SHORT REPORT

Internal iliac vein thrombosis in pediatric Crohn's disease☆

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Abstract

Thromboembolic events are one of the important extraintestinal manifestations of inflammatory bowel diseases that are associated with considerable morbidity and mortality. Iliac vein thrombosis is rarely reported in inflammatory bowel diseases. A 9.5 year-old girl was presented with joint pain, nausea, vomiting and weight loss. She was diagnosed with Crohn's disease and right internal iliac vein thrombosis. With the implementation of immunosuppressive and anticoagulant therapies clinical picture has improved and thrombosis has resolved. Timely diagnosis and early treatment of extraintestinal complications of inflammatory bowel diseases might be lifesaving.

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1. Introduction

Inflammatory bowel diseases (IBD) are associated with various extraintestinal manifestations.1 Among these, thromboembolic events are one of the major causes of morbidity and mortality.2 Diverse risk factors for thromboembolism are present in IBD; namely, factors that are acquired during active disease such as hypercoagulable state and factors that are already present such as inherited causes of thrombophilia.2,3 Approximately 90% of venous thromboembolism episodes in childhood have an underlying condition.4 Although IBD is associated with various venous thromboses, association of iliac vein thrombosis and inflammatory bowel disease is rare. We present a 9.5 year-old child with Crohn's disease and internal iliac vein thrombosis.

2. Case report

A 9.5 year-old girl was presented with epigastric, right groin and ankle pain, and nausea and vomiting of 1 month

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duration. The pain was worse after meals, severe, non-radiating and cramping in nature. She lost 5 kg in the previous month. There was no fever, swelling or redness in the joints. She was constipated. There was no history of diarrhea and blood in stool.

Her past medical history was unremarkable except for premature adrenarche which she was being followed for 15 months. She was not using any drugs for treatment.

On presentation the initial physical examination revealed an exhausted 9.5 year-old girl with epigastric and right groin pain on palpation. There was no swelling, warmth or erythema in the lower extremities. Axillary temperature was 37.3 °C. Laboratory tests indicated an active inflammatory process with sedimentation rate of 68 mm/h, C reactive protein of 6.8 mg/dL (normal <0.5), and fibrinogen of 611 mg/dl (normal 100–300). Complete blood count revealed a white blood cell count of 9600/mm³, hemoglobin of 11 g/dl, hematocrit of 33% and platelets of 684,000. Fecal calprotectin was 843 μg/gr (N <50). Serological tests for EBV, CMV and Salmonella were negative as well as autoimmunity markers, including ANA, ds-DNA, and ANCAs.

Occult blood in stool was positive. The results of a comprehensive metabolic panel, urinalysis, as well as levels of amylase were all within normal limits. Upright and supine radiographs of the abdomen revealed no abnormality. Hip joint ultrasonography was normal and no effusion was seen in hip joints. Abdominal ultrasonography revealed thickening of the terminal ileum wall. At this time, she developed severe right lower quadrant pain. Abdominal CT scan revealed thickening of the wall of the ascending colon, cecum, and terminal ileum. There were multiple pericecal lymph nodes. There was an evidence of partial thrombus in the right internal iliac vein (Fig. 1).

Before the implementation of anticoagulant therapy esophagogastroduodenoscopy (EGD) and colonoscopy were performed. EGD revealed edematous, hyperemic and ulcerated corpus and antrum. The duodenum and esophagus seemed to be normal. Histopathological examination showed lymphoplasmocytic and neutrophilic leukocyte infiltration in the lamina propria of the corpus and antrum. Colonoscopic examination showed evidence of active colitis with ulcers and erosions in both terminal ileum and colonic segments. Histopathological examination demonstrated cryptitis, crypt abscess and granuloma-like formations in terminal ileum. Colonic biopsy specimens showed local irregularities in the crypts, cryptitis and lymphoplasmocytic and neutrophil leukocytic infiltrations in the lamina propria. With these results, she was diagnosed with Crohn’s disease and internal iliac vein thrombosis.

Pathergy test was performed to exclude Behcet’s disease and was found negative. Anticardiolipin and antiphospholipid antibodies were negative. Patient was found to be heterozygous for factor V Leiden mutation, while PT 202100 and MTHFR mutations were negative. Factor VII activity was 267% (53–170), factor V and XIII activities were within normal limits. Homocysteine level was normal. Protein C and protein S activities were 136% and 78% normal, respectively.

Prednisolone (60 mg/day), 5-ASA (30 mg/kg/day), and heparin infusion for iliac vein thrombosis were started. At the 10th day of heparin treatment, repeated Doppler ultrasonography demonstrated persistence of partial thrombus allowing blood flow in the right internal ileac vein. She was discharged on warfarin, prednisolone and 5-ASA at the 20th day of hospitalization. At the end of the 1 month treatment her complaints decreased. Azathioprine was added to her treatment regime at the 1st month of therapy while prednisolone was being tapered.

Three months after the diagnosis, repeated abdominal CT demonstrated thickening of the wall of the terminal ileum. There was no evidence of thrombus in the right iliac vein. Prednisolone treatment was stopped at the 5th month of treatment. Five months after the discontinuation of prednisolone, she started to experience occasional bloody stools and acute phase reactants became positive. For this reason prednisolone treatment was instituted again. Thirteen months after the diagnosis, repeated colonoscopy showed completely normal macroscopic and microscopic findings. Prednisolone was tapered slowly. At the 15th month of diagnosis warfarin treatment was stopped. After 24 months of diagnosis, she was in remission on azathioprine (1.5 mg/kg/day).

3. Discussion

Approximately 90% of episodes of venous thromboembolism in childhood have an underlying, serious condition as an etiological factor causing the thrombosis. These conditions include central venous catheters, malignancy, trauma, surgery, congenital heart disease and other malformations of the vascular system, renal disease and autoimmune diseases such as systemic lupus erythematosus, and IBD. Moreover defects affecting the physiological anticoagulant system and deficiencies of protein C and S might contribute to venous thromboembolism.

Inflammatory bowel disease is closely associated with venous thrombosis. Presence of IBD was shown to increase TE risk 3.6 fold in adults and 1.8 fold in pediatric patients. Thromboembolism frequently, but not necessarily, occurs during active inflammation phase. Components of hemo- stasis, i.e. platelets, coagulation and fibrinolysis, are affected in favor of a hypercoagulable state in IBD. Inflamed mucosal microvasculature in IBD was thought to activate platelets to overexpress CD40 ligand which in turn might contribute to increased prothrombotic state. Activity of factors V, VII, and VII were increased. The role of the congenital thrombophilic factors such as factor V Leiden, MTHFR mutations were negative. Factor VII activity was 267% (53–170), factor V and XIII activities were within normal limits. Homocysteine level was normal. Protein C and protein S activities were 136% and 78% normal, respectively.

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Figure 1  CT scan shows partial thrombus in the right internal iliac vein (arrow).
prothrombin G20210A and MTHFR mutations in thrombosis in patients with IBD remains controversial.\textsuperscript{8,9} Pancolonic involvement with active disease, increased fibrinogen and platelet count, and heterozygote Factor V Leiden mutation and increased activity of Factor VII might all have contributed to the thrombosis to some extent in our patient. Illofemoral deep vein thrombosis is infrequent in children. Isolated iliac vein thrombosis was rarely associated with IBD.\textsuperscript{10} Obstruction of one or both iliofemoral veins might be asymptomatic or cause swelling and pain in the lower extremity or thigh and might result in pulmonary embolism.\textsuperscript{11} Our patient had only right groin pain that might be attributable to deep vein thrombosis.

Treatment of deep vein thrombosis is divided into two major modalities; mainly surgical and medical. Surgical thrombectomy is reserved for acute life-threatening conditions. Medical treatment is composed of unfractionated or low molecular weight heparin as the initial therapy and oral anticoagulants such as warfarin as the maintenance therapy.\textsuperscript{5} It was recommended that, in the first episode of thrombus, with the persistence of chronic clinical risk factors, anticoagulant therapy had to be continued for 12 months. Our patient was managed successfully with initial heparin therapy for 10 days and maintained on warfarin as well as IBD therapy. Partial and complete resolution of thrombus was achieved at 10th day and 3rd month of treatment respectively. Physicians caring for IBD patients should give proper attention to the unusual signs, like groin pain in our patient, in the course of disease and increased venous thromboembolism risk should be kept in mind. Once thrombus is developed long-term patient management, including control of disease activity and the treatment of thrombosis are important to prevent complications.

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GB carried out the follow-up of patient, collected the data and drafted the manuscript.

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SAE carried out the follow-up of patient, participated in the design and coordination of the study and helped to draft the manuscript.

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