SHORT REPORT

Idiopathic myointimal hyperplasia of mesenteric veins and pneumatosis intestinalis: A previously unreported association

Raquel García-Castellanos, Raquel López, Vicente Moreno de Vega, Isabel Ojanguren, Marta Piñol, Jaume Boix, Eugeni Domènech, Eduard Cabré

A G-I Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain
B Department of Pathology, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain
C Endoscopy Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain
D Department of Surgery, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain
E Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Barcelona, Spain

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Abstract

Idiopathic myointimal hyperplasia of mesenteric veins is a very rare disease occurring in young male patients, with no more than eight cases reported in the world literature. It causes venous ischemia in the sigmoid colon and rectum that clinically resembles inflammatory bowel disease. Pneumatosis intestinalis is also a rare condition usually associated to a wide range of diseases including bowel ischemia. We herein report on a case of pneumatosis intestinalis associated to idiopathic myointimal hyperplasia of mesenteric veins. To our knowledge, this is the first report of such an association, and the first one of idiopathic myointimal hyperplasia of mesenteric veins occurring in a female patient as well.

1. Introduction

Idiopathic myointimal hyperplasia of mesenteric veins (IMHMV) is a very rare disease that was firstly described by Genta and Haggitt in 1991. To date, there are only eight cases reported in the world literature, all of them occurring in young male patients. IMHMV usually presents with rectal bleeding and other symptoms that closely resemble those of inflammatory bowel disease. The diagnosis is made at the histopathological examination of the surgical specimen, which exhibits a proliferation of smooth muscle cells in the intima of veins and venules in the territory of the lower mesenteric vein, whereas arteries are normal. Although the pathogenic mechanisms for IMHMV are unknown, its clinical course is benign and without relapses after resection.
Pneumatosis intestinalis (PI) is also an infrequent condition characterized by the presence of gas within the wall of the gastrointestinal tract. Although PI may occur as a primary disease, it is mostly associated with a variety of underlying conditions. However, an association of PI with IMHMV has never been reported.

We herein report on a case of PI associated to IMHMV. To our knowledge, this is the first report of such an association, and the first one of IMHMV occurring in a female patient as well.

2. Case report

A 32-year-old woman, without remarkable medical or surgical history arrived at the emergency department with pain in the lower left quadrant of the abdomen in the previous month together with low-volume diarrheal stools (6–7 per day) with blood and mucus. The patient did not report fever, weight loss, or extraintestinal symptoms. She was an occasional smoker, and the epidemiological history only disclosed the intake of raw fish two weeks before. There was no history of recent travel abroad, and she was not on oral contraceptives or other chronic medications.

The physical examination was unrevealing except for a hard 15 × 4 cm abdominal mass, in the lower left abdominal quadrant. A CT scan showed thickening of the bowel wall and the surrounding fat involving the rectum, sigmoid and descending colon (Fig. 1). Blood tests yielded normal values, with the exception of high acute-phase reactants (C-reactive protein 53 mg/l; ESR 52 mm/h; serum fibrinogen 873 mg/dl). Stool culture and examination for parasites and ova, as well as fecal Clostridium difficile toxin assay all yielded negative results. Antibodies against hepatitis B, hepatitis C, and human immunodeficiency viruses were also negative. A colonoscopy revealed some bubble-like elevated areas, extending from 7 cm of the anal margin to the splenic flexure, which went flat when pricked with the biopsy forceps, and were are typical of PI (Fig. 2). Rectal biopsies showed unspecific minimal changes with Congo red negative staining. A barium meal and follow through of the small bowel was normal.

A tentative diagnosis of primary PI was made. The patient was treated with oxygen therapy and oral metronidazole with marked clinical improvement in spite that the abdominal mass persisted, and she was discharged from the hospital to be followed on an outpatient basis. Two weeks later, however, the patient was re-admitted to the hospital because of worsening of pain in the lower left abdominal quadrant, palpation of tender mass in that area, diarrhea and increasing rectal bleeding.

The patient’s blood tests were again normal, except for mild anemia and elevated acute-phase reactants. A new proctosigmoidoscopic examination (Fig. 3) showed severe

Figure 1 Abdominal CT scan showing marked thickening of the sigmoid colon and the surrounding fat.

Figure 2 Endoscopic conventional (Panel A) and narrow-band imaging (Panel B) views of the sigmoid colon showing bubble-like areas which collapsed after pricking with biopsy forceps, consistent with pneumatosis intestinalis.

Figure 3 View of the second endoscopic examination showing extensive mucosal involvement with ulcers covered with fibrinous material.
pain and progressive anemia that required transfusion of four units of packed red cells. Total parenteral nutrition was started. A new abdominal CT scan showed marked thickening of wall of the left colon with severe involvement of pericolic fat and the presence of free peritoneal fluid. The mucosal biopsies taken on the second colonoscopic examination showed changes consistent with ischemic colitis. A diagnostic work-up to rule-out vasculitis (i.e., serum autoantibodies including antinuclear and anti-cardiolipin antibodies, cryoglobulins, periungueal capillaroscopy, and muscle biopsy) and thrombophilia (prothrombin time, activated partial thromboplastin time, protein S, protein C, activated protein C resistance, antithrombin III, factor V Leiden) were all negative. A mesenteric angiography showed some hypertrophic neoformed collateral vessels in the recto-sigmoid area (Fig. 4).

On the light of these findings, and because the persistence of rectal bleeding with increasing transfusion requirements, as well as abdominal pain unresponsive to continuous administration of morphine, surgical treatment was indicated about three months after the onset of symptoms. A sigmoidectomy with by Hartmann-type terminal colostomy was performed.

**Figure 4**  Lower mesenteric angiography showing some hypertrophic and collateral vessels in the area of rectum and sigmoid colon.

involvement from 5 cm of the anal verge with ulcers covered with fibrin, suggestive of pseudo-membranous colitis. This prompted empirical therapy with oral vancomycin while waiting for the result of a new *C. difficile* toxin assay (which was indeed negative). Few hours later, her clinical condition worsened with abundant rectal bleeding, severe abdominal

**Figure 5**  Macroscopical view of the surgical specimen. (Panel A): There are bluish areas in the serosa with several bubbles scattered over its surface, typical of pneumatosis intestinalis. (Panel B): Once opened, it showed an extremely hard bowel wall with superficial mucosal ulcerations, and markedly thickened pericolic fat. The sharp clear-cut edge between the involved and uninvolved colon (arrows) suggests an ischemic etiology.

**Figure 6**  Panel A: Histological view of the sigmoid wall showing signs of mucosa ischemia with superficial ulceration as well as fibrosis and hyalization of the lamina propria. Also, there is a marked proliferation of hyperplasic veins (H&E, ×40). Panel B: This proliferation of hyperplasic vessels was also seen in the muscular propria (H&E, ×100). Positive immunohistochemistry for the endothelial marker CD34 confirms their vascular nature (Panels B and C, ×100).
Macroscopically, the surgical specimen showed an extremely hard bowel wall with superficial mucosal ulcerations, markedly thickened pericolic fat, and bluish areas in the serosa with several bubbles scattered over its surface, typical of PI (Fig. 5). Of note, there was a sharp clear-cut edge between the involved and uninvolved colon, suggesting the vascular etiology of the disease (Fig. 5B).

Histological examination revealed mucosal ischemic changes with superficial ulcerations as well as fibrosis and hyalinization in the lamina propria. In addition, there was a marked proliferation of venous vessels with thickened walls in the submucosa, the muscular propria and the serosa (Fig. 6). These veins exhibited marked hyperplasia involving the intima and muscular layers consistent with IMHMV (Fig. 7A and B). Elastin and actin stains allowed the confirmation of the venous nature of the involved vessels, and the muscular origin of the hyperplasic cells in the venous wall, respectively (Fig. 7C and D). Also, some subserosal cysts negative for endothelial CD34 marker immunohistochemistry, and typical for PI, could be seen (Fig. 8).

The postoperative period was uneventful. Seven months later, the colostomy was closed and the bowel continuity was restored with a termino-terminal colo-rectal anastomosis. At the time of writing this report (24 months after the sigmoidection), the patient remains symptom-free. A CT scan and a colonoscopic examination do not show any abnormality.

3. Discussion

Mesenteric ischemia is a condition usually occurring in the elderly and is mostly due to arterial thromboembolic disease. Less often, mesenteric ischemia is due to venous occlusion due to venous thrombosis. Non-thrombotic occlusion of the mesenteric veins is rare and has been described to occur in vasculitis (e.g. systemic lupus erythematosus), Behçet disease or the so-called enterocolic lymphocytic phlebitis, also termed mesenteric inflammatory veno-occlusive disease (MIVOD). IMHMV is an extremely rare cause of venous mesenteric ischemia. To our knowledge only eight cases have been reported in the literature (Table 1). The present case fits well with the clinico-pathological features of IMHMV that has been described to occur in young otherwise healthy individuals, presenting as insidious subacute abdominal pain with rectal bleeding that may resemble inflammatory bowel disease. Indeed, in our case this was the first diagnostic possibility on the light of the first CT scan findings. However, endoscopic findings ruled out this diagnosis. Also, the second endoscopy showed features which might fit within inflammatory bowel disease, but this was not considered due to the previous clinical course.

As in the majority of (but not all) previous cases, the sigmoid colon was involved with changes of subacute and chronic ischemia and the presence of veins with thickened walls.
walls with myointimal hyperplasia that occludes their lumen. These changes confer an “arterial” appearance to the involved veins. However, elastin stain allowed the confirmation of the venous nature of these vessels and distinguish them from normal arteries (Fig. 7C). Indeed, this is of utmost diagnostic importance since one of the previously reported cases had been initially diagnosed of fibromuscular arterial hyperplasia. The absence of vascular or perivascular inflammatory changes supports the diagnosis of IMHMV rather than MIVOD. Although, some authors have suggested that IMHMV would be a late stage of MIVOD, the involvement of colon, cecum and terminal ileum in MIVOD vs. sigmoid colon and rectum in IMHMV argue against this hypothesis. Other authors have proposed the term enterocolic lymphocytic phlebitis as an umbrella entity to include MIVOD and IMHMV, since both entities share some pathological features.

Although one case of myointimal hyperplasia of the mesenteric veins in association with hereditary thrombophilia has been described, the cause of IMHMV remains elusive. On the basis of the predominant involvement of sigmoid colon in young people who are prone to develop recurrent volvulus of this segment of the colon, it has been speculated that hyperplastic changes in the mesenteric veins would be the result of an as yet undetected arteriovenous fistula which would develop in the sigmoid mesocolon as a result of traumatic injury caused by intermittent torsion or stretching of this segment occur-

**Figure 8** Pneumatosis intestinalis was present in the subserosa, as cysts devoid of endothelium (Panel A, H&E, ×40), as confirmed by the absence of CD34 expression on immunohistochemistry (Panel B, ×40).

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**Table 1** Cases of IMHMV reported to date.

<table>
<thead>
<tr>
<th>Case #</th>
<th>Ref. #</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Presenting symptoms</th>
<th>Involved site</th>
<th>Endoscopic appearance</th>
<th>Complication</th>
<th>Time to surgery</th>
<th>Follow-up</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>30</td>
<td>M</td>
<td>Abdominal pain</td>
<td>Sigmoid</td>
<td>Stricture</td>
<td>Obstruction</td>
<td>1 month</td>
<td>7 years</td>
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<tr>
<td>2</td>
<td>1</td>
<td>38</td>
<td>M</td>
<td>Rectal bleeding</td>
<td>Sigmoid</td>
<td>Ulcerative colitis</td>
<td>Perforation</td>
<td>&gt;6 months</td>
<td>2 years</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>25</td>
<td>M</td>
<td>Diarrhea</td>
<td>Sigmoid</td>
<td>Ulcerative colitis</td>
<td>Bleeding</td>
<td>3 months</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>58</td>
<td>M</td>
<td>Constipation</td>
<td>Sigmoid</td>
<td>IBD</td>
<td>N/A</td>
<td>&gt;12 months</td>
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<tr>
<td>5</td>
<td>1</td>
<td>67</td>
<td>M</td>
<td>Diarrhea</td>
<td>Sigmoid</td>
<td>Ischemia?</td>
<td>Bleeding</td>
<td>2 months</td>
<td>2 years</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>22</td>
<td>M</td>
<td>Rectal bleeding</td>
<td>Rectum</td>
<td>IBD</td>
<td>Bleeding</td>
<td>5 months</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>38</td>
<td>M</td>
<td>Rectal bleeding</td>
<td>Sigmoid</td>
<td>Perforation</td>
<td>Bleding</td>
<td>6 months</td>
<td>18 months</td>
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<tr>
<td>8</td>
<td>4</td>
<td>31</td>
<td>F</td>
<td>Diarrhea</td>
<td>Descending colon</td>
<td>Perforation</td>
<td>Blending</td>
<td>3 months</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>Present</td>
<td>32</td>
<td>F</td>
<td>Abdominal pain</td>
<td>Sigmoid</td>
<td>Pneumatosis intestinalis + Bleeding</td>
<td></td>
<td>3 months</td>
<td>2 years</td>
</tr>
</tbody>
</table>

N/A: Non-available; IBD: Inflammatory Bowel Disease. *Reinterpretation of the case reported in reference #16.*
ring, for instance, during exercise. Such a “traumatic” pathogenic mechanism is supported by the finding of a greater prevalence of focal myointimal hyperplasia of the mesenteric veins in resected bowel specimens which had undergone pre-resection trauma (i.e. volvulus/intussusception, incarcerated hernia, stoma takdow down etc.), as compared to those which had not.

Besides the fact that this is the first reported female patient with IMHMV, a feature that renders the present case unique is its association with PI. This is also a rare entity with a reported crude incidence of about four cases per year in some referral centers. PI is a pathological sign rather than a disease as it occurs in the setting of a wide array of clinico-pathological conditions, although in a minority of cases no causative factor could be found. Hence, the prognosis of PI mostly depends on the nature of the underlying disease. Three possible sources of intramural gas in the bowel have been proposed for PI: a) gas in the intestinal lumen, b) bacterial production of gas, and c) pulmonary gas. The later could account for those case of PI associated to asthma or chronic obstructive pulmonary disease, whereas a combination of luminal and intramural bacterial gas would explain the development of PI associated to gastrointestinal disease where disruption of the mucosal barrier occurs, including intestinal ischemia. In this sense, the development of PI in the present case should be viewed as an early ischemic phenomenon secondary to IMHMV.

In summary, despite its rarity IMHMV should be suspected in young patients with features of ischemic colitis of the sigmoid area. Although mucosal biopsies may on occasion be helpful for the diagnosis, this mostly relies on the histological examination of the surgical specimen. Surgical resection of the involved segment is always curative, as no recurrence has been reported on the long time.

References