

Atypical presentation of acute idiopathic megacolon in a 14-year-old patient

Running head: Unusual acute megacolon

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Introduction

In clinical practice the term “megacolon” is used to indicate a marked dilatation of the cecum and the sigmoid colon (>12 and 6.5 cm, respectively) (1). From a clinical standpoint, a megacolon can be classified as chronic or acute depending on its clinical presentation. Chronic megacolon typically refers to a congenital disorder in which the enteric nervous system (ENS) supplying the colon does not develop properly, thereby leaving the distal segments of the viscus without myenteric and submucosal ganglia (i.e. Hirschsprung's disease) (2). Other cases of non-aganglionic chronic megacolon can be secondary to variety of conditions such as Chagas' disease and neurodegenerative diseases (e.g. Parkinson's and Alzheimer's diseases), leading to or associated with ENS abnormalities (3). The acute form of megacolon, also referred to as Ogilvie's syndrome, is characterized by a predominant involvement of the cecum and right colon usually affecting elderly patients undergoing surgery (e.g. orthopedic procedures) or taking medications altering gut motility (e.g. opioids or antidepressants) (4). Some forms of acute megacolon, however, can be idiopathic in origin since no underlying etiology can be identified.

Patients with acute idiopathic megacolon usually have a longstanding history of constipation, often accompanied by laxative abuse, and their clinical presentation is characterized by abdominal distension and severe pain with radiological evidence of stool impacted in the colon and rectum (1, 4).

The case herein reported represents an unusual form of acute idiopathic megacolon characterized by massive descending and sigmoid colon distension complicated with a volvulus in a 14-year-old boy with no Hirschsprung's disease. In addition, just to increase the peculiarity of this case report, the patient had an unremarkable clinical record, and never suffered from chronic constipation in the past.

Case Report

A 14-year-old boy came to the Emergency Unit of St. Orsola-Malpighi Hospital because of severe abdominal pain, bloating and distension, vomiting and failure to pass gas and stool. His clinical history was unremarkable with the patient conducting a very healthy life, practicing sports and attending school with excellent records up to the onset of the acute episode. His sister, parents and paternal and maternal 1st degree relatives did not complain of chronic constipation nor of any other systemic diseases. On admission, the physical examination revealed a markedly distended abdomen, with tenderness evoked by superficial palpation, tympanitic at percussion and absence of borborygmi. No cardiologic or pneumologic abnormalities were observed. The body mass index was normal for his age and body temperature was 37°C. Blood tests revealed mild leukocytosis (WBC: 9.2×10^3 mmc), heamoglobin 15.4 gr/dL, hematocrit 45.4% and platelets 300×10^3 μ L. Kidney, liver and pancreatic tests were normal. Reactive protein C was below the detection limit.

X-ray examination of the abdomen showed dolichocolon with a large dilatation of the sigmoid colon (about 6-7 cm). A mechanical obstruction was excluded by a CT scan which disclosed a highly dilated sigmoid colon containing feces; the distal portion of sigma was reduced in size, suggesting a volvulus of the sigmoid colon (Figure 1).

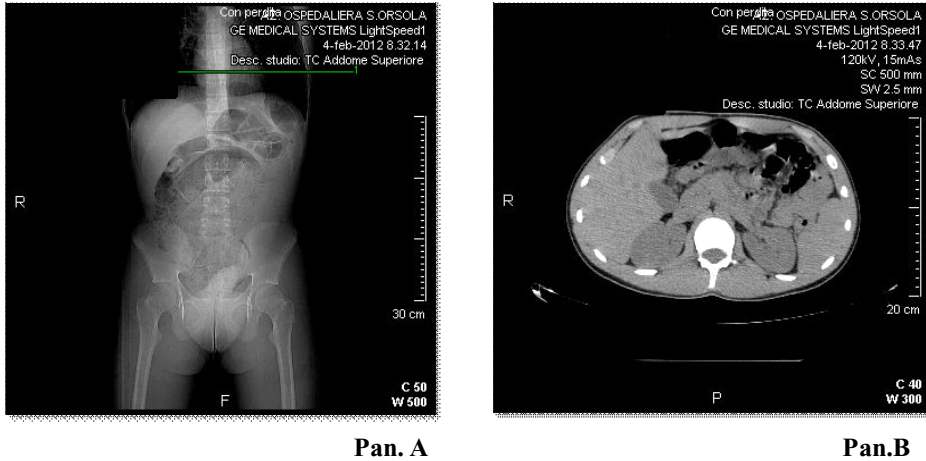


Figure 1. CT examination. Panel A: shows the marked dilatation of the sigmoid colon with a cut-off point suggestive of occlusion like due to a volvulus as illustrated in Panel B.

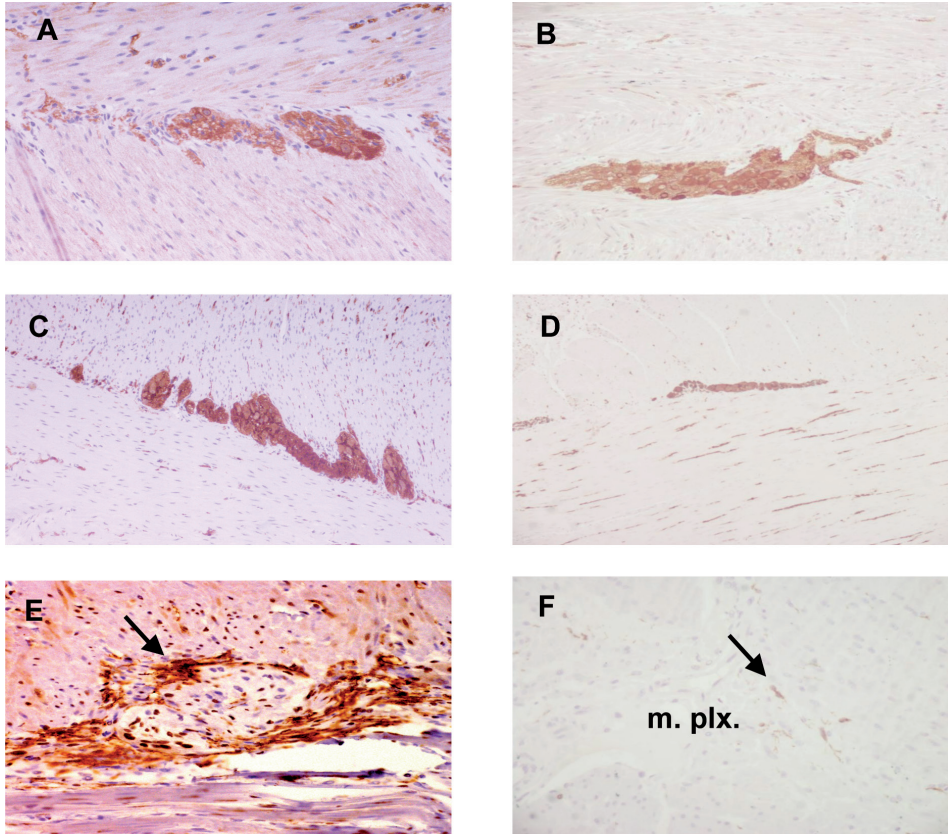


Figure 2. Representative example illustrating NSE (A & B), S-100 β (C & D) and c-Kit (E & F) immunolabeling in the herein presented patient (B, D, F) compared to a age-sex matched control (A, C, E). Note the normal appearance of NSE and S-100 β immunoreactive patterns in the myenteric plexus of the patient's specimen (B and D) vs. control (A and C, respectively). In contrast, c-Kit immunolabeling showed a marked depletion of interstitial cells of Cajal (arrows) around a myenteric plexus (m. plx.) in the patient's sigmoid colon (F) vs. control (E). ABC immunoperoxidase technique. Original magnifications (from the microscope objectives): 15x in A, C and F; 10x in B and 5x in D; 20x in E.

Because of the intense abdominal pain and evidence of a volvulus at CT scan, the patient was referred to the emergency surgery and operated on the same day of sigmoidectomy with side-to-side anastomosis. The post-operative phase was uneventful and the patient recovered fully after few days. The macroscopic resected specimen confirmed the radiological diagnosis of volvulus and the routine H&E histopathological examination showed a diffusely ischemic colon wall with no other detectable abnormalities. The immunohistochemical analysis, using antibodies directed to identify the neuron specific enolase (NSE), a general pan-neuronal marker, the S-100 β , a glial cell marker and c-Kit, one receptor expressed by interstitial cells of Cajal (ICC), was performed in order to establish whether neuro-muscular abnormalities would have a contributory role in the marked dilatation observed in this case. The results showed that, compared to age and sex-control specimens from subjects undergoing surgery for uncomplicated neoplasia, there was only a marked depletion of the c-Kit immunolabeled ICCs (Figure 2).

The patient was discharged in good general health after eight days from admission and he is still in good clinical condition.

Discussion

The observed patient represents a very uncommon disease in clinical practice. In fact, the exact prevalence of acute megacolon (or acute colonic pseudo-obstruction/Ogilvie's syndrome) is unknown, but may be inferred from the incidence of large bowel obstruction where it is responsible for at least 20% of cases (5, 6). It occurs in about 1% of hospitalized patients undergoing orthopaedic procedures, including lower limb joint replacement and spinal operations (7). Also, about 0.3% of patients with severe burns can develop marked distension of the colon (8). None of these clinical situations applied to our patient.

Indeed, the reason to present this case of acute (idiopathic) megacolon was due to a number of unusual features. First, compared to classic acute colonic pseudo-obstruction, which is diagnosed in elderly cases with recent surgery and/or treated with drugs interfering with gut transit (4), the reported patient was young, had no history of chronic constipation and did not take any medicine. Secondly, male gender, Caucasian origin, and low fiber diet should be protective factors as anatomical and epidemiological data indicate (9). Thirdly, Ogilvie's syndrome affects the right side sections of the colon, while, in this case the predominant involvement of the disease was the sigmoid colon complicated by a volvulus. This finding was initially interpreted as a possible Hirschsprung's disease not diagnosed during childhood. However, the histopathological analysis of the sigmoid colon revealed a normal appearance of the ENS and related ganglia as indicated by immunohistochemical analysis of NSE. In this line, also S-100b resulted in a nice labeling of glial cell component associated to the ENS. In contrast, c-Kit immunolabeling of ICCs showed a reduced network of these cells around myenteric plexus and throughout the muscular layer. Thus, taking the histopathological features together, Hirschsprung's disease could be ruled out, while, on the other hand, there was an overall reduction of ICC networks. This is a result which has been previously reported in patients with severe slow transit constipation undergoing colectomy for laxative unresponsiveness (10). The reason why a non-constipated patient should display a histopathologic pattern of a slow transit constipation-type (i.e. reduced ICC network) remains an unclear aspect and raises questions which go far beyond the purpose of this report. Furthermore, the mechanisms involved in sigmoid dilatation, such as that observed in the herein described case, remain undefined. Whether ICC network is selectively decreased in the sigmoid area or rather diffused to other parts of the colon (or even to extra-colonic segments of the alimentary tract) cannot be extrapolated by the available surgical specimen. Likewise the presence of an abnormal ICC network in this patient cannot be excluded from the lack of clinical manifestations, since the histopathologic abnormalities had remained asymptomatic up to the onset of the acute episode.

Furthermore, another aspect which deserves discussion pertains to the possibility that the mechanical complication (i.e. volvulus) occurred in this patient could have played a role in the reduced ICC network. Indeed, in a previous case report, we described a patient with a congenital mechanical obstruction of the gut (Ladd's band) with a marked reduction of the ICC in the dilated segments above the mechanical obstruction, but not in the apparently normal segments below the fibrotic band (11). Although from a single case, that report suggested that a mechanical component may alter the c-Kit expression and therefore the ICC density in any layer of the gastrointestinal tract, including colon. Clearly, this possibility requires further data to be confirmed.

The pathophysiology of acute megacolon is obscure. A variety of hypotheses regards an imbalance between extrinsic autonomic innervation (12, 13). Although these neural mechanisms can be possible on the basis of association with prevertebral and retroperitoneal trauma or disease (14-16), there is no direct evidence in their support. Nonetheless, the favourable response to anti-cholinesterase drugs (e.g. intravenous neostigmine) used in patients with acute colonic pseudo-obstruction supports a possible decrease of parasympathetic activity (4). In addition to the parasympathetic component, some experimental evidence indicates that stretch-sensitive mechanoreceptors, located in the gut wall, may also contribute to self-maintenance of colonic contractile inhibition, with a likely active role in our patient (17). Why visceral dilatation should follow such impairment of motility is unknown. Given the prominent regulatory role exerted by the ENS, one cannot discard the possibility that a functional impairment of the intrinsic innervation may also have contributed to the clinical picture of the

present patient. Factors altering the morpho-functional integrity of the ENS, including mild inflammatory stimuli, allergens, gut microbiota changes, neurotropic viruses can all evoke neural dysfunction and related colonic dysmotility and distention. These functional changes in the ENS may not be necessarily associated with neural degeneration and loss (18, 19).

In conclusion, this case clearly shows that acute megacolon can occur at any age and be not preceded by major diseases or trauma. A multidisciplinary approach may lead to appropriate diagnosis and management of such difficult cases. Emergency surgery may prevent life-threatening complications such as colonic hemorrhage, ischemia and perforation.

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