

CLINICAL STUDY

Deep vein thrombosis associated with celiac disease

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Abstract: *Introduction:* Cases of venous thrombosis associated with celiac disease have been rarely published. We report a case of celiac disease associated with deep venous thrombosis in the left leg.

Material and methods: A 44-year old man was admitted to the hospital due to diarrhea, which was present for three months. The diarrhea was present 5–6 times a day and was neither mucous nor bloody. Microscopic examination of feces was normal. No pathogenic microorganisms were isolated in culture. Esophagogastro-duodenal endoscopy showed bulbar and post-bulbar mucosal granularity. Jejunal biopsy revealed flattening of mucosa and cellular infiltration of lamina propria with plasma cells and lymphocytes. The IgA anti-gliadin antibodies and IgA anti-endomysium antibodies were positive. The diagnosis of celiac disease was made and gluten-free diet was started. On the seventh day of hospitalization, a marked swelling, erythema and pain developed in the left leg. Doppler ultrasonographic examination revealed an acute thrombotic process in the left proximal venous system. Investigations for the causes of thrombotic status were negative. The long term outcome is favorable with gluten-free diet and warfarin treatment.

Discussion: It should be kept in mind that there is a tendency toward thromboembolic events in patients with celiac disease, especially during an acute phase of the disease (Ref. 5). Full Text (Free, PDF) www.bmj.sk.
Key words: celiac disease, venous thrombosis, thrombophilia.

Besides predisposing hereditary conditions, arterial and venous thrombotic events have been reported also during the course of acquired systemic diseases. Celiac disease is a chronic, immune-mediated enteropathy, mostly associated with malabsorption caused by gluten intolerance. Celiac disease is associated with several extraintestinal conditions such as type I diabetes mellitus, Sjögren disease, etc. Venous thrombosis has been rarely reported. Budd-Chiari syndrome associated with intraabdominal venous thrombosis represents the majority of the reported cases. Although an intraabdominal thrombosis have been reported, development of venous thrombosis in the extremities is rare in patients with celiac disease. In this study, we present a patient hospitalized for diarrhea with subsequent development of deep vein thrombosis in the left leg and the review of literature.

Case report

A 44-year old man was admitted to the hospital due to diarrhea which was present for three months. The diarrhea had the frequency 5 to 6 times a day and was not mucous neither bloody. On physical examination, abdominal tenderness and pretibial edema was noted with no other remarkable finding. Hemoglobin

was 11.7 g/dl. Ferritin level was 427.2 ng/ml (range 28–365 ng/ml), serum iron level 12 µg/dl (25–156), serum folate level 1.4 ng/ml (2.7–34), serum vitamin B12 level 124 pg/ml (200–900). The total binding capacity of iron was 66 µg/dl (250–425). The total serum protein and albumin levels were 38 g/l (64–83) and 23 g/l (35–54), respectively. Microscopic examination of feces was normal. Pathogenic microorganisms were not detected in the culture of feces. Abdominal ultrasonographic examination was normal. Esophagogastroduodenal endoscopic examination showed bulbar and post-bulbar mucosal granularity. Histological examination of jejunal biopsy revealed flattening of mucosa and cellular infiltration of lamina propria with plasma cells and lymphocytes. The number of intraepithelial lymphocytes was also increased. The anti-gliadin antibody IgA and anti-endomysium antibody IgA were positive. The diagnosis of “celiac disease” was made and gluten-free diet was started. On the seventh day of hospitalization, a marked swelling, erythema and pain developed in his left leg and the Homan’s sign was positive. Doppler ultrasonographic examination revealed an acute thrombotic process in left external iliac vein, main femoral vein, proximal part of vena saphena magna, deep and superficial femoral vein and area extending to the middle part of popliteal vein. Enoxaparin 1 mg/kg bid subcutaneously was started. Examinations on factor V Leiden, prothrombin 20210 gene mutation, lupus anticoagulant and anticardiolipin antibodies were negative. Serum homocystein level and activities of protein C and S were normal. Enoxaparin treatment was switched to warfarin after two weeks. The long term outcome is favorable with gluten-free diet and warfarin treatment.

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Discussion

There is some data proving a causal relation of procoagulation state in the promotion of thromboembolism in celiac disease. In some cases, thromboembolism has been attributed to acquired hyperhomocysteinemia as a consequence of folic acid and vitamin B12 deficiency (1). Bahloul et al reported a patient with celiac disease who developed cerebral venous thrombosis (2). The etiologic investigation revealed the protein S deficiency. Karoui et al also reported a patient with portal vein thrombosis and celiac disease (3). In this patient, the anticardiolipin antibody IgG and anti-beta2 glycoprotein antibodies were positive. Lee and Pulido described a woman with non-ischemic central retinal vein occlusion associated with celiac disease (4). They suggested that dehydration due to diarrhea and celiac disease or hyperviscosity from the circulating anti-gliadin antibodies might cause a thrombotic event. In our patient, plasma homocystein level and activities of protein C and S were normal. Factor V Leiden, prothrombin 20210 gene mutation, lupus anticoagulant and anticardiolipin antibodies were negative. We could not define an etiological factor for thrombotic tendency in our case. In literature, in most cases the etiological factor could not be determined. The exact causes of thrombosis in patients with celiac disease are yet unknown.

Saibeni et al studied the frequency of hyperhomocysteinemia, which is a risk factor for thrombosis, in patient with celiac disease (5). They found that hyperhomocysteinemia, which is a re-

sult of vitamin deficiency caused by malabsorption, is more frequent in patients with celiac disease compared to the control group. Because we could not demonstrate hyperhomocysteinemia despite the presence of vitamin deficiencies in our patient, we could not make this factor liable for the thrombosis process.

In summary, it should be kept in mind that there is a tendency to thromboembolic events in patients with celiac disease, especially during an acute exacerbation of the disease.

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