

Could the Complications of Megacolon be Avoided by Monitoring the Risk Patients? Cases Report

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Rezumat

Ar putea fi evitate complicațiile megacolonului prin monitorizarea pacienților la risc? Prezentare de caz

Prezentăm 2 cazuri de megacolon asociat cu accident cerebrovascular și consum de substanțe neuropsihiatrice.

Cazul 1: o femeie de 75 de ani cu diabet zaharat, hipertensiune, tahicardie cu fibrilație atrială, revărsate pleurale bilaterale și accident cerebral hemoragic în antecedente a fost internată în unitatea noastră. Aceasta prezenta afectarea OTS, distensie abdominală cu ileus paralic. Examenul CT a relevat distensie colonică, cu impactare severă a materiilor fecale. În timpul intervenției chirurgicale s-a decelat volvulus sigmoidian.

Cazul 2: un bărbat de 59 de ani cu istoric de oligofrenie a fost internat cu diagnosticul de abdomen acut. Prezenta stupor și ileus paralic cu distensie abdominală. CT-ul abdominal a relevat dolichosigmoid, cu impactare a materiilor fecale. Pacientul a fost supus unei laparotomii, în timpul căreia s-a decelat o perforație de 2 mm la nivel sigmoidian. Colonul sigmoid avea un diametru de 28 cm și o lungime de 75 cm. Chiar dacă o corelație clară nu a fost încă stabilită, anomaliile de reglare a motilității gastrointestinale pot avea loc la diferite nivele la pacienții cu afecțiuni psihiatrice sau

cerebrovasculare, sau care consumă medicamente cu proprietăți anticolinergice, motiv pentru care ar trebui atent monitorizați. Scopul este acela de a stabili precoce un diagnostic de anomalie a funcției colonice, în vederea evitării unor complicații potențial fatale.

Cuvinte cheie: obstrucție colonică, megacolon, oligofrenie, procedură Hartmann, boală Hirschsprung

Abstract

We report 2 cases of megacolon associated with cerebrovascular accident and neuropsychiatric drug consumption.

Case report 1: a 75-year-old woman with diabetes mellitus, hypertension, tachycardia with atrial fibrillation, bilateral pleural effusions and previous cerebral hemorrhage was admitted in our hospital. She presented clouded sensorium and abdominal distension, with closed alvus. The CT scan showed a distension of the colon, with severe fecal impaction. A volvulus of the sigma was found at surgical intervention.

Case report 2: a 59-year-old man with a medical history of oligophrenia was admitted to our hospital for acute abdomen. He presented stupor and closed alvus with abdominal distension. The abdominal CT scan showed a dolichosigma, with fecal impaction. The patient was submitted to a laparotomy and a two millimetres perforation of the sigma was found. The sigma had a diameter of 28 cm and a length of 75 cm. Even if a clear correlation has not been found yet, anomalies of the regulation of the gastro-intestinal motility can occur at different levels in patients with psychiatric or cerebrovascular diseases and drug consumption with anticholinergic properties, and they should be carefully monitored. The purpose is an

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early diagnosis of colon function anomalies in order to avoid potentially fatal complications

Key words: colonic occlusion, megacolon, oligophrenia, Hartmann procedure, Hirschsprung's disease

Introduction

Megacolon is characterized by a pathological, enormous and permanent increased size of the colon or part of it, with thickening of its muscle layers. (1,2) Different causes can lead to megacolon, but usually they are very difficult to identify, and in these cases the disease is termed idiopathic (3). During childhood, the most important cause is Hirschsprung's disease (HD), which is characterized by a congenital aganglionosis of the enteric nervous system of the colon. (4)

On the opposite adults are rarely affected by HD and usually other causes must be sought. Among these causes, chronic constipation, infectious illnesses (like Chagas disease or other infectious colitis complicated by toxic megacolon), diabetes mellitus, organic diseases, myxedema, connective diseases and above all, some neuropsychiatric diseases and drug consumption must be considered.

We report 2 cases of acquired megacolon with the aim of underlining the relationship between megacolon, neuropsychiatric and neurovascular diseases and drug consumption.

Cases Report

Case 1. A 75-year-old woman presented at our hospital with a 2 day history of abdominal pain, located in all quadrants.

Her general condition was deteriorated, with clouded sensorium and abdominal distension. Alvus was closed, but neither nausea nor vomit were present.

Her medical history was significant for diabetes mellitus, hypertension, tachycardia with atrial fibrillation, bilateral pleural effusions and previous cerebral hemorrhage that resulted in hemiplegia with right hemiparesis. The patient was taking insulin, an antiarrhythmic drug (verapamil hydrochloride) for the atrial fibrillation, acetylsalicylic acid and an anxiolytic drug (diazepam).

Laboratory tests showed white blood cells count, AST and ALT within normal range. Glucose (146 mg/dl; range 65-120), azotemia (57 mg/dl; range 10-55), LDH (679 U/l; range 300-600), CPK (230 U/l; range 26-170) were increased.

Red blood cells ($3.60 \times 10^6/\mu\text{L}$; range 3.78-5.20), haemoglobin (10.60 g/dl; range 11.60-14.90), hematocrit (31.30%; range 34.90-43.90), sodium (121 mEq/l; range 134-150) and potassium (2.9 mEq/l; range 3.6-5.5) were slightly decreased.

The abdominal X-ray detected marked colonic distention with fecal residue but it did not show the presence of free peritoneal air.



Figure 1. The sigmoid colon was 60 cm in length



Figure 2. Marked dilatation of the sigmoid colon that reached almost 20 cm

The CT scan showed distension of the colon, with severe fecal impaction, until the middle portion of the descending colon. At this level, a concentric thickening of the walls of the gut with reduction of the lumen seemed evident. Downstream from the fecal impaction, the descending colon, the sigma and the rectum appeared empty.

Due to the patient's clinical situation and to the radiological examination with the diagnosis of abdominal occlusion, the patient was submitted to surgical intervention.

By laparotomy, a dolichosigma of 60 cm and brownish colour twisted on itself (volvulus) was found (Fig. 1). After derotation of the volvulus, the color of the dolichosigma remained brownish (Fig. 2), so a sigmoidectomy was decided for.

Anatomopathological examination of the specimen showed the presence of a chronic mucosal inflammatory infiltrate. Moreover, sub-mucosal and muscle interstitial congestion was found.

The postoperative period was uneventful. The patient pre-

sented flatulence five days after the procedure. 14 days after the procedure a new cerebral ischemic episode with language disjunction occurred. For this reason the patient was transferred to the department of neurology.

Case 2. A 59-year-old man was transferred from the department of internal medicine to our department for acute abdomen, caused by a dolichosigma perforation. The patient's general condition was deteriorated and he presented stupor. The alvus was closed. He presented abdominal distension and at the auscultation of the abdomen there were no bowel sounds.

His medical history was positive for oligophrenia, and for this, the patient was treated with neuroleptic and anxiolytic drugs (olanzapine, lorazepam and biperidene chlorhydrate).

Laboratory tests showed an increase of: white blood cells ($32.30 \times 10^3/\mu\text{L}$; range: 4.00-10.40) with an elevated rate of neutrophils ($27.1 \times 10^3/\mu\text{L}$; range: 1.7-8.2), AST (43 U/L; range 13-41), LDH (1505 U/L; range 300-600) and CPK (240 U/L; range 38-190). On the other side, red blood cells ($3.68 \times 10^6/\mu\text{L}$; range 4.10-5.50), hemoglobin (9.70 g/dl; range 12.70-16.60), hematocrit (30.10%; range 38.60-48.0), total proteins (3.3 g/dl; range 6.0-8.4), calcium (7.1 mg/dl; range 8.2-10.2), amylase (17 U/L; range 36-128), and lipase (18 U/L, range 22-51), were decreased.

The abdominal CT scan showed a marked thickening wall dolichosigma, with fecal impaction. Fecal material was present also in the remaining portions of the colon, but it was not increased in size. Intraperitoneal free air was also found.

Due to the clinical examinations the patient was submitted to laparotomy. In the peritoneal cavity there were free feces due to a two millimetre perforation of the antimesenteric wall of the sigma, leading to fecal peritonitis. The sigma was very dilated with a diameter of 28 cm and a length of 75 cm and the perforation was due to the enormous pressure inside the dilated sigma (Figs. 3, 4).

Because of the bowel and the peritoneal conditions we performed a left hemicolectomy and a colostomy, according to Hartmann's procedure. Pathological examination of the specimen showed only an inflammation of the gut wall.

The postoperative period was uneventful and the patient was discharged on the 7th day but died 9 days after of causes not related to the surgical procedure.

Discussion

Megacolon is a very diffuse pathology that can be the consequence of different disorders.

The normal function of the colon is regulated by the nervous system which acts on different levels and that can be divided in intrinsic and extrinsic nervous system. (5) The intrinsic nervous system or enteric nervous system is represented by the Meissner's and Auerbach's plexus which are respectively found in the submucosal and in the muscular layer of the bowel; the extrinsic nervous system or extraenteric nervous system acts through the sympathetic and parasympathetic nervous systems which transfer to the periphery the information coming from the central nervous system and

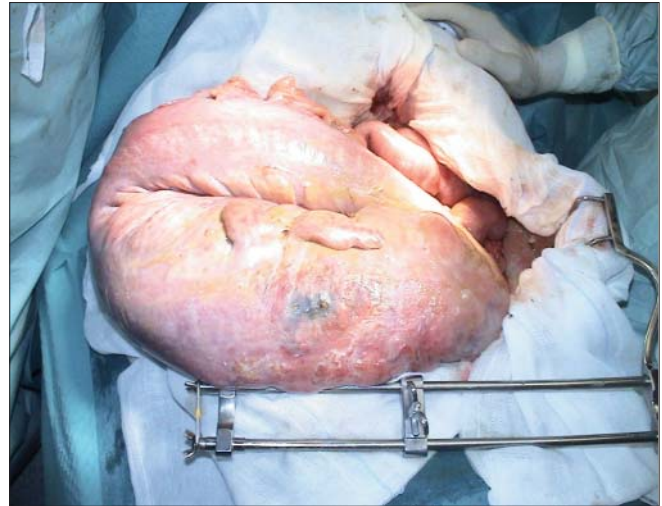


Figure 3. The sigmoid colon was 75 cm in total length and occupied almost the entire abdominal cavity

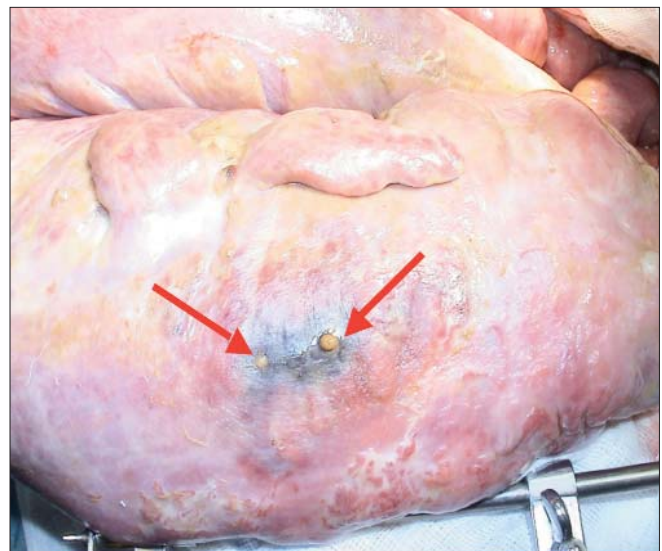


Figure 4. The diameter of the sigmoid colon was 28 cm. The extreme diastatic tension caused the perforation (arrows)

then can modulate the activity of the colon according to the information received.

Therefore, alterations of the normal function of the enteric or extraenteric nervous system can result in anomalies of the normal motility of the colon and, finally, to megacolon. Recently, other factors have also been considered for explaining the pathophysiology of megacolon, as abnormalities of the interstitial cells of Cajal or alterations of smooth muscle cells within the gut wall. (4,6)

Megacolon can be either congenital or acquired, but the true etiology is often difficult to find.

The congenital megacolon is mainly the result of Hirschsprung's disease (HD), which is the result of congenital absence of intramural ganglionic cells in the distal intestine.

This condition can be familial (5-20% of the cases) (7), but in most cases it is a sporadic form.

Different gene mutations have been assumed, but probably the main alterations concern mutations of gene RET (7), which is very important for the normal formation of the enteric ganglia. Naturally, HD is a typical condition of the childhood, but it can also be present in adults. In adulthood the incidence is unknown and can be the consequence of a missed diagnosis in childhood. (4)

Because of the aganglionosis, the upstream bowel gradually becomes hypertrophic and dilated with the intent to make the intestinal content in the part of the aganglionic segment progress. Surgery is often the only therapeutic alternative.

When megacolon occurs in adulthood different etiologies have to be evaluated. A cause is often difficult to find and for this reason it is termed idiopathic megacolon (IM). (4) The exact incidence of the IM is unknown. (6)

The same structures altered in the other cases of megacolon, as the intrinsic nervous system and the extrinsic nervous system, the interstitial cells of Cajal, or the smooth muscle cells are also involved in IM (6), but without the typical abnormalities that can be found in other pathologies, as in HD. (1)

Other times, an etiology is identifiable. A very common cause is Chagas' disease (CD), which is an infectious disease caused by *Trypanosoma cruzii* protozoan.

It is a great problem in Latin America, where millions of people are infected. (8,9)

In the colon, the problems are related to the destruction of the enteric nervous system with inflammation (8), hipoganglionosis (2), reduction of the interstitial cells of Cajal (9) and some degree of fibrosis. (8,9) It is still not clearly known if this is the direct result of the infection, of the consequent inflammation or of a cross-reactivity among antigens in common between the parasite and some components of the wall of the colon. (9)

CD is not the only cause that can lead to an involvement of the peripheral nervous system in the colon and therefore to problems of intestinal motility. Other rare causes of peripheral neuropathy must be taken into consideration since they can determine constipation and megacolon. These can be a paraneoplastic neuropathy (especially as the result of an underlying lung small cell carcinoma, thymoma, breast cancer or Hodgkin's disease)(5,10,11,12), a connective tissue disease (as scleroderma) (13) and myxedema (14). Sometimes also primary muscle diseases, as myotonic dystrophy, can lead to megacolon. (16)

As mentioned above, the enteric nervous system is not the only one that can be involved in the pathogenesis of megacolon. The autonomic nervous system and the central nervous system as well can be affected by pathologies that can have an impact on the functionality of the colon.

Diabetic neuropathy is certainly the most frequent and known cause of autonomic neuropathy (5,15). The gastrointestinal system can be involved on different levels, including the stomach, the small and the large intestine. (16) The clinical manifestation is represented by diarrhoea, but also by constipation. On the other side, different studies have been conducted to find a correlation between neuro-

logical diseases and abnormalities of the bowel motility.

In some pathologies, gastrointestinal disorders are normally present. The typical example is Parkinson's disease (PD), in which the reduction of the bowel movements, determining constipation (5,17), is characteristic. The main problem in PD concerns the dopaminergic deficiency at the level of the substantia nigra, but also the dorsal motor nucleus of the vagus and the myenteric plexus of the gastrointestinal tract seem directly involved, in fact typical Lewis bodies have been also found in those structures. (5,17)

Delayed colonic transit can be also present in other neurological diseases such as multiple sclerosis, where the pathogenesis of the gastrointestinal disorders is not well known, or in patients with spinal cord pathologies, where the pathogenesis is also quite unknown, but it is probably due to an involvement of the sympathetic function of the spinal cord. (5)

Stroke can also be associated with constipation and megacolon, but a direct correlation has not been found yet. The etiopathogenesis is probably multifactorial, because often these conditions occur in elderly patients, forced to bed rest, submitted to multitherapy, with other pathologies. It is the case of the patient of the case report 1, where her clinical history is positive for cerebral hemorrhage, diabetes mellitus and atrial fibrillation, for which the patient was treated with an antiarrhythmic drug based on verapamil hydrochloride, that can cause constipation. (15)

Therefore, in this case a valid cause of megacolon is not known. The etiology is probably multifactorial, since the nervous system that regulates the colon function could be impaired on different levels, because of the various pathologies that affect the patient.

In the second case report the most likely explanation for megacolon is in the interaction between the antipsychotic drugs and the structures that regulate the normal function of the colon.

Constipation is a well-known collateral side effect of antipsychotic drugs. Constipation is often severe and it can lead to fecal impaction, megacolon, perforation and also, in some cases, death. (18) There are many classes of psychotropic drugs that must be carefully monitored during their use.

Many studies have been made on drugs with anticholinergic properties. (19,20,21) One of these drugs is Clozapine, an atypical antipsychotic drug used in cases of schizophrenia. Among the various collateral effects, constipation occurs in 14-60% of the patients that use this drug. (19,20) The pathophysiology of the constipation seems to be due to a decreased intestinal motility as a result of its anticholinergic properties, (19,20) acting as antagonist of the M3 and M5 receptors. (19)

If underestimated and not treated, constipation can complicate into an intestinal pseudo-obstruction, fecal impaction and colon perforation. In the most severe cases, death has also been reported as a complication of fecal vomitus aspiration, shock and pulmonary edema, and necrotizing colitis. (20)

Another atypical antipsychotic drug is Risperidone, that has a 5HT-2 receptors and D-2 dopamine receptor antagonism

mechanism. The anticholinergic properties of Risperidone are not known yet, but a case of megacolon in a schizophrenic patient using this drug has been described. (22)

Another drug with anticholinergic properties is Imipramine, a tricyclic antidepressant. The principal complication of this drug is to the cardiovascular system, but also constipation and other gastrointestinal problems have been documented: Ross et al. reported a case of toxic megacolon due to an Imipramine overdose. (21)

Also, narcotic drugs used for a long time in the management of pain cause constipation, that occurs in more than 90% of the patients that make use of such drugs. (23-24)

Opioids act on gastrointestinal tract opioid- μ -receptors (23,24) that are found in the submucosal and myenteric plexus, (25) leading to a decreased acetylcholine release, with consequent reduction of the normal colon function. (24)

The impaired motor activity, associated with decreased secretion of ions and fluids (25), is the basis of constipation that can also bring to serious consequences, with potential risk of death for the patient, if not well treated. (23,24)

In case report 2, the patient used psychiatric drugs. They are probably the cause that has led to megacolon. Particularly the drug based on biperidene chlorhydrate, which has well-known anticholinergic properties. (26)

Conclusion

Cerebrovascular accidents, especially in elderly patients with deteriorated general conditions, and psychiatric patients treated with antipsychotic drugs can be affected by problems which delay the intestinal transit, with constipation, faecal impaction, up to megacolon with risk of perforation and consequent peritonitis. Thus, in the most severe cases the risk of death is not to be underestimated. For this reason, it is necessary to monitor the intestinal function of the patients that make use of determined psychiatric drugs attentively, so as to make it possible to set an early diagnosis of colon function anomalies and to be able to act before the onset of potentially fatal complications.

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