

Crohn's disease with isolated esophagus and gastric involvement

İzole özofagus ve mide tutulumlu Crohn hastalığı

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Isolated esophagus and stomach involvement in Crohn's disease is rather rare. We present here a female patient aged 35 years, who presented with complaints of fatigue, difficulty in swallowing, nausea, and vomiting, and who was diagnosed as esophago-gastric Crohn's disease.

Crohn hastalığında izole özofagus ve mide tutulumu oldukça nadirdir. Biz 35 yaşında, halsizlik, yutma güçlüğü, bulantı, kusma yakınması ile gelen ve özofago-gastrik Crohn hastalığı tanısı alan kadın olguyu sunduk.

Key words: Crohn's disease, esophagus, stomach

Anahtar kelimeler: Crohn hastalığı, özofagus, mide

INTRODUCTION

Crohn's disease (CD) is an idiopathic, chronic, and inflammatory disease of the gastrointestinal tract characterized by the segmented, transmural involvement of the tract. Ileocolonic involvement is seen in about 40% of the cases, small intestines are involved in about 30%, and colonic/anorectal involvement is seen in about 40% (1). Gastro-duodenal involvement is seen in 0.5-13% of the patients with ileocolonic disease (2, 3). Isolated esophagus and stomach involvement is rather rare (4).

CASE REPORT

A female patient, aged 35 years, was admitted to our clinic with complaints of fatigue, difficulty in swallowing, nausea, vomiting and pain in stomach after eating, and loss of body weight. Her complaints had started about eight years previously. She had undergone endoscopic examinations in various centers with the pre-diagnosis of tumor in the stomach. In a hospital where she was hospitalized for exploration, laparotomy and partial splenectomy had been performed; biopsies were taken from stomach and mesenteric lymphadenopathies without resection, with the surgical pre-diagnosis

of inoperable gastric tumor. The results of pathological examination had indicated an inflammatory reactive lymphoid hyperplasia. She was discharged without any therapy with the recommendation of follow-up visits.

She described pain starting in the epigastric region and spreading to the sides simultaneously with eating, and had experienced these symptoms for the last year. Nausea and vomiting accompanied this pain. If she did not eat, the symptoms did not occur and she was comfortable. She described difficulty in swallowing when eating solid food, and had lost about 10 kg.

There were no distinguishable features in her personal or family histories. She did not consume alcohol or smoke.

Vital signs were normal in her physical examination. She had a pale and thin appearance, and her general condition was determined as medium. There were rugae in the corners of her mouth and aphthous ulcers on tongue. Examinations of other systems were normal.

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Laboratory findings: Hb: 4.45 g/dl, white blood count: 10,200/mm³, platelet count: 109,700/mm³, and MCV: 57 fl. Fasting blood sugar: 46 mg/dl, total protein: 6.8 mg/dl, albumin: 3.0 g/dl, AST: 19 U/L, ALT: 12 U/L, GGT: 61 U/L, ALP: 158 U/L, calcium: 8.02 mg/dl, ionized calcium: 4.08 mg/dl, sodium: 139 mmol/L, potassium: 4.17 mmol/L, and chlorine: 101 mmol/L.

Ferritin was found to be 77.1 ng/ml (normal value: 11.0-306.8), Mate, 3.13 ng/ml (normal value > 3.0), vitamin B12 223 pg/ml (normal value: 120-600), AFP <0.605 ng/ml (normal value: 0-7), CEA: 0.474 ng/ml (normal value: 0-3.4), CA 125: 34.63 U/L (normal value: 0-35), CA 19-9: 9.16 U/ml (normal value: 0-39), and CA 15-3: 26.23 U/ml (normal value: 0-25).

Abdominal ultrasonography and upper gastrointestinal tract endoscopic examination were planned. On abdominal ultrasonography, a lymphadenopathy package with hypoechoic signals in inner regions with dimensions 7.5 cm x 4.5 cm was observed close to the left lobe of the liver and heart. The residual spleen was observed in the spleen region. Echoes of both kidneys were increased by grade 1. A diffuse and heterogeneous thickening in the wall of the stomach close to 12 mm in the thickest part was observed.

On the endoscopic examination of the upper gastrointestinal tract, upper and middle parts of the esophagus were normal. Esophagus was hyperemic in the lower end, and diffuse ulcerations were observed there. Biopsies were taken. Lumen was narrowed because of ulcerations (Figure 1). En-

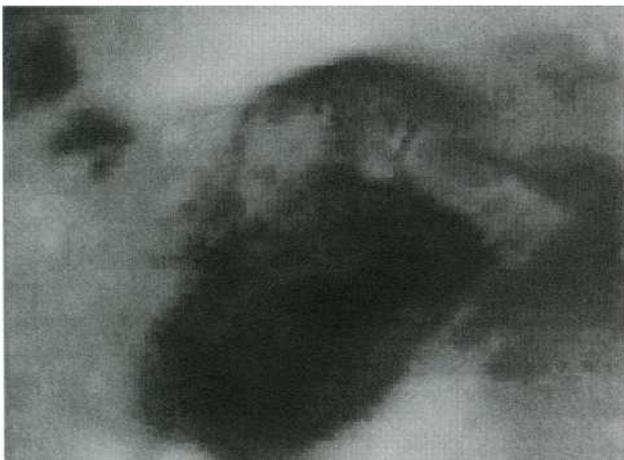


Figure 1. Endoscopic view of the esophagus. The hyperemic mucosa and diffuse ulcerations can be seen in the lower end of the esophagus

doscope had to be forced to advance it to the stomach. Mucosa and pleats of the stomach had a normal appearance. Diffuse ulcers with rough and granulated surroundings with diameters of 1-3 cm were observed in the antrum and corpus of the stomach. Mucosa there had the appearance of paving stones. There were mucosal nodulations in places, and biopsies were taken. The expansion of the lumen in the antrum was not sufficient, the antrum and pylori were narrowed, and the endoscope had to be forced to advance it to the duodenum (Figure 2). The bulbous and the second part of the duodenum were normal.



Figure 2. Endoscopic view of the antrum, corpus, and pylori in the stomach. Mucosa with paving stone appearance, diffuse polypoid lesions, mucosal nodulations, and narrowed pylori can be seen

Following the pathological examination of the biopsy samples, the following was reported: "Material consists of superficial gastric mucosa, and masses of fibrinous exudate that is either free or continues with mucosa. The superficial epithelium of the mucosa shows hyperplasia of varying degree, and it has formed a villous pattern. Neutrophil leukocytes are present within the superficial epithelium as solitary or in groups. Partially inflammatory infiltration, and partially a granulation tissue rich in capillaries are observed in the stroma. Areas of fibrosis are observed on one side of these granulation tissues. Two of the samples consist entirely of tissue pieces that show diffuse fibrosis having a few atrophic glandular structures. In the base of one of the samples that is consistent with the base of ulceration, and that has an intensive

mass of fibrin and exudate on the surface, fibrosis and intensive lymphoid infiltration are observed. Pathological diagnosis: Crohn's disease, stomach" (Figures 3, 4).

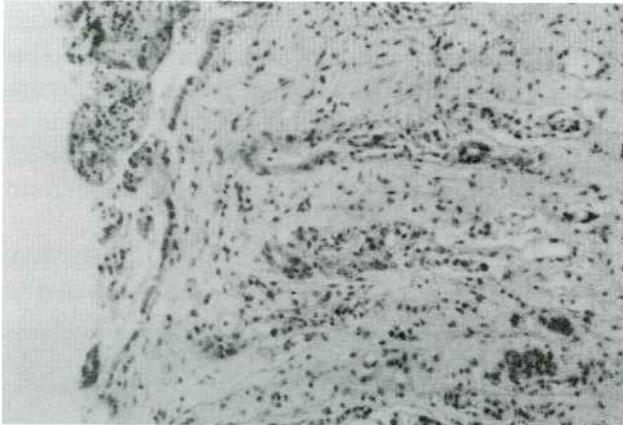


Figure 3. Intensive fibrosis and granulation tissue in the mucosa are observed on histopathological examination



Figure 4. Intensive lymphoid infiltration and fibrosis in the mucosa are observed on histopathological examination

Following the diagnosis of the case as CD in stomach, passage X-rays of the small intestines and lower gastrointestinal system endoscopic examination were performed to determine whether or not other parts of the gastrointestinal system were involved; both were evaluated as normal.

In the thoraco-abdominal tomography, conglomerated lymph nodes were observed in para-esophageal and para-vertebral regions that continued up to the cardio-esophageal junction and contained calcifications in millimetric dimensions. The liver was larger than normal with regular contours. In

the sub-diaphragmatic region, there was a heterogeneous mass lesion with areas of hypodense necrosis measuring 7 x 9 cm within the neighborhood of the liver. Walls of the stomach were thick and had an edematous appearance. The spleen was not observed, and a structure with a diameter of 2 cm in the spleen region was consistent with an accessory spleen.

Blood transfusion of 5 units and fluid replacement therapy were performed since the patient was overly anemic and dehydrated because of vomiting. Corticosteroid therapy (60 mg/day), and IV H₂ receptor antagonist therapy (4x1) was started. She was able to receive orally in two weeks, thus I.V. therapy was replaced with oral therapy. Corticosteroids were reduced to 40 mg/day. Omeprazole 40mg/day (oral) and azathioprine 100 mg/day were added to the regimen. Bone mineral densitometry (BMD) examination was performed to exclude possible osteoporosis because of corticosteroid therapy and deficiency in intake. According to the results of BMD, femur neck (Z score -2.35) and Ward's triangle (-2.77) were osteopenic, inter was porous (-2.80), and L₁, L₂, L₃, and L₄ were osteopenic (Z scores 0.90, -1.51, -2.07, and -1.69, respectively). Calcium and vitamin D were added to the therapy.

Almost one month had passed until re-hospitalization of the patient. Nausea and vomiting had reduced, and the patient had begun to gain weight. Upper GIS endoscopic examination was repeated. Ulcers in the antrum and corpus had disappeared; diffuse polypoid lesions were present and the mucosa had a paving stone appearance. Monolithiasis of white color was observed in the esophagus. Ulcerations and erosion in the lower end of the esophagus and cardia continued. Lumen was still partially narrowed, but it was possible to advance to the stomach without forcing the endoscope.

Nausea and vomiting of the patient was improved, and hemoglobin value increased to 12 g/dl. Corticosteroid dosage was reduced to 10 mg by reducing it 5 mg each week. The patient took 10 mg/day corticosteroid and 100 mg/day azathioprine together for three months, then corticosteroid was stopped. The patient is being followed with 100 mg/day azathioprine, and she is still asymptomatic.

DISCUSSION

Crohn's disease is a chronic inflammatory disease of the gastrointestinal system that can involve any

part of the system from the mouth to the anus. Gastroduodenal involvement is rather infrequent (0.5-13%) (2, 3, 5). In general, histological changes in stomach and duodenum are present in patients with CD with a ratio of 20-40%. A clinically symptomatic disease, however, is seen with a ratio of 4% (4). Generally, proximal CD is seen many years later than distal CD (7).

Isolated gastric CD, however, is rare (8). In isolated gastric CD, other parts of the gastroduodenal system, and small and large intestines are entirely normal. In a study by Dutch University, which is the greatest study published to date, 940 patients who were diagnosed between 1934-1994 were studied, and it was found that only seven had isolated gastric CD (5, 9, 10). Our case also had isolated gastric CD. The results of her small intestine X-rays and colonoscopic examination were normal.

The symptoms of gastric CD are nausea, vomiting, epigastric pain, and weight loss (8,10). These symptoms arise from peptic ulcers and/or obstruction in the outlet of the stomach (1). In our case also, nausea and vomiting were predominant. In addition, the patient had dysphagia, and she had difficulty in swallowing solid food. In this case, involvement of the esophagus in an early stage was also present.

Endoscopic findings of proximal CD resemble that of distal CD, and include mucosal edema, focal and diffuse erythema, nodular lesions, erosion, and ulcers (11). In the series of Nugent, friability, ulcerations, and stricture were reported (9). In our case, there were endoscopic lesions, nodular lesions in the antrum and corpus, and diffuse ulcerations. Nodulations were observed in places. Endoscopic lesions are most frequently seen in the antrum in gastric CD (12, 13).

Isolated esophageal involvement in CD is again rather rare (14). When the literature is reviewed, it is seen that Dancygier and Frick (15) had reported the number of isolated esophageal CD cases as less than 80 as of 1992. Geboes et al. (16) reported the esophageal involvement in patients with CD as nine cases out of 500. Our case was not an isolated esophageal Crohn's case, however, it accompanied the gastric involvement. The esophagus was hyperemic and there were ulcerations in the endoscopic examination. The lumen was narrowed because of the ulcerations. In a study performed in Leiden University, which is considered as one of

the reference centers of inflammatory intestinal diseases, only seven of the patients had esophageal involvement out of 72 who were diagnosed as proximal CD. Only one of them accompanied gastric and duodenal CD (5).

The most frequent symptom in esophageal CD is dysphagia. It arises from mucosal ulcerations in the initial stage, and in later stages from formation of stricture. In more advanced stages of esophageal involvement, however, formation of fistulas has been described (14).

Histological findings of gastric CD resemble that of distal Crohn's. The most widely used histological finding in the diagnosis is the presence of granulomas. However, granulomas may not always be present. Granuloma is seen in only 9% of the cases. Acute inflammation is generally found (with a ratio of 56%) (10-17). CD is histologically found in the antrum with a ratio of 41.5%, followed by the corpus (37.1%), the bulbus (13%), and the duodenum (12.1%). The major site of involvement is the antrum (13). In our case, granulation tissue was also observed in histological examination.

There are controlled data for the treatment of gastroduodenal CD. H₂ receptor blockers or proton pump inhibitors are recommended as the initial therapy (1). Miehsler et al. (18) described symptomatic recovery in 10 cases with upper gastrointestinal symptoms with omeprazole, and Woolfson and Greenberg (19) described the same in four cases with non-obstructive gastroduodenal CD. Grübel et al. (10) reported no response with proton pump inhibitors in four cases with gastroduodenal CD.

Mesalamine, corticosteroids, 6-mercaptopurine, azathioprine, and infliximab are empirically used for the treatment of CD (1). Mesalamine can be effective by partially dissolving in the stomach and proximal small intestines. It has been reported in some small retrospective studies that CD in early stages responds to corticosteroids; however, there are no data regarding the long-term use. Promising results about 6-mercaptopurine or azathioprine therapies have been described in some small series (6, 20). There are no prospective, controlled studies about the use of infliximab in gastroduodenal CD. Grübel et al. (10) reported that they had given infliximab (5 mg/kg) in infusions in three dosages at the 0, 2nd, and 6th weeks to two of their cases, and that the ulcerations resolved in the first

case after the second dosage; however, the second case required surgical treatment because of refractory strictures, although the large jejunal ulcer resolved.

In our case, treatment with H₂ receptor blockers and corticosteroids was started as the initial therapy, and maintenance therapy was applied with azathioprine 100 mg/day.

Surgical therapy in CD can be indicated for ulcers

not responding to medical therapy, massive bleeding, in gastric outlet obstructions for which balloon dilatation is unsuccessful, or in cases where gastric fistulas have developed (1). Recurrence after surgical therapy is common, and re-operations are frequently required (5, 9).

As a result, isolated gastric Crohn's disease is a rare disease that imitates gastric tumors with difficult diagnosis and treatment; these two conditions can rarely be present together (21).

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