Delayed laparoscopic cholecystectomy in a case of acute cholecystitis and intestinal malrotation type I

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Abstract

In adults, intestinal malrotation is an oligosymptomatic entity that is occasionally discovered during the course of diagnostic studies for other causes. In the case described herein, intestinal malrotation was discovered during investigation for cholelithiasis and acute cholecystitis. Malrotation may occur due to alterations in the asymmetric cellular dynamics of the mesentery responsible for intestinal shortening and unilateral retraction, this may occur as a secondary event following alterations in the expression of homeodomain transcription factors. The incidental finding of asymptomatic intestinal malrotation in adults does not preclude its surgical treatment. However, when intestinal malrotation is associated with cholecystitis, due to cholelithiasis, it is advisable, to first treat the cholecystitis conservatively, in our case, and then perform partial adhesiolysis of the Ladd bands that hinder access to the cystic area and carry out cholecystectomy by elective laparoscopy.

Introduction

Intestinal malrotation (IM) is caused by the abnormal rotation and fixation of the middle segment of the primitive intestine between the fourth and twelfth week of gestation.[1] This segment is suspended from the dorsal mesentery (DM), which connects the intestinal tube to the dorsal wall of the body and is derived from the mesoderm. Malrotation occurs in approximately 1 in 6000 newborns, and its most frequent clinical presentation is during the early or neonatal period, in 40 to 50% of cases, symptoms present during the first week of life.[2] However, in many cases malrotation is not detected or diagnosed because it remains asymptomatic, even into adult life.[3] Unfortenately, in 70% of children intestinal malrotation is associated with a range of other abnormalities, including atresia duodenal or small bowel stenosis, Ladd's bands, Meckel's diverticulum, intusception, omphalocele, gastroschisis, diafragmatic hernia and even Hirchsprung's disease.[4] In adults, malrotation is not commonly associated with other abnormalities. The clinical presentation of this condition varies from non-specific symptoms, such as erratic colic pains, which may or may not occur with diarrhea, or constipation, which can cause a significant delay in diagnosis. Futhermore, malrotation can be discovered incidentally during the course of diagnostic studies for other pathologies, such as malnutrition, malabsorption, protein losing enteropathy, small bowel volvulus with ischemia and/or necrosis, shock or as in the case presented herein, acute cholecystitis and cholelithiasis associated with type I malrotation (Table 1).[5-9]

Case Report

A 60-year-old man presented to the Emergency Department with abdominal pain in the epigastrium and mesogastrium. The patient had experienced a slow and progressive onset of symptoms which eventually reached significant intensity but without irradiation, this was accompanied by abdominal distension, nausea, vomiting, dyspepsia and constipation. Two years previously, the patient had consulted with a medical specialist to seek advice over episodes of dyspepsia with flatulence and occasional vomiting, gastroscopy revealed mild chronic gastritis while colonoscopy, carried out via the hepatic angle, due to poor tolerance, revealed multiple sigmoid diverticula.

Upon admission, blood count was 11,000/mm^3 with 24% lymphocytes, and 208,000 platelets, hemoglobin was 16.1 g/dl and hematocrit was 46.6% (normal range 35.9-44.6). All biochemical tests were within the normal range. Simple radiological assessment of the abdomen showed an anomalous distribution of gas patterns, with dilatation of the small bowel loops in the right hemiabdomen. Abdominal ultrasound showed no vascular alterations or organomegalies except for a supernumerary spleen (1.8 cm in size) in the infrahiliar region. The vesicular wall was thickened (>4 mm) with microlithiasis. The patient was thus diagnosed with acute cholecystitis Grade I, according to criteria specified in the Tokyo Guidelines 2018.[6] Thoracoabdominal computed tomography (CT) and virtual colonoscopy, performed by radiologists after the administration of oral and intravenous contrast, revealed the anomalous disposition of the small bowel loops in the right hemiabdomen, and the large intestine in the left hemiabdomen, while also revealing the cecum and terminal ileum in the lower midline to the umbilical region (Figures 1 and 2), diverticula were also observed in the sigmoid region. For this reason, the patient was admitted into the hospital, and placed on a strict diet. He also received decompression via a nasogastric tube, serum therapy, antibiotics and prokinetics. He was discharged ten days later. Due to pressure in our health care area, the patient underwent laparoscopic surgery two months later. Surgery involved lysis of the fibrous Ladd bands that extended from the cecum to the sub-hepatic area and abdominal wall, which hindered access to the Calot triangle, and cholecystectomy. Surgical outcome was favorable, and the patient was discharged after 3 days. Written informed consent was obtained from the patient in order for us to publish this case report and accompanying images.

Discussion

It is rare to discover type I intestinal malrotation during the course of diagnostic studies for cholecystitis. In our patient, we made a diagnosis of IM while investigating the gastrointestinal tract by CT or colono-

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graphy due to recurrent abdominal pain. These techniques are currently the most commonly used diagnostic methods because they makes it possible to observe rotation of the intestinal loops and their relationship with the mesenteric vessels and other viscera.[7,8] According to the classic description by Snyder and Chaffin, the primitive midline intestine, rectus and the midline, grows disproportionately compared to the rest of the embryo and determines the U-shaped herniation in the umbilical cord by the sixth week of gestation and the beginning of the 180º rotation process in a counter-clockwise direction on the axis of the superior mesenteric artery (SMA). The latter remains in the duodenojejunal loop to the right, posterior and inferior, and the loop of the colon, to the left and higher. Snyder and Chaffin describe the first stage of *non-rotation*, or stage I, as when the middle intestine returns to the abdominal cavity without having rotated more than the first 90º, in other words movement only occurs in the horizontal plane.[9] Thus, the pre-arterial segment, which will constitute the small intestine, is located in the abdomen to the right of the SMA, whereas the post-arterial segment, which eventually becomes the distal ileum and the right half of the colon, are located on the left side of the SMA, with the middle line crossing the ileum distally, from right to left, to reach the cecum. At present, the origin of these malrotations is thought to lie in cellular alterations that occur in the mesentery. The DM of the embryonic intestine is initially a completely symmetrical structure, consisting of four functionally distinct compartments: the left epithelium and mesenchyme, and the mesenchyme and the right epithelium. Subsequent cellular changes are required in each compartment in order to initiate rotation. Previous experimental studies, in birds and mice, unequivocally demonstrate an asymmetric evolution, presenting a dense mesenchyme and columnar epithelium on the left side; on the right side, the mesenchyme cells are dispersed and the epithelium is cuboidal. This asymmetry in cellular dynamics during the embryonic period are due to the differential expression of a range of transcription factors in either compartment of the mesoderm. On the left side, transcription factors such as Pitx2 and IsI1, which act downstream of Nodal, and the adhesion molecule, N-Cadherin, which acts downstream of Pitx2, almost exclusively predominate. Pitx2 is a paired-type homeobox gene which enhances a non-canonical Wnt pathway to activates the formin, Daam2, which interacts and binds adhesion complexes mediated by N-Cadherin to the actin cytoskeleton, thus determining a polarized condensation in the

Table 1. Classification of small bowel rotation anomalies, based on the classic description of Snyder and Chaffin.[9]

Type defect	
I	Non-rotation
IIa	Lack of duodenum rotation
IIb	Reverse rotation of the duodenum
IIc	Reverse rotation duodenum, colon rotation
IIIa	Normal rotation duodenum, colon not rotation
IIIb	Incomplete fixation of the hepatic angle of the colon
IIIc	Incomplete blind fixation and its mesentery
IIId	Internal hernias

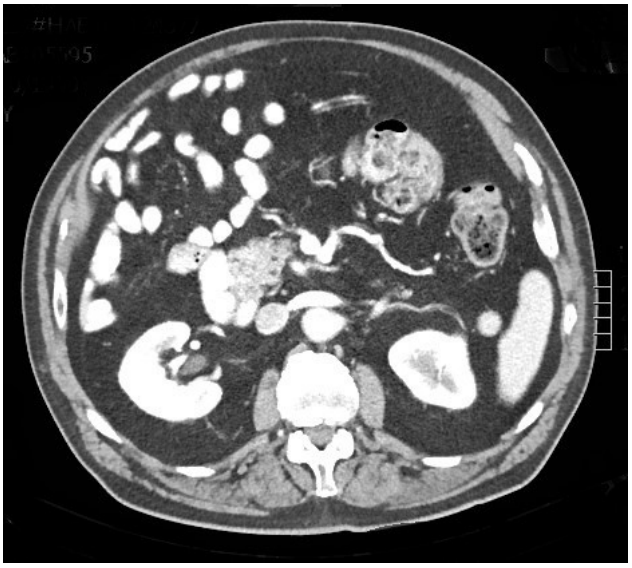

Figure 1. Computed tomography of the abdomen with contrast showing the arrangement of the small and large intestines in different locations of the abdomen.

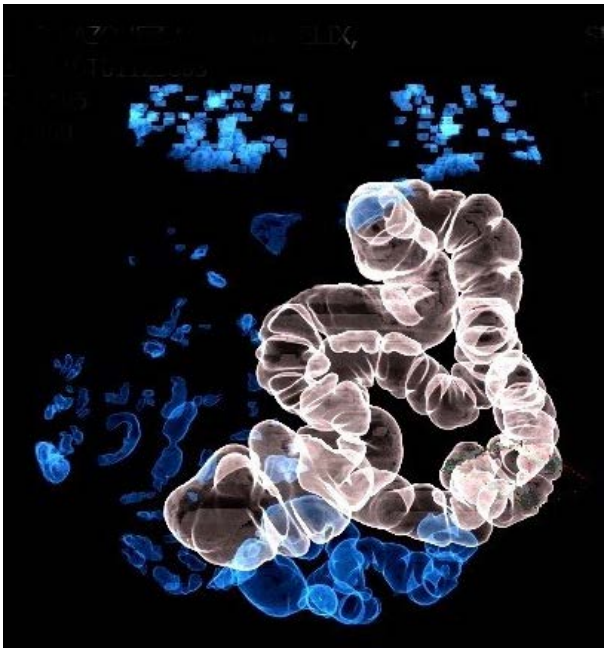

Figure 2. Computed tomography and colonography image showing the presence of the small intestine on the right and colon on the left.

left DM. Other positive mediators of the Wnt pathway, which have been described in the left DM, are the Frizzled 4 receptors and Gpc3; inhibitors of Wnt, such as Sfrp, are expressed exclusively on the right side of the DM.[10-12]

In humans, it is plausible that there are also alterations in the expression of transcription factors required for morphogenetic events during the asymmetric formation of the intestine, in the determinants of early fixation and during the stabilization of the intestine, causing IM.

These, and other basic questions, such as whether the origin of alterations in the expression of transcription factors are due to gene dysregulation, *de novo* germline mutations, somatic mutations or mosaicism, require future research investigations.[13]

IM manifests clinically more frequently in childhood and may be associated with other morphological alterations of the intestine. However, the clinical manifestations in adults are less frequent and are due to mechanical problems that are expressed as episodes of abdominal pain, vomiting and even malnutrition due to volvulus or changes in peristaltic movement. It has been suggested that the persistence of IM could underlie the appearance of other anomalies, such as diverticula, eventually inducing pancreatitis or even colon cancer.[14,15] We hypothesize that the presence of duodenocolic and duodenojejunal bands can affect drainage from the bile duct and become an etiopathogenic factor in the formation of cholelithiasis and cholecystitis, as in the case described herein.

When malrotation is detected, either as chronic episodes or as emergencies, surgical treatment is recommended because this allows efficient exploration and resolution of the precise cause.[16] The most frequent surgical procedure utilized in such cases is that described by Ladd, which involves lysis of adhesions in the duodenum, caecum, colon and small intestine.[17]

However, in adults, IM is asymptomatic. Consequently, the management of patients with incidental findings is still the subject of controversy. The arguments in favor of surgery in such cases are that the risk of acute problems throughout life, such as volvulus, can affect 20% of cases and that elective surgery carries less risk than emergency surgery.[18] However, the Ladd procedure is not exempt from postoperative complications in previously healthy people.[19]

Furthermore, there are no established criteria to guide clinical management in patients when IM is associated with acute cholecystitis. Currently, Grade I cholecystitis is a subsidiary of laparoscopic early cholecystectomy, a procedure associated with low morbidity and mortality. However, when associated with IM, it is possible that the existence of fibrous bands, or other abnormalities, may hinder access to the cystic area with inflammation. Furthermore, dissection of the structures in this area, and the risk of conversion to open surgery, represent adverse conditions that can be avoided by deferring surgery and limiting treatment to the partial lysis of Ladd bands and elective cholecystectomy.

Conclusions

In adults, asymptomatic IM is a rare entity which can be discovered during the course of investigations for other causes. In our patient, we detected IM while carrying out investigations for cholelithiasis and cholecystitis. Malrotation occurs because of alterations in the asymmetrical cellular dynamics of the mesentery responsible for intestinal shortening and unilateral retraction, this may occur as a secondary event following alterations in the expression of homeodomain transcription factors, and is frequently associated with the presence of fibrous bands. When both entities, intestinal malrotation and cholecystitis, are associated it is possible that the presence of inflammation and fibrous bands in the sub-hepatic area may render early cholecystectomy much more difficult. As a result, our patient received medical treatment and deferred surgery was scheduled for adhesiolysis of the sub-hepatic fibrous bands and laparoscopic cholecystectomy. Our patient's favorable outcome suggests that this procedure can be a recommended as a good therapeutic option.

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