

# Idiopathic Myenteric Ganglionitis Underlying Acute 'Dramatic' Intestinal Pseudoobstruction: Report of an Exceptional Case

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## Key Words

Idiopathic constipation · Acute intestinal pseudoobstruction · Myenteric ganglionitis

## Abstract

Inflammation of the myenteric plexus of the gastrointestinal tract is a very rare pathological condition, with few reports in the medical literature. This pathological condition causes atonic gut motor dysfunction and is principally secondary to other diseases, being reported nearly solely as a paraneoplastic phenomenon in neuroendocrine lung tumors, including small cell carcinomas or neuroblastomas. In addition it can also be associated with disorders of the central nervous system, although it has rarely been described in Chagas disease. It has been named 'idiopathic myenteric ganglionitis' because no apparent causes can be demonstrated. We report the clinicopathologic findings of an exceptional case of a young woman affected by severe chronic constipation suddenly changing into acute intestinal pseudoobstruction with dramatic evolution. Relationships between ganglionitis, idiopathic constipation and acute intestinal pseudoobstruction as well as therapeutic implications are discussed.

## Case Report

A 29-year-old female was admitted to our department in April 2005. She presented with a twelve-year history of constipation. The patient was initially treated by sacral neuromodulation [1]. The definitive implantation of a permanent impulse generator (Interstim 3023, Medtronic) months after was performed after a temporary trial period of stimulation. Electrode implantation caused no complications and six months later her general condition was improved. She had regained weight, defecations continued with a good daily rhythm without straining or abdominal pain. The patient declared to be fully satisfied by the improvement to her quality of life.

Suddenly, eight months after the permanent implantation, the situation dramatically changed. The patient had again severe constipation and abnormal abdominal distension. We performed an abdominal X-ray showing marked distension of the whole bowel, particularly of the colon. After a brief observation period, air fluid levels increased and the colon reached an enormous dilation. CT scan demonstrated no mechanical obstruction, there seemed to be a deteriorating intestinal pseudoocclusion (Ogilvie syndrome). The patient's serious general condition and the presence of free air in the peritoneum forced us to operate on her. The length and volume of the colon were enormously increased and the wall was thin and perforated in the cecum. The terminal tract of the small bowel was also dilated. A total colectomy with ileorectal anastomosis was performed.

Histological findings revealed a diffused and dense inflammatory infiltrate restricted to all myenteric plexuses (fig. 1, fig. 2) and to some submucosal plexuses (fig. 3), associated with degenerative features and concurrent loss of ganglion cells. In some plexuses, ganglion cells were absent. Inflammatory infiltrate was mixed in nature, being composed of lymphocytes, plasma cells and eosinophils. Lymphocytes were the predominant cell types in most plexuses. The same histological findings were found in the terminal ileum which was apparently affected.

Immunohistochemical study (fig. 4) revealed that most lymphocytes were CD3+ and CD4+ and only scattered lymphocytes were CD8+ or CD20+; a normal number and distribution of interstitial cells of Cajal stained with c-kit (CD117) was demonstrated. No pathological changes were observed in the mucosa and submucosa, with the exception of a mild and specific inflammatory infiltrate in the colonic mucosa. The histological findings, and particularly the presence of the just described subclasses of lymphocytes, allowed the diagnosis of 'acute pseudoobstruction due to idiopathic immune-mediated myenteric ganglionitis'.

Unfortunately surgery did not resolve the illness. After a period of relative healthiness, three months after the operation the abdomen was again dilated and the peristalsis stopped. New air fluid levels were present on X-ray. No evidence of mechanical obstruction was present on CT scan. Rectoscopy confirmed perviety of the ileorectal anastomosis done in the previous operation. The patient was given total parenteral nutrition and at the same time we attempted a course of pulse-dosed steroid treatment (100 mg i.v. methylprednisolone daily for ten days). The patient did not get any benefit and her clinical condition deteriorated. We attempted a jejunostomy to obtain decompression of the small bowel, but the patient's condition quickly worsened until she eventually died.

## Discussion

Although the cause of idiopathic severe chronic constipation has never been completely clarified, almost all pathological clues have been described to be of degenerative character and/or alterations of the neuropeptide levels. An underlying inflammatory neuropathy may be responsible for chronic constipation/megacolon, usually secondary as in Chagas and paraneoplastic diseases. Recently, idiopathic forms of chronic constipation/megacolon have been described with autoimmune enteric ganglionitis underlying chronic idiopathic constipation and subsequent megacolon [2].

Chronic intestinal pseudoobstruction, characterized by a loss or failure of intestinal peristalsis without organic causes occluding the lumen, appears to be characterized by frequent pseudoocclusive episodes, which can simulate mechanical occlusion. In chronic intestinal pseudoobstruction also different pathological clues have been noticed. The clues affect either the myogenic and/or the neurogenic part of the intestinal wall in mitochondrial myopathies and in progressive systemic sclerosis; more frequently an enteric ganglionitis can be secondary to different conditions, including inflammatory and paraneoplastic disease, or more rarely can be idiopathic [3].

Because of recent reports in literature [2, 3] we speculate that in our case, ganglionitis of the myenteric plexus was present since the first observation with clinical signs of chronic constipation/megacolon with a subsequent 'dramatic' change into an acute pseudoobstruction, because of the worsening of the autoimmune inflammation. This consideration gives us interesting perspectives in the treatment of severe constipation.

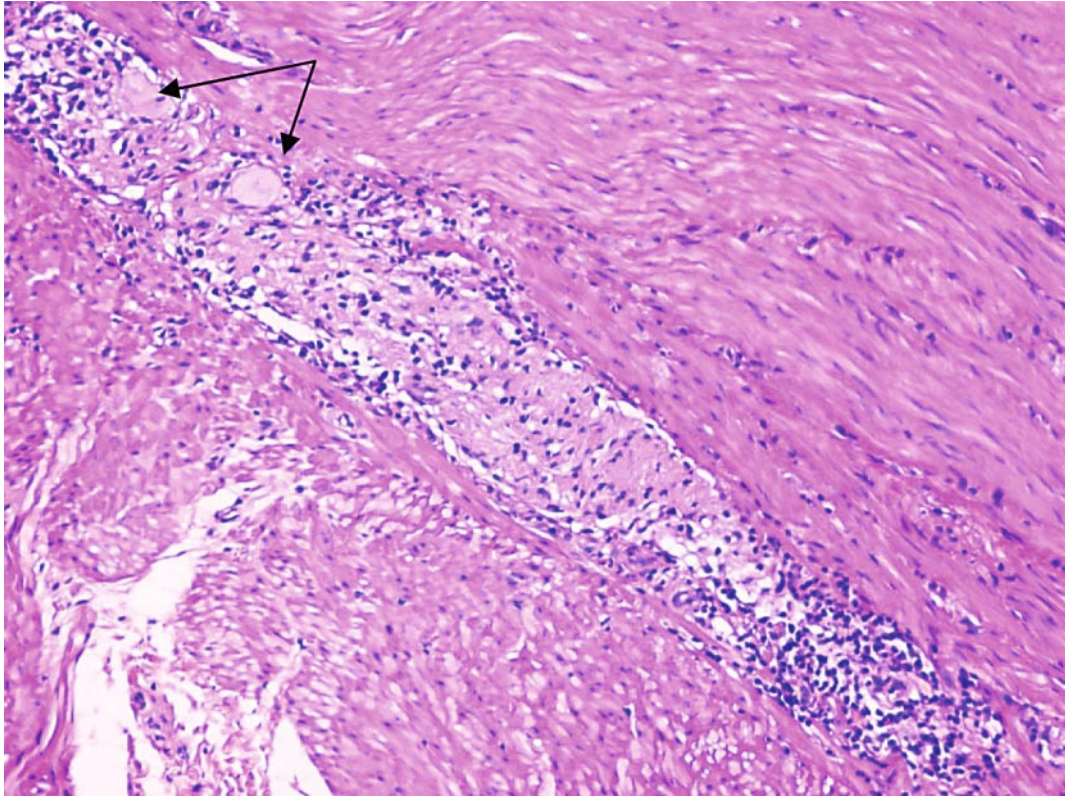
Pharmacological treatment of severe idiopathic chronic constipation (and of chronic pseudoobstruction) is reported in the scientific literature with various types of prokinetics: cisapride, metoclopramide, domperidone, octreotide, prostigmina, erythromycin, etc. However, the disordered motility is resistant to treatment and prokinetic drug therapy is generally disappointing. Recently some encouraging results have been reported regarding the first experiences in treatment by sacral neuromodulation [1]. If the cause of severe chronic constipation is an autoimmune ganglionitis, we can also attempt immunosuppressive therapy [4, 5]. In hindsight, we should suspect intestinal ganglionitis as a cause of severe constipation.

Nowadays, a secure diagnosis concerning the existence of enteric ganglionitis can be confirmed only by histological sampling from full-thickness samples of the intestinal wall, and this is possible, except for the rectum, only in patients undergoing intestinal surgery. Antineuronal circulating antibodies, such as the antineuronal antinuclear ANNA-1, the anti-HU (antineuronal nuclear antibody), the anti-YO (anti Purkinje cell protein cytoplasmatic antibody) or other circulating antineuronal antibodies expressed in ganglionitis, are not reliable for diagnosis. However, in presence of any suspicion when intestinal occlusion is not secondary to mechanical causes, we should not hesitate to obtain a full-thickness biopsy of the intestinal wall, even if surgery is required. This way a short operation can avoid a long series of useless surgical procedures. Once we have a firm diagnosis, patients can benefit immediately from immunosuppressive treatment with high-dosed steroids and/or immunosuppressive drugs, also in association with permanent sacral nerve stimulation, which can help patients with complete failure of intestinal motility.

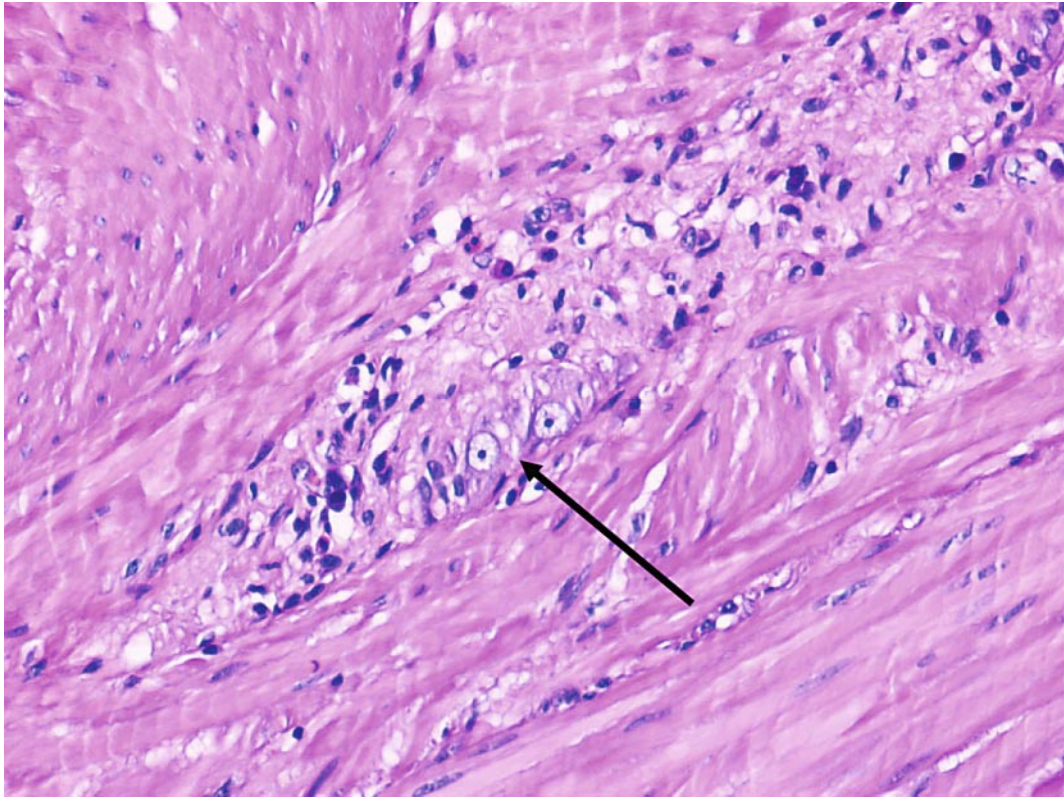
### Conclusion

The reported case is exceptionally rare, in fact we found only one analogous case of mortality in a young adult due to acute intestinal pseudoocclusion with known primary visceral myopathy [6] in the literature. However we can draw some conclusions: (1) When severe chronic constipation is present, we must consider that this can be due to an inflammatory process of the myenteric plexus and thus might evolve into severe pseudoocclusion. (2) Only a full-thickness biopsy can offer a firm diagnosis: if we suspect ganglionitis we should try absolutely to obtain it. (3) With a firm diagnosis of ganglionitis we can treat the disease in time, not only during the exacerbation but also in the chronic stadium, by high doses of corticosteroids [4, 5], NPT, etc. (4) In a part of rare perforative complications, surgery is not indicated in intestinal pseudoocclusion, except for full-thickness biopsy or decompressive procedures.

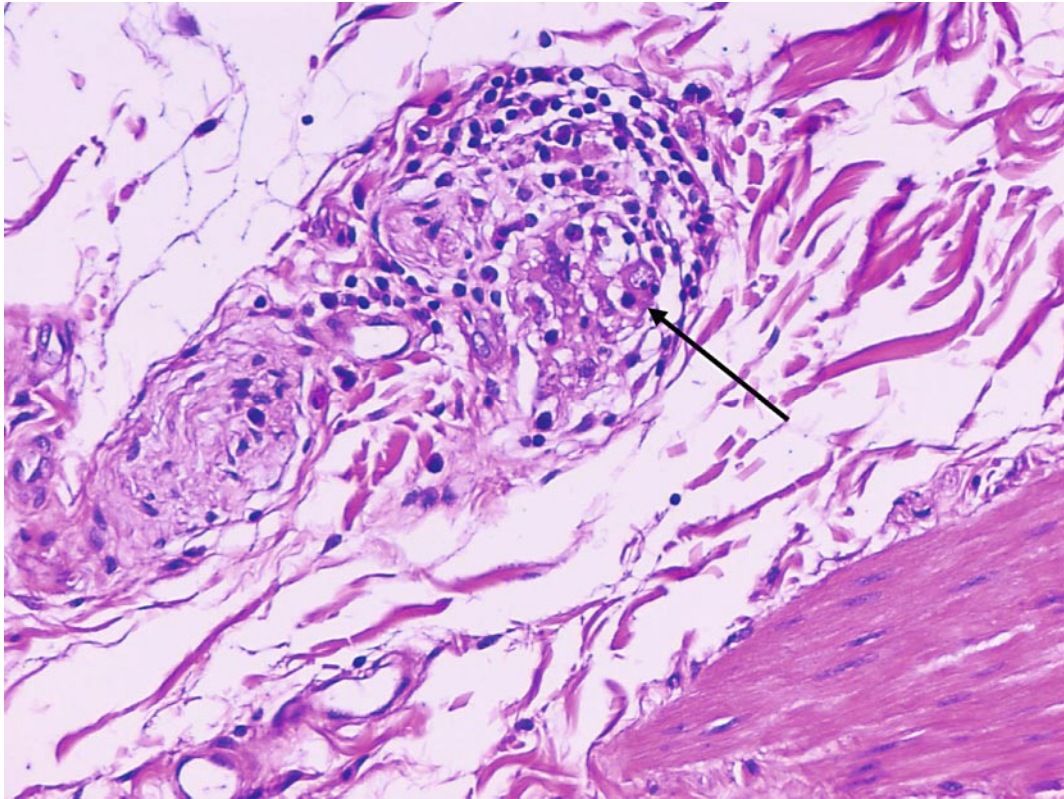
**Fig. 1.** Myenteric plexus with severe inflammatory infiltrate. Inflammatory cells are present both at the periphery and within the plexus in direct contact with Schwann and residual ganglion cells (arrows) showing degenerative changes.



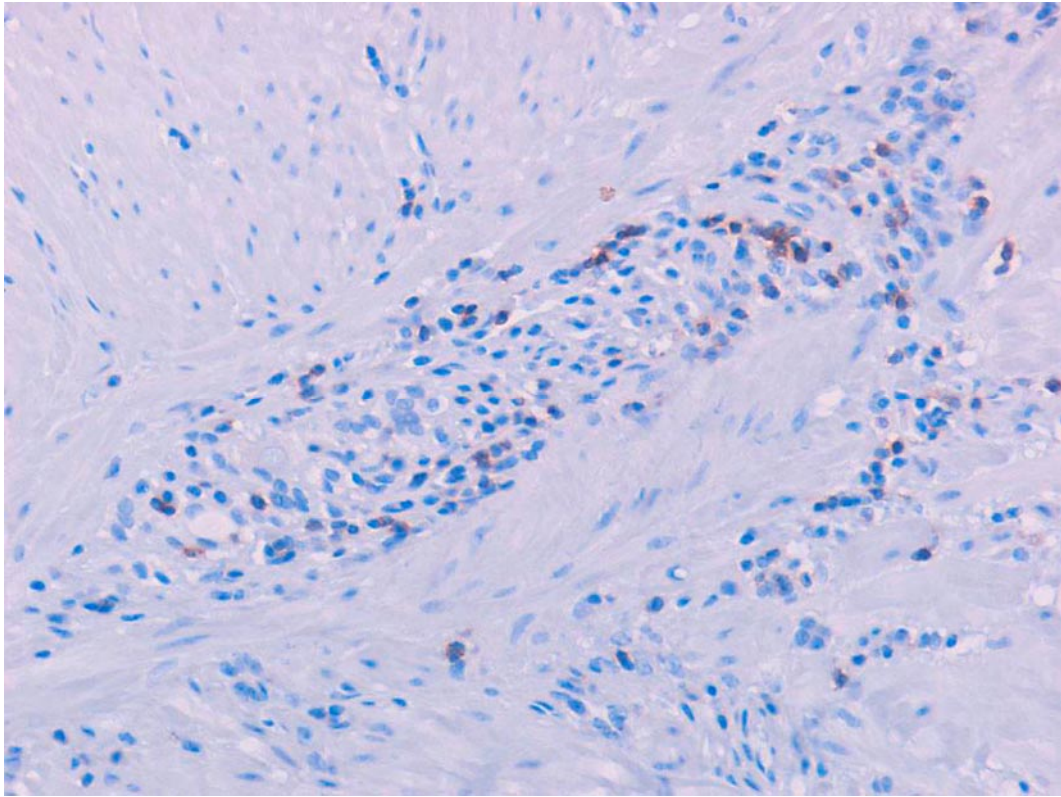
**Fig. 2.** High magnification of myenteric plexus showing lymphocytes, plasma cells and eosinophils. Residual damaged ganglion cells are still preserved (arrow).



**Fig. 3.** Submucosal plexus showing inflammatory infiltrate; some lymphocytes invade the cytoplasm of ganglion cells (arrow).



**Fig. 4.** Myenteric plexus. Immunohistochemical staining with CD3 antibody showing that most lymphocytes are T in nature.



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