

Image Quiz for Surgeons

Chirurgia (2013) 108: 584-588
No. 4, July - August
Copyright © Celsius

Solitary Ganglioneuromatosis of the Descending Colon, Presenting as Giant Retroperitoneal Tumour

I.N. Mateş¹, C. Iosif², D. Dinu¹, S. Constantinoiu¹

¹St. Mary Department of General and Esophageal Surgery, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

²Department of Pathology, St. Mary Clinical Hospital, Bucharest, Romania

Rezumat

Ganglioneuromatoză solitară a colonului descendent, ca tumoră retroperitoneală gigantică

Ganglioneuromul este o tumoră benignă a sistemului nervos autonom, localizarea colică la adulți este neobișnuită. Există trei pattern-uri: ganglioneurom polipoid, polipoză ganglioneuromatoasă și ganglioneuromatoză difuză. Ultimul este asociat frecvent cu neurofibromatoza tip 1 și neoplazia endocrină multiplă tip 2b. O femeie de 68 ani, acuzând doar o ușoară constipație, a fost internată pentru o tumoră voluminoasă în flancul stâng; CT, urografia și irigografia au demonstrat o formațiune retroperitoneală (sarcom retroperitoneal?). Intraoperator, formațiune tumorală de 16/10/11 cm, solidă și încapsulată, atașată pe fața retroperitoneală al colonului descendent, fără leziune mucoasă macroscopic; diagnosticul patologic al piesei rezecate (rezecție tumorală en-bloc cu colectomie limitată): ganglioneuromatoză intramurală colică. Anamnezic, prin examen clinic și explorări endoscopice, nu s-a putut demonstra concomitența sau agregarea familială a unui sindrom cu transmitere genetică. La adulți, ganglioneuromatoza transmurală nu este obligatoriu asociată cu neurofibromatoza tip 1 sau neoplazia endocrină multiplă tip 2b; proliferarea tumorală adesea simulează cancerul în virolă și

diagnosticul este obținut prin examenul patologic al piesei rezecate. Cazul relatat de noi este particular; țesutul lax retroperitoneal a favorizat dezvoltarea lentă a ganglioneuromatozei intramurale, sub forma unei tumori retroperitoneale gigante fără nici o evidență radiologică care să sugereze originea sa colică.

Cuvinte cheie: ganglioneurom colic, ganglioneuromatoză intestinală, tumoră retroperitoneală

Abstract

Ganglioneuroma (GN) is a benign neoplasia of the autonomous nervous system, colonic GN is uncommon in adults. There are three subgroups: polypoid GN, ganglioneuromatous polyposis and diffuse ganglioneuromatosis. Ganglioneuromatosis is highly-associated to neurofibromatosis type 1 (NF1) and multiple endocrine neoplasia type 2b (MEN2B). A 68-year-old female, with a discrete retarded emission of stools, was admitted for a large tumor in the left flank; CT scan, urography and barium enema demonstrated a large retroperitoneal mass, presumed as sarcoma. Open surgery discovered a 16/10/11 cm solid and encapsulated tumor, attached to the retroperitoneal descending colon, with no macroscopic mucosal involvement; the pathologic diagnosis of the resected specimen (en-bloc tumorectomy with limited colectomy) was intramural colonic ganglioneuromatosis. Anamnesis, physical examination and complete endoscopic explorations showed no evidence of personal bearing or familial aggregation of genetic syndromes. In adults, association of transmural ganglioneuromatosis to NF1 or MEN2B is not mandatory; presentation often mimics obstructive carcinoma and positive diagnosis is provided by

Corresponding author:

Ioan Nicolae Mateş, MD, PhD
St. Mary Department of General and
Esophageal Surgery
37-39 Mihalache Ion Blv, sector 1, 011172
Bucharest, Romania
E-mail: ioan.mates@gmail.com

pathological examination of the resected specimen. In this peculiar case, the loose tissue of the retroperitoneal space favoured a slow development of intramural ganglioneuromatosis, presenting as a gigantic retroperitoneal mass with no radiological evidence of its colonic origin.

Key words: colonic ganglioneuroma, intestinal ganglioneuromatosis, retroperitoneal tumor

Introduction

Ganglioneuroma (GN) is a rare, benign and well-differentiated, slow-growing and indolent neoplasia of the autonomous nervous system, characterized by an overgrowth (hyperplasia) of mature ganglion cells and satellite (supporting) cells; colonic GN is uncommon. It may be discovered at any age, with different clinical and prognostic significance in infants and adults; it may be a solitary lesion or a component of a systemic syndrome. There are three subgroups, each with a different degree of GN formation: polypoid GN, ganglioneuromatous polyposis and diffuse ganglioneuromatosis.

Ganglioneuromatosis is highly-associated to von Recklinghausen's disease - neurofibromatosis type 1 (NF1) and multiple endocrine neoplasia type 2b (MEN2B), especially in adults with nodular intramural or transmural proliferation (neural hyperplasia in all layers of the bowel wall, including the myenteric plexus). There are a few reported cases of solitary transmural ganglioneuromatosis in adults, unassociated to systemic genetic syndromes; typically, presentation is similar to annular-obstructive carcinoma and definitive diagnosis is provided only by the pathological examination of the resected specimen.

Case report

A 68-year-old old female, with no significant medical history, was admitted for surgical treatment of an abdominal tumor, discovered by self-abdominal palpation. Her only complaint was a discrete retarded emission of stools. A large (20/15 cm), solid and indolent mass was evident at palpation in the left flank; laboratory blood tests were normal. Previous to admission, computer tomography (CT, native + iv contrast), described a 12.6/11/15.6 cm well-defined, inhomogeneous (even to late contrast), retroperitoneal formation in the left flank, in contact with the anterior parietal peritoneum and exerting a compressive effect on the intestinal loops (Fig. 1), presenting strict delimitation to the inferior pole of the kidney and psoas muscle (Fig. 2); a retroperitoneal sarcoma was suspected. Urography: huge, homogenous opaque image in the left flank; midline-displacement of the left lumbar ureter. Barium enema: midline and anterior (Fig. 3) displacement of the descending colon.

Open surgery (midline abdominal incision) disclosed the presence of a large retroperitoneal bulk in the left flank, with



Figure 1. CT scan, iv contrast: well-defined, inhomogeneous, retroperitoneal formation in the left flank

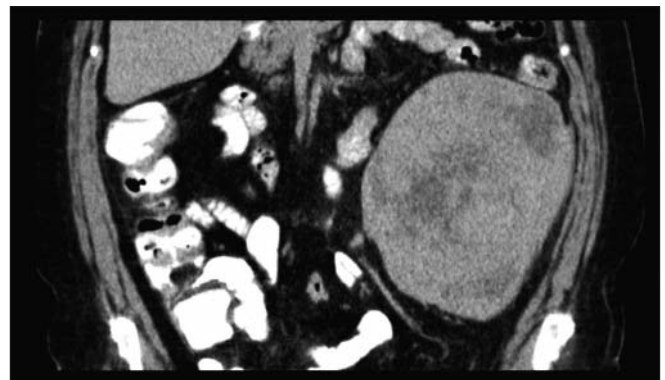


Figure 2. CT reconstruction



Figure 3. Barium enema, lateral view: anterior displacement of the descending colon, far-away from the lumbar vertebrae axis

obvious displacement of the descending colon. A thickened peritoneal fascia of the left colic gutter was incised (sigmoid to left flexure); blunt digital- dissection of the tumor and complete

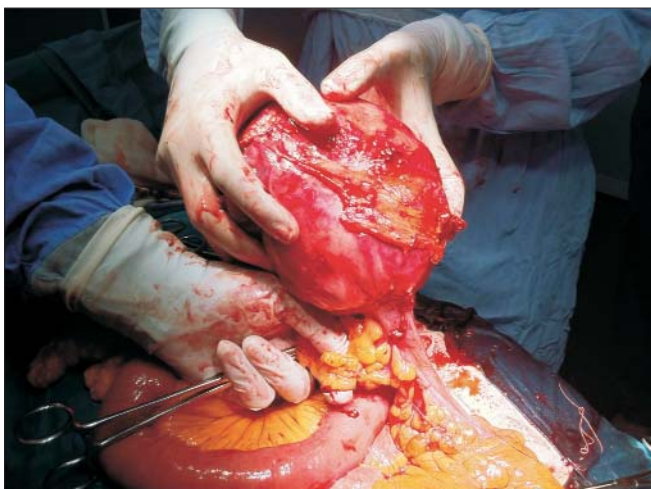


Figure 4. Complete dissection of the retroperitoneal tumour; limited attachment to the descending colon

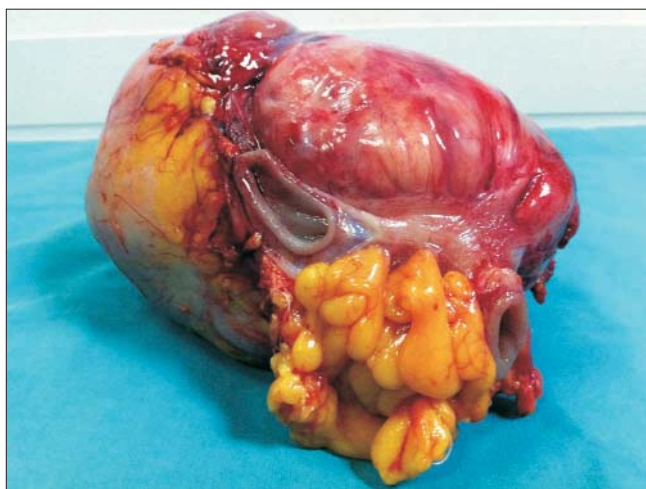


Figure 5. Resected specimen

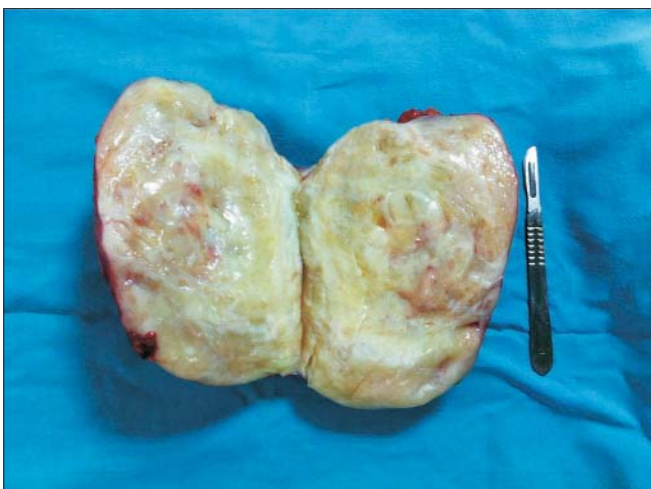


Figure 6. Sectioned resected specimen

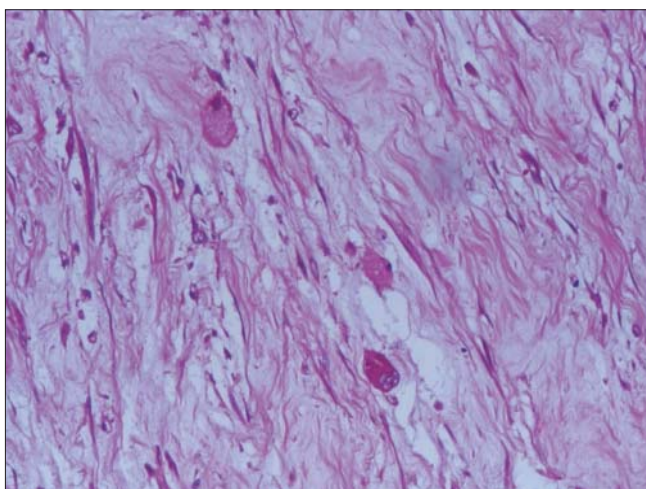


Figure 7. Microscopy, hematoxylin-eosin (x10 objective): scattered ganglion cells in a neuromatous stroma

mobilization of the left colon. The tumor was attached to a 5 cm- long segment of the descending colon, on the opposite site from its mesentery, but sharing the same vascular sources (Fig. 4); later confrontation of CT imaging with surgical reality demonstrated that attachment of a digestive segment to the mass (clearly visible in Fig. 1) was misinterpreted as digestive compression, so presumption of a digestive tumor was neglected. En-bloc resection of the tumor along with a limited colectomy was practiced (Fig. 5). Grossly the aspect was that of a 16/10/11 cm solid and encapsulated tumor, with no mucosal involvement, fasciculated and white-yellowish on section (Fig. 6). The patient was discharged 9 days later.

Histology displayed a relatively uniform appearance with few ganglion cells arranged in small clusters or scattered in a loose stroma (Fig. 7) with bland, spindle-shaped cells with Schwannian features. The tumour cells lacked other features of malignancy showing no mitosis and only mild nuclear pleomorphism. Immunohistochemical staining (Fig. 8) showed strong immunoreactivity for neuron-specific enolase (NSE) and

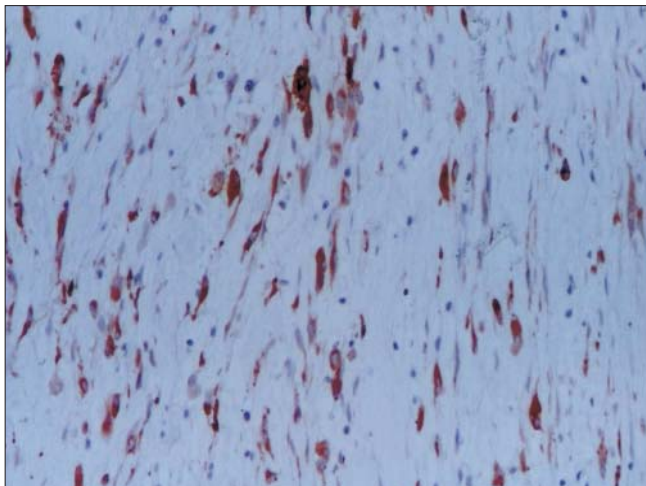


Figure 8. Immunohistochemical staining (x10 objective): strong immunoreactivity for NSE in ganglion cells and spindle cells

S100 protein, but SYNAPTO and NFT were negative; immunostaining for anti-CD117 and DOG-1 for interstitial cells of Cajal was negative, as well as for CROMO and Ki67. Diagnosis: intramural ganglioneuromatosis. There was no clinical or pathological evidence of NF1 or MEN2B; anamnesis was negative for familial aggregation of other genetic syndromes. Upper-GI endoscopy was normal; no associated polyposis, non-familial adenomatous polyposis or adenocarcinoma was demonstrated by colonoscopy and follow-up examination discovered no relapse 9 months later.

Discussions

Ganglioneuroma (GN) is a rare, benign and well-differentiated, slow-growing and indolent neoplasia, of the autonomous nerve system that can be found in diverse anatomic sites. Gastrointestinal GN are equally distributed between males and females and can be discovered at any age (1). Colonic GN are uncommon (2-4) but appear to be largely centered in the left colon and rectum (1,5). Microscopically, there is an abundance of mature ganglion cells, associated to hyperplasia of spindle Schwann cells - forming nerve fibres; immunohistochemically, the ganglion cells are positive for neuron-specific enolase (NSE), neurofilaments (NFT) and synapto-physin (SYNAPTO), whereas the Schwannian components are positive for S100 protein and often for glial fibrillary acidic protein (1).

Although GN may be a solitary finding, it is commonly identified as a component of systemic syndromes. A long-term follow-up study (5) demonstrated three subgroups, each with a different degree of GN formation (6):

- polypoid GN. The usual presentation is a colonoscopic discovery, with no characteristic symptoms, of solitary or low number of, pedunculated or sessile small-sized (11-20 mm) polyps, covered by normal or discoloured mucosa (endoscopically indistinguishable from hyperplastic or adenomatous polyps), with limited endoscopic ultrasound involvement of the mucosa or submucosa. None of these patients present NF1. Endoscopic mucosal resection provides positive and differential diagnosis to hyperplastic polyps, hamartoma, true adenoma, as well as definitive curative treatment (4,7).
- ganglioneuromatous polyposis. The condition is similar to polypoid GN and described by multiple (more than 20) GN sessile or pedunculated polyps (4). It may be associated in adults to multiple cutaneous lipomas or skin tags (5,6), but children occasionally present Cowden's disease (multiple hamartoma syndrome), non-familial colic polyposis or juvenile polyposis (8). GN polyposis may be an incidental colonoscopic finding; occasionally endoscopic exploration is motivated by constipation or bleeding; colectomy is the best option.
- diffuse ganglioneuromatosis. Intestinal ganglioneuromatosis has two morphological patterns, mucosal or transmural; both variants are described in children. Based on clinico-pathologic and immunohistochemical studies, it was suggested that mucosal ganglioneuromatosis might represent a distinct entity, with a lower

morbidly rate compared to the transmural variant - characterised by neural hyperplasia in all layers of the bowel wall, with predominant involvement of the myenteric plexus (9). Mucosal intestinal ganglioneuromatosis is essentially described in children and rarely in adults - presenting distinctive features from that observed in children (10). Diffuse murally extending ganglioneuromatosis is highly-associated to NF1 and MEN2B (1,5), but genetic association is not mandatory in adults (10,11). Typically, nodular intramural or transmural proliferation is discovered in adults; the tumour growth is solid and voluminous, annular (developing a napkin-ring constriction); most patients are operated for partial/complete colonic obstruction presumed as secondary to carcinoma (2,10,11,12); it may distort the architecture of the surrounding tissue, but occasionally there is no luminal surface ulceration of the lesion (11). There are few reported cases associated to sporadic colonic adenocarcinoma, but the significance of this association is undetermined; a common molecular mechanism involved in both entities is controversial.

Conclusion

We report a solitary, unusual, giant (16/10/11 cm) colonic intramural ganglioneuromatosis of the descending colon in an adult female, simulating a retroperitoneal sarcoma; preoperative radiological investigations were unable to suspect its colonic origin. The tumour was indolent and exerted only a slight colonic compression. Its gross macroscopic appearance was of a large, solid and encapsulated mass attached to the colon, with no luminal surface lesion; the microscopic diagnosis was a surprise: intramural ganglioneuromatosis.

Ganglioneuromatosis is usually confined to the mucosa and rarely transmural, in adults. There are scarce reported-cases of solitary colonic diffuse ganglioneuromatosis (unassociated to NF1 or MEN2B), most of them discovered in adults so our present study confirms previous reports. The transmural variant is described as a luminal-constrictive, progressive formation, with clinical and radiological features resembling carcinoma; diagnosis is always dependent on the microscopic examination of the resected specimen. To the best of our knowledge, this is an exceptional case-report of a solitary, giant colonic intramural ganglioneuromatosis, presenting as a retroperitoneal mass.

References

1. Miettinen M, Fletcher CDM, Kindblom L-G, Tsui WMS. Mesechimal tumors of the colon and rectum. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, editors. WHO Classification of Tumours of the Digestive System. IARC: Lyon 2010, p. 182.
2. Bibro MC, Houlihan RK, Sheahan DG. Colonic ganglioneuroma. Arch Surg. 1980;115(1):75-7.
3. Soccorso G, Puls F, Richards C, Pringle H, Nour S. A ganglioneuroma of the sigmoid colon presenting as leading point of intussusception in a child: a case report. J Pediatr Surg. 2009;44(1):e17-20. doi: 10.1016/j.jpedsurg.2008.10.037.

4. Fiori E, Pozzessere C, Lamazza A, Leone G, Borrini F, Schillaci A, et al. Endoscopic treatment of ganglioneuroma of the colon associated with a lipoma: a case report. *J Med Case Rep.* 2012 Sep 14;6(1):304. doi: 10.1186/1752-1947-6-304.
5. Shekitka KM, Sobin LH. Ganglioneuromas of the gastrointestinal tract. Relation to Von Recklinghausen disease and other multiple tumor syndromes. *Am J Surg Pathol.* 1994;18(3):250-7.
6. Chan OT, Haghghi P. Hamartomatous polyps of the colon: ganglioneuromatous, stromal, and lipomatous. *Arch Pathol Lab Med.* 2006;130(10):1561-6.
7. Mendez MI, Pereda T, Rodriguez FJ, Funez R, Sanchez A. Solitary colonic polypoid ganglioneuroma. *Diagn Pathol* 2008;3:20.
8. Dellinger GW, Lynch CA, Mihas AA. Colonic ganglioneuroma presenting as filiform polyposis. *J Clin Gastroenterol* 1996;22:66-70.
9. d'Amore ES, Manivel JC, Pettinato G, Niehans GA, Snover DC. Intestinal ganglioneuromatosis: mucosal and transmural types. A clinicopathologic and immunohistochemical study of six cases. *Hum Pathol.* 1991;22(3):276-86.
10. Chambonnière ML, Porcheron J, Scoazec JY, Audigier JC, Mosnier JF. Intestinal ganglioneuromatosis diagnosed in adult patients. *Gastroenterol Clin Biol.* 2003;27(2):219-24. French.
11. Ledwidge SF, Moorghen M, Longman RJ, Thomas MG. Adult transmural intestinal ganglioneuromatosis is not always associated with multiple endocrine neoplasia or neurofibromatosis: a case report. *J Clin Pathol.* 2007;60(2):222-3.
12. Lazar AM, Brătucu E, Straja ND, Daha C, Marincea M, Cirimbei C, et al. Primitive retroperitoneal tumors. Vascular involvement--a major prognostic factor. *Chirurgia (Bucur).* 2012;107(2):186-94.