

RECURRENT ISCHEMIC COLITIS IN A PATIENT WITH LEIDEN FACTOR V MUTATION AND SYSTEMIC LUPUS ERYTHEMATOUS WITH ANTIPHOSPHOLIPID SYNDROME

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Abstract

Ischemic colitis results from insufficient blood supply to the large intestine and is often associated with hypercoagulable states. The condition comprises a wide range presenting with mild to fulminant forms. Diagnosis remains difficult because these patients may present with non-specific abdominal symptoms.

We report a 51-year-old female patient with known Leiden factor V mutation as well as systemic lupus erythematosus along with antiphospholipid syndrome suffering from recurrent ischemic colitis. At admission, the patient complained about abdominal pain, diarrhea and rectal bleeding lasting for 24 hours. Laboratory tests showed an increased C-reactive protein (29.5 mg/dl), while the performed abdominal CT-scan revealed only a dilatation of the descending colon along with a thickening of the bowel wall.

Laparotomy was performed showing an ischemic colon and massive peritonitis. Histological examination proved the suspected ischemic colitis. Consecutively, an anti-coagulation therapy with coumarin and aspirin® 100 was initiated. Up to the time point of a follow up examination no further ischemic events had occurred.

This case illustrates well the non-specific clinical presentation of ischemic colitis. A high index of suspicion, recognition of risk factors and a history of non-specific abdominal symptoms should alert the clinicians to the possibility of ischemic disease. Early diagnosis and initiation of anticoagulation therapy or surgical intervention in case of peritonitis are the major goals of therapy.

Key words: Ischemic colitis, factor V Leiden mutation, lupus erythematosus, antiphospholipid syndrome, therapy.

INTRODUCTION

Ischemic colitis is considered as disease of the elderly population resulting from insufficient blood supply to the large bowel. It is often associated with hypercoagulable and abnormal portal states [1, 2]. In cases of adequate collaterals, intestinal vein thrombosis does not inevitably lead to bowel infarction since in this case the venous drainage is secured, therefore haemorrhagic infarction is prevented.

However, ischemic colitis comprises a wide spectrum of presentation forms, ranging from mild to ful-

minant. Diagnosis remains difficult, because it can affect individuals without known predisposing disorders and these patients may present non-specific abdominal symptoms [3, 4]. So far, two different types of ischemic colitis have been described. First, a gangrenous form associated with transmural necrosis and secondly, a milder transient form with reversible lesions to the mucosa and sub mucosa [5].

We report the case of recurrent ischemic colitis in a female patient with Leiden factor V mutation and systemic lupus erythematosus with antiphospholipid syndrome.

CASE REPORT

A 51-year-old female patient was admitted to our university hospital with a 2-day history of cramp-type abdominal pain with rectal bleeding and diarrhea. The clinical examination showed diffuse abdominal tenderness, with signs of peritonism. The patient's body temperature was 37.7°C, the peripheral pulse was 85 beats/minute, and the blood pressure was 125/70 mmHg. Complete blood counts, electrolytes, liver function tests, renal function, urinalysis, amylase and lipase were all within normal range. Calcitonin was 0.7 ng/ml (normal: <0.5 ng/ml) and C-reactive protein was 29.5 mg/dl (normal: <0.5 mg/dl), indicating severe inflammation, but however of very unspecific character.

The medical history of the patient presented a thrombosis of vena jugularis and vena brachiocephalica that had occurred six years ago. Furthermore, the patient developed an ischemic colitis of the coecum six years ago, as well as of the sigma seven years ago. Both times, surgical resection of coecum and parts of the sigmoid colon were performed as therapeutic regime. Thereafter, heterozygosity for factor V Leiden mutation was diagnosed and long-term anticoagulation treatment with coumarin was initiated. Weekly controlled international normalized ratio values had consistently remained within the therapeutic range of 2.5-3.5. The additional medical history included a systemic lupus erythematosus and antiphospholipid syndrome, with primary diagnosis 15 years ago. The patient's sister was also diagnosed with systemic lupus erythematosus.

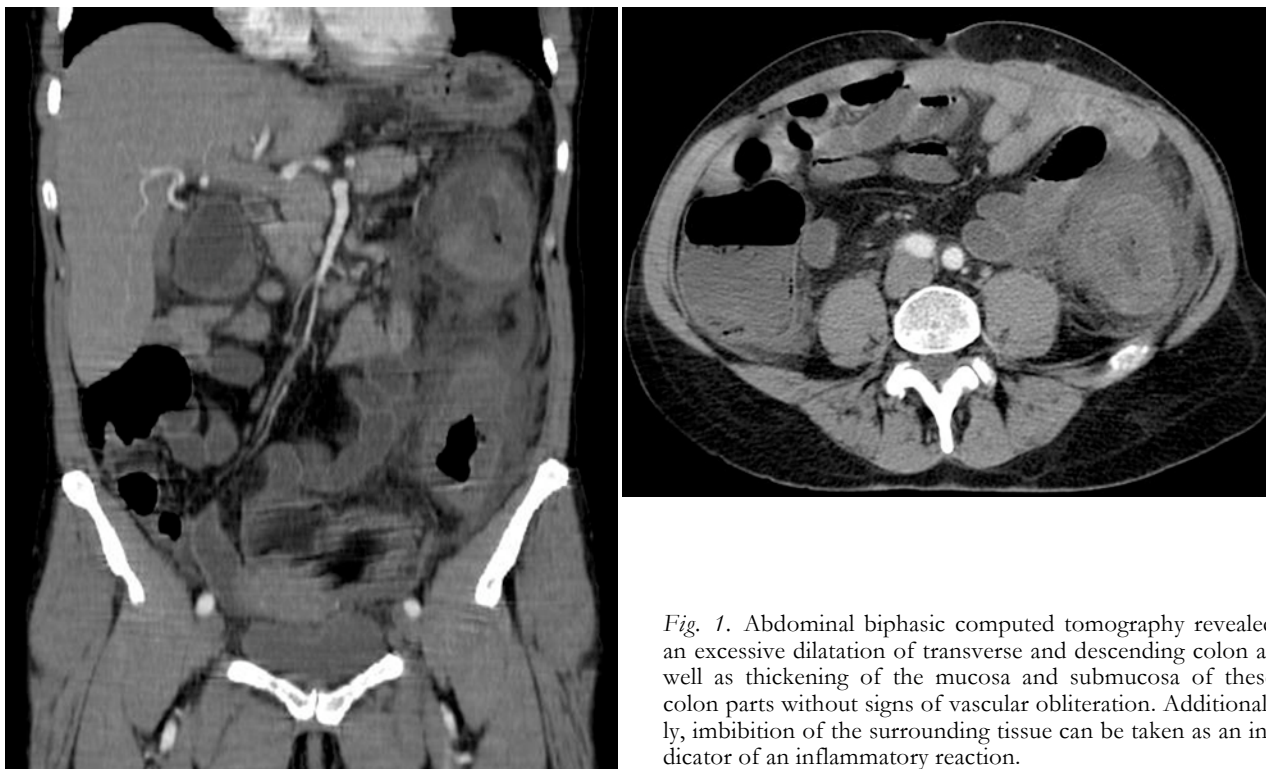


Fig. 1. Abdominal biphasic computed tomography revealed an excessive dilatation of transverse and descending colon as well as thickening of the mucosa and submucosa of these colon parts without signs of vascular obliteration. Additionally, imbibition of the surrounding tissue can be taken as an indicator of an inflammatory reaction.

Clinical examination showed signs of peritonism and ultrasound of the abdomen revealed a dilatation of the colon lumen. Abdominal biphasic computed tomography revealed an excessive dilatation of the transverse and descending colon as well as thickening of the segmental wall of these colon parts without signs of vascular obliteration (Fig. 1).

Because of these findings, our patient underwent surgery. During surgery, an ischemic disaffection of the descending colon was visible along with signs of massive peritonitis, but without apparent involvement of the large bowel-supplying vessels. Therefore, the descending colon was resected and consecutively a protective ileostoma was constructed. Histological examination of the resected colon presented an ischemic colitis with thrombosis of the mucosal veins and venules.

After surgery the patient recovered well and was discharged from the hospital two weeks thereafter. An anti-thrombotic therapy with coumarin and aspirin® 100 was initiated. Up to a follow up examination 18 months after surgery, the patient had not developed any further thrombotic or ischemic events.

DISCUSSION

Different studies regarding the epidemiology of ischemic colitis have shown incidence rates ranging from 9.9 to 47 per 100.000 per person years. However, many cases of ischemic colitis still seem to be underdiagnosed. Therefore, the true incidence of ischemic colitis remains unclear. Several reasons may explain this underestimation of ischemic colitis, including its various presentation form and the fact that most patients are not hospitalized or do not seek for medical help [6-8].

Several, different comorbidities have been described in patients with ischemic colitis. In most patients hypertension (51% - 57%) can be found, 30% - 51% of the patients show cardiovascular diseases and 9% - 30% have renal failure or nephropathy. Diabetes mellitus can be found in up to 25%. Finally, an association with cancer or chronic respiratory diseases can be seen in some patients [2, 3, 9, 10].

Thrombosis, embolism, shock, trauma, decreased cardiac output, arrhythmia, vasculitis or disorders of coagulation are considered as risk factors of ischemic colitis. In some cases, drugs such as meloxicam, pseudoephedrine or immunosuppressive agents have been also described as risk factors [1, 11, 12].

Hypercoagulable states such as factor V Leiden, Prothrombin G20210A, Antithrombin III and mutation of the methylene tetrahydrofolate reductase gene are predisposing factors for the development of an acute mesenteric ischemia. A clinical trial comparing patients who developed an acute mesenteric ischemia with normal controls regarding prothrombotic disorders revealed a higher prevalence of prothrombotic disorders in patients with acute mesenteric ischemia [2]. In our case, the combination of systemic lupus erythematodes with antiphospholipid syndrome and a heterozygous factor V Leiden mutation could be the reason for developing recurrent ischemic colitis.

In general, ischemic colitis may affect any part of the intestinal tract. The left colon flexure seems to be the most susceptible area regarding ischemic injury because this area has the potential to suffer from an incomplete anastomosis between the superior and inferior mesenteric arterial circulation. Retrospective studies showed that in most cases of ischemic colitis the left colon segment were involved (40% - 47%). The right colon (ascending colon) is only affected in 30% - 33%,

the left colon flexure in 18%-28% and the transverse colon in 20% - 25% [3,9].

In the majority of the cases an early diagnosis of colon ischemia is difficult and therefore requires a high index of clinical suspicion. Clinical examination reveals abdominal pain in more than 68% of the patients, and the majority complains about diarrhea, melaena or rectal bleeding. Peritoneal signs can be present in only 11% of patients. In few cases, a temperature increase above 38.5°C can be found and a drop of systolic blood pressure below 90 mmHg. Routine laboratory tests are unhelpful or unspecific [3, 9].

The abdomen is easily accessible to ultrasound; however, ultrasound exams have several limitations such as overlay by gastrointestinal gas, obese patients and the experience of the examiner. Ultrasound has a sensitivity of 93% in detecting a colon wall thickening. But the specificity of bowel wall thickening is low [1, 13]. Angiography is the golden standard imaging method in cases of an embolism or thrombosis of the mesenteric vessels. In our case, only small vessels were obstructed and therefore, angiography could not help to find the diagnosis. Some authors suggest additional colonoscopy with biopsy to confirm the diagnosis of ischemic colitis in these cases [10, 13-16].

The treatment of ischemic colitis usually consists of anticoagulation alone or in combination with surgery. In single cases, alternative therapeutic treatment with prostaglandin E1 has been reported. The presence of peritoneal signs indicates a surgical exploration, since bowel infarction has probably occurred already. Subsequent management is dictated by the surgical findings, ranging from small segmental infarction to necrosis of the entire bowel with or without perforation. Systemic heparin therapy after operation should be initiated with a bolus injection of 5000 IU, followed by a continuous infusion adjusting the applied dose leading to an activated partial thromboplastin time twice as high than normal. Once the absence of an ongoing ischemia is proven an oral anticoagulation therapy with coumarin should be started [15, 17, 18].

In cases of coagulation abnormalities and/or vascular diseases patients might develop recurrent ischemic events as demonstrated in our case. Sometimes, oral anticoagulation does not prevent from thromboembolic or ischemic events. We started a therapy with coumarin and aspirin® 100 after surgical intervention and had no further complications during follow up.

The majority of patients with ischemic colitis do survive with conservative therapy. Patients, who require surgery, have a high mortality rate due to a delayed diagnosis, especially if the disease occurs in the ascending colon. The extent of the disease is not itself associated with a poor prognosis [3, 9].

CONCLUSION

Ischemic colitis occurs most commonly in elderly patients with co-morbid conditions such as hypertension or diabetes. However, this disease can be also seen in younger patients with coagulation and vascular abnormalities as described in our case. Adequate patients' management during and after operation is necessary for the patients' outcome. Due to a delayed diagnosis,

the prognosis might be poor, especially if the ascending colon is affected [4, 9, 15].

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Received: February 13, 2007 / Accepted: January 15, 2008

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