in adults with abdominal lymphangiomas: 100% of adult lymphangioma patients are females aged between 38 and 66 years (7). Jain et al. reported a 15-year-old female patient with small-bowel lymphangioma. Lin et al. reported a 38-year-old female patient with duodenal lesions (12,19). Our patient was a 44-year-old female with lymphangiomas of the ileum and jejunum.

Abdominal lymphangiomas have variable clinical manifestations, such as nonspecific abdominal pain, painless abdominal mass, and if complicated due to infection, bowel obstruction, hemorrhage, and ascites presenting as acute abdominal swelling. Lymphangioma can also be asymptomatic (20). In adult patients, clinical presentation is milder and lasts months or years before diagnosis (4). One study reported that symptom duration in five pediatric patients was acute, ranging from 3 days to 2 months. In contrast, in nine adult patients, symptom duration ranged from 2 weeks to 1 year, and four adult patients were asymptomatic. In our case, the main symptom was abdominal distension and pain (10). Protein-losing enteropathy is an uncommon presentation of abdominal lymphangioma, which is already a rare disorder. One case reported a 32-year-old woman with hypoalbuminemia and colonic lymphangiomatosis. Another case report showed a 38-year-old woman with hypoproteinemia and gastrointestinal bleeding diagnosed with abdominal lymphangiomatosis (1,12). Our patient had hypoalbuminemia that persisted for more than 1 year.

Abdominal ultrasonography can show well-circumscribed cystic lesions with multiple thin septa (21). On a CT scan, lymphangioma manifests itself as a unilocular or multilocular septate cystic mass, with enhancement of the wall and septum by a contrast medium with fluid attenuation present. Ultrasonography and CT can determine the tumor's size, location, and cystic nature, but an accurate diagnosis is not possible with these methods (20). It is suggested that MRI is more useful for assessing disease severity (6). Mesenteric lymphangioma is a thin- walled cystic mass, which has a yellow external surface, and the lymphatic spaces are filled with proteinaceous eosinophilic fluid (20).

Complete surgical removal is suggested as the treatment of choice for symptomatic and asymptomatic patients alike (22,23). Reported recurrence rates for complete resection are between 0% and 27% (24). Our patient's follow up after resection was normal with no signs of recurrence.

Lymphangioma of the abdomen is a very uncommon disease, which does not have any characteristic symptoms. Nevertheless, this rare disease should be suspected in patients with unexplained hypoproteinemia.

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