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# Crohn's colitis with extraintestinal manifestations: a case report

## Çeşitli ekstraintestinal bulguları olan bir Crohn kolitisli hasta: Olgu sunumu

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*The etiopathogenesis of inflammatory bowel disease remains unclear, with various extraintestinal features often found with the disease. Sometimes more than one extraintestinal finding is found in the same patient. In this case report, a patient with more than one extraintestinal manifestation of Crohn's disease is presented. Extensive thrombi in the venous system and pyoderma gangrenosum in the left lower extremity was observed but there was complete recovery following treatment with both systemic and topical agents.*

**Key words:** Crohn's disease, extraintestinal manifestations.

*İnflamatuar barsak hastalıklarının etiyolojisi henüz tam olarak aydınlanmamıştır. İnflamatuar barsak hastalıklarında çeşitli ekstraintestinal bulgular görülebilir. Bu bulguların etyopatogenezinde pekçok teori ileri sürülmektedir. Ekstraintestinal bulguların bazen birden fazlası aynı hastada görülebilmektedir. Burada tartışılan olgu; bir Crohn hastası olup, birden fazla ekstraintestinal bulgusu vardı; venöz sistemde yaygın trombozlar ile sol alt ekstremitede pyoderma gangrenosum izlenmiş olup; bulgularda gerek sistemik, gerekse topikal tedavi ile düzelme sağlanmıştır.*

**Anahtar kelimeler:** Crohn hastalığı, ekstraintestinal bulgular.

## INTRODUCTION

Inflammatory bowel disease (IBD) is a group of diseases characterised by inflammation and mucosal injury of the small intestines and colon. Anemia, malabsorption, cholelithiasis and nephrolithiasis are the most frequently observed complications that are directly associated with IBD. Also, in both Ulcerative Colitis (UC) and Crohn's Disease (CD), extraintestinal manifestations may occur in various organs and tissues. Thus, IBD is considered to be a systemic disease.

In a large series of patients, the incidence of extraintestinal involvement has been reported to be 25%-36% (1, 2). Thus in a least a quarter of patients, more than one extraintestinal manifestation can be seen. Of these, the most frequently observed is the triad of joint, occular and skin involvement (3).

In this report we present a case of Crohn's colitis in which pyoderma gangrenosum, thrombosis and presence of anticardiolipin antibodies was observed, the latter of which has not been reported to be associated with Crohn's colitis in the literature.

## CASE

A 40-year-old female was referred to our department with a diagnosis of CD and pyoderma gangrenosum. She presented with a four month history of bloody diarrhea and a painful ulcerated lesion located on the back of her left thigh. She also had complaints of abdominal pain, bloody mucousy diarrhea, weakness, loss of appetite and weight loss. Past medical history included one miscarriage and a traffic accident. On physical examination, her body temperature was 37°C, the spleen was palpable approximately 7 cm from the costal arc and an ulcerated, oozing lesion, 20 cm x 25 cm, was observed on the posteriomedial part of her left thigh (Figure 1). Laboratory analysis showed a hemoglobin value of 10.8 gr/dl, hematocrit 32.8%, leukocyte count of 6100/mm$^3$, platelet count of 181000/mm$^3$ and an erythrocyte sedimentation rate (ESR) of 42mm/hr. Her blood biochemistry revealed CRP 96mg/dl, albumin 3.1gr/dl and normal liver and kidney function tests.

The activity index of Crohn's disease (CDAI) was calculated to be 281. ANA, anti-dsDNA, anti-HIV,

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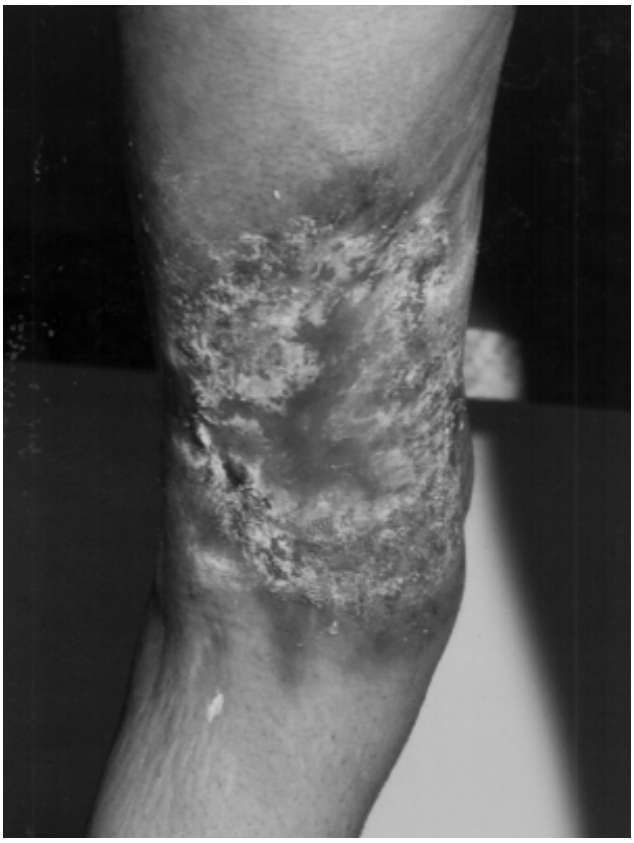

**Figure 1.** Ulcerated oozing lesion on the posteriomedial part of the patients left thigh.

HbsAg, anti-HBs, and anti-HCV were all negative. Histopathologic examination of the specimen taken from the lesion on her left thigh supported a diagnosis of pyoderma gangrenosum.

Colonoscopic studies revealed hyperemic, friable, deep, scattered ulcers 4-5 mm in diameter, polypoid lesions, mucosal bridging, and intermittent pale and hollow areas in the mucosa of the rectum, sigmoid and descending colon (Figure 2). Due to the narrowing in the lumen of the proximal parts of the colon, it was not possible to access the descending colon. Biopsies were taken and the histopathologic reports supported the diagnosis of CD. At double contrast colon examination, a narrowing, that did not obstruct the passage, was found in a six cm segment of the splenic flexura. Upper gastrointestinal x-ray series, including the small intestine, were normal.

At abdominal and portal venous ultrasonography, dilated and thickened walls of bowel segments, splenomegaly, recanalised thrombus in the splenic and portal veins, total occlusion of the right portal vein branch and a recanalised thrombus in the left branch with collaterals in the splenic hilus were found. During the examinations, complaints of pain and swelling in the left leg by the patient prompted a bilateral lower extremity venous Doppler ultrasonographic examination. Thrombi were found in the left main femoral vein and its branches and in the popliteal vein.

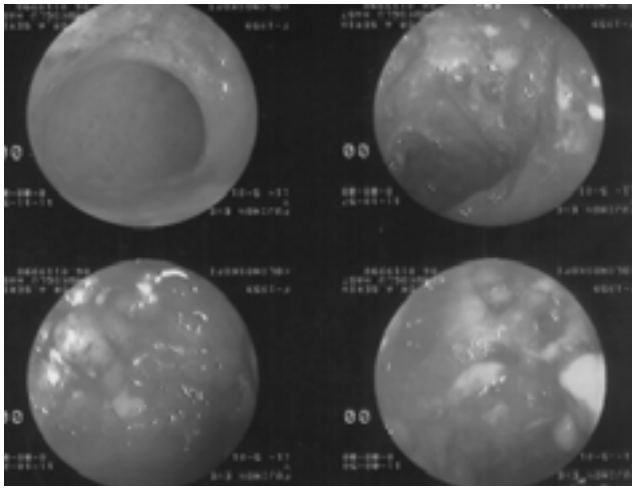

**Figure 2.** Colonoscopic appreance of the mucosa of the rectum,sigmoid and descending colon

Tests carried out to clarify the etiology of thrombosis showed levels of antithrombin-III, proteins C and S, factors V and VIII and APC resistance to be within normal limits. The anticardiolipin antibody (ACL) IgM level was found to have increased to 1.6 MPL (normal range 0-1.1). ACL IgG was negative.

The patient was put on a diet rich in calories but deficient in fiber and given oral prednisolone 40 mg/day together with topical oral care as recommended by dermatologists. Anticoagulant therapy was initiated with heparin then later followed by warfarin. Four weeks after the initiation of treatment, improvement in both the clinical and laboratory parameters was observed with an approximately 50% recovery in the lesion on the thigh. The steroid dose was gradually decreased and oral 5-ASA (Salofalk, 2gr/day) was added to the treatment regime. Anticoagulant therapy and wound care were continued.

Three months later the patient had no complaints except for occasional swelling. Defecation frequency decreased to one-three times per day, was formed and contained neither blood nor mucus. She had no fever, abdominal pain, nausea or vomiting. Her appetite was good with a 7 kg gain in

weight. The wound on her thigh had almost disappeared and systemic examination revealed no abnormal finding except for splenomegaly. She had a decrease of 175 points in the CDAI. Her hemoglobin was 13.2 gr/dl, hematocrit 40%, leukocyte count 12900, platelet count 153000, ESR 8 mm/hr, albumin 4.3 gr/dl, and CRP was negative. Her echocardiographic and thorax computerised tomographic findings were normal.

## DISCUSSION

Various extraintestinal findings are observed in IBD. Although these usually occur during the course of IBD, they may also appear before the bowel symptoms and even after colectomy. These extraintestinal findings are found more frequently in CD than in UC and in Crohn's colitis, are found more frequently than in the small intestine itself (3). More than one finding can also be found at the same time, with erythema nodosum, arthritis and uveitis most frequently being found together. We did not come accross any research in the literature associating IBD with pyoderma gangrenosum, thrombosis and ACL antibodies, as seen in our patient.

Various skin lesions have been reported in IBD. Of these, the most frequently observed are erythema nodosum and pyoderma gangrenosum, both seen in 5% of patients (4). Pyoderma gangrenosum occurs most frequently in the lower extremities but can also be found in the face and even in the oral cavity. Although it has no correlation with the severity of the bowel disease, it generally appears during the active phase. It has been reported to occur at incision sites caused by trauma (7,8). Our patient stated that the lesion on her thigh appeared after the traffic accident she suffered.

The risk of both arterial and venous thrombosis is increased in IBD. In contrast to the rate of 39% found in autopsy series, in the clinical setting it is seen in only 1-3% of cases (7). Deep vein thrombosis usually causes pulmonary emboli with a high mortality risk. Thrombi may also form at different sites such as the cerebral arteries and sinuses, coronary vessels, hepatic veins, mesenteric arteries and veins, gonadal veins and retinal vessels (7,9,10). Although the etiopathogenesis of thrombosis seen in IBD is not fully understood, coagulation problems have been reported. In the active disease, factors V and VIII and fibrinogen are increased, whereas antithrombin III and proteins C and S levels have been found to be low (9,10). Active protein C resistance is an important cause (11). Fibrinolytic activity is decreased whilst the platelet count, activity and spontaneous platelet aggregation are increased.There was no thrombocytosis in our patient and the proteins C and S, factors V and VIII, and antithrombin III levels were normal.

During remission, the previously increased coagulation factors and platelet counts return to normal. However, the abnormalities in fibrinolysis and spontaneous platelet aggregation and the increased risk of thrombosis have been shown to continue during remission (12-14). In CD in particular, the increase in the ACL titer is reported to raise the risks of both venous and arterial thrombosis. However, no correlation is observed between the degree of disease activity and the titer of ACL antibodies (15). The ACL IgM titer in our patient, who also had a history of miscarriage, was increased.

Although some authors report that treatment of IBD results in resolution of the hemostatic abnormalities (9), in view of the fact that recurrent thromboembolic events can still occur, long term use of anticoagulants are considered appropriate (9,15).

Pyoderma gangrenosum responds well to systemic and/or topical steroids, topical antibiotics and to cyclosporine or FK-506 treatment in resistant cases. While topical treatment is usually prescribed systemic treatment of the bowel disease is in fact adequate for healing of the lesion (7). With both prednisone 40 mg/day and topical treatment, we observed a decrease in the activity index of CD and also recovery of the thigh lesion of our patient. During the follow up period, there was no incident of thromboembolism. The patient was therefore discharged with the recommendation that the steroid dose be tapered and finally stopped with 5-ASA and anticoagulant treatment continuing under out patient follow-up.

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