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# Solitary plexiform neurofibroma determining pyloric obstruction: a case report

## *Neurofibroma plexiforme solitário determinando obstrução pilórica: relato de caso*

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### ABSTRACT

Solitary gastric plexiform neurofibroma (PN) is a very rare tumor that originates from the peripheral nerves. PN is a rare cause of pyloric obstruction. A 58 year-old man, reported epigastric discomfort, nausea, and vomiting for two months. Upper digestive endoscopy showed a moderate/accentuated pyloric stenosis. Computed tomography (CT) and echoendoscopy revealed a pyloric nodule. The patient underwent to distal gastrectomy. Macroscopically, a gray nodule measuring  $1.1 \times 1.0 \times 1.0$  cm was identified. Using microscopy, a benign tumor composed of enlarged tortuous nerve fascicles showing a neurofibromatous proliferation with mild atypia and myxoid matrix was found. The lesion showed positive immunoexpression for S100, Leu7, and epithelial membrane antigen (EMA), and was negative for CD117, DOG-1, desmin, and smooth muscle actin. The diagnosis of PN was then determined.

**Key words:** neurofibroma; pylorus; gastric cancer; gastrointestinal tract; pathology.

### INTRODUCTION

Primary gastric neurogenic tumors are rare. They are found into two major groups: those arising from the peripheral nerve sheath origin (schwannomas, neurofibromas, ganglioneuromas, neuromas, and perineuromas), and those of sympathetic or chromaffin system (neuroblastomas, ganglioneuromas, and paragangliomas). Gastric neurofibromas develop either as sporadic isolated lesions or as a more diffuse involvement in neurofibromatosis type 1 (NF1) patients. Isolated gastric neurofibromas are uncommon lesions related to bleeding, melena, pain, and obstruction. Plexiform variant is a subtype of neurofibroma that usually compromises soft tissue and rarely affects gastric wall<sup>(1, 3, 4, 6, 13, 16, 18)</sup>. Herein, the authors report an uncommon case of solitary gastric plexiform neurofibroma (PN), and discuss pathologic and clinical findings of this tumor.

### Case report

A 58-year-old man was admitted to hospital service referring epigastric discomfort, episodes of nausea, and vomiting for

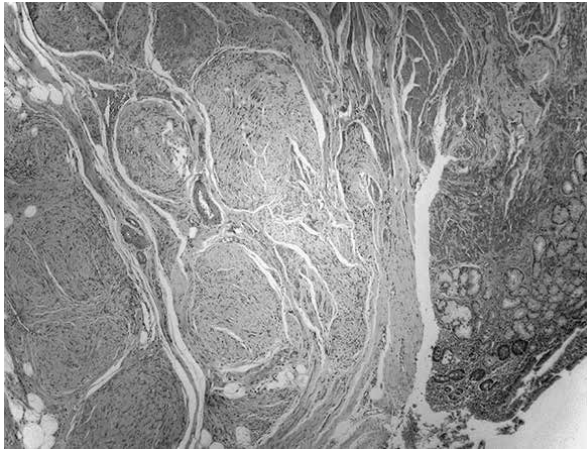
two months. Physical examination revealed discrete epigastric pain on abdominal palpation. Other organs and systems have not showed clinical alterations, as there was no previous history of relevant disease. Upper gastrointestinal endoscopy showed areas of enanthematous gastritis at the antrum and a moderate to accentuated pyloric stenosis. Biopsy specimen contained moderate chronic gastritis. *Helicobacter pylori* were not found. Computed tomography (CT) scans revealed thickening area of pylorus. Upper digestive echoendoscopy revealed a wall pyloric nodule measuring 1.0 cm in diameter. Chest and central nervous system CT/magnetic resonance imaging (MRI) scans did not show abnormalities. The patient underwent distal gastrectomy. Macroscopically, a gray oval nodule measuring  $1.1 \times 1.0 \times 1.0$  cm was identified; it was affecting the muscular layer of the pylorus and perigastric tissue. Using microscopy, a benign soft tissue tumor was found. The process was composed of enlarged tortuous nerve fascicles (**Figure 1**), showing neurofibromatous proliferation with elongated, mildly atypical cells with oval to elongate nuclei (**Figure 2**). Neoplastic cells were loosely dispersed in a moderately myxoid matrix. Some collagen fibers were

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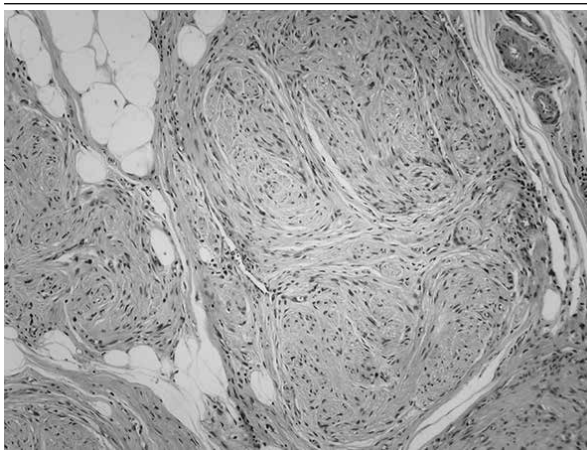
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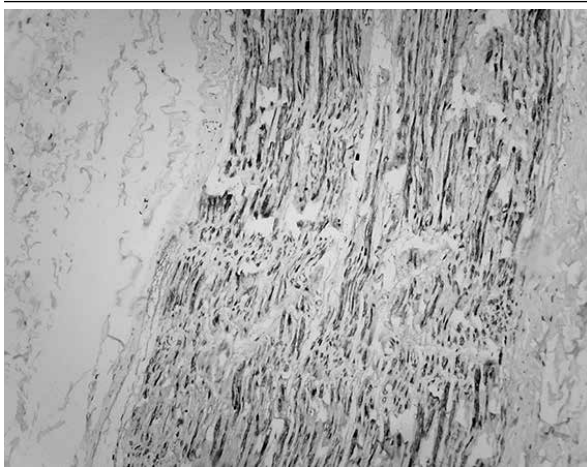
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**FIGURE 1** – Plexiform neurofibroma: tortuous expansion of multiple nerve fascicles caused by neurofibroma cells, affecting gastric wall, HE, 40×  
HE: hematoxylin and eosin stain.



**FIGURE 2** – Plexiform neurofibroma: a benign soft tissue tumor composed of cells which have oval to elongate normochromatic nuclei, expanding the nerve fascicle, HE, 200×  
HE: hematoxylin and eosin stain.



**FIGURE 3** – Plexiform neurofibroma: positive immunoreactivity for S100 antibody, streptavidin-biotin, 200×

seen. The lesion showed positive immunoexpression for S100 (**Figure 3**), Leu7, and epithelial membrane antigen (EMA) (rare peripheral cells), and was negative for CD117, DOG-1, desmin, and smooth muscle actin. The diagnosis of PN was then determined. No other clinical evidences of NF1 were found.

## DISCUSSION

Neurofibromas are well-differentiated, benign peripheral sheath tumors consisted of Schwann, perineurial-like, and fibroblasts cells, and cells with intermediate features. Residual myelinated or unmyelinated axons are often present. Many of these lesions are associated with a recognizable nerve. In general population, neurofibromas are much more sporadic than associated with neurofibromatosis. Neurofibromas occur in a variety of architectural types, including cutaneous (localized and diffuse), intraneural (localized or plexiform type), massive soft tissue tumors (composed of both diffuse and plexiform elements), and visceral. The clinical presentation and gross appearance differ considerably between the different forms. As isolated lesions, both plexiform and massive soft tissue tumors are almost pathognomonic of NF1, although there are cases in which the syndrome is not identified, at least at the time of surgery. PN are related to alterations in the NF1 gene, including secondary, somatic mutations. Visceral neurofibroma consists of solitary or multiple, sporadic or NF1-associated neurofibromas of localized or plexiform type. Viscera affected include the small bowel, mesentery, large bowel, stomach, liver, and the genitourinary tract. Laryngeal or cardiac lesions are rare<sup>(1-3, 5, 9, 10, 12, 14, 17)</sup>.

PN is defined as a neurofibromatous involvement of multiple fascicles of a nerve, and often of its branches. PN most often presents in children of either sex, and less frequently occurs in young adults. The tumor arises mostly in large nerves related to cervical, brachial, or lumbosacral plexuses. Most visceral and mesenteric neurofibromas are of the plexiform type. PN of major nerves are considered a precursor lesion to the majority of malignant peripheral nerve sheath tumors. Malignant transformation occurs in 5% of sizable plexiform tumors, but is a rare event in diffuse cutaneous and massive soft tissue neurofibromas. PN associated to NF1 essentially always develop during early childhood, often before the cutaneous neurofibromas have fully developed<sup>(1, 2, 5, 12, 14, 15, 19-21)</sup>. In the present case, the authors describe a PN originated in the pylorus which determined gastric obstruction. The **Table** shows some cases of gastrointestinal PN found in the international literature compared with our case study.

TABLE – Summary of some published cases of gastrointestinal PS

Authors	Age/gender	Clinical findings	Topography	Treatment modality	Outcome
Beck <i>et al.</i> <sup>(4)</sup>	14/F	Hematemesis	Stomach	Gastrectomy	Unavailable
Ganeshan <i>et al.</i> <sup>(7)</sup>	67/M	Dysphagia	Esophagus	Esophago-gastrectomy	Unavailable
Leslie <i>et al.</i> <sup>(11)</sup>	76/F	Abdominal pain	Small bowel	Partial enterectomy	Died due lung adenocarcinoma
Park <sup>(15)</sup>	11/M	Abdominal discomfort	Ileum	Partial tumor resection	No clinical evidence of tumor growth after 10 months
Rezende <i>et al.</i> <sup>(18)</sup>	42/M	Abdominal discomfort, black stools, and anemia	Antrum	Distal gastrectomy	No evidence of recurrence after 36 months of follow-up
Present report	58/M	Epigastric discomfort, nausea, and vomiting	Pylorus	Distal gastrectomy	No evidence of recurrence after 03 months of follow-up

PS: plexiform schwannoma; F: female; M: male.

PN more commonly consists of grossly expanded nerves or nerve fibers which are largely replaced by neurofibromatous tissues. These expanded nerves form thick, convoluted cords and nodules macroscopically. PN have smooth glistening external surface. The cut surface of PN is uniformly light tan or gray, glistening, semitranslucent, firm, and without hemorrhage or necrosis. In the gastrointestinal tract, PN usually determines a nodular lesion affecting muscular layer and perivisceral adipose tissue. Less commonly, PN extend from the submucosa across the muscularis mucosae into the mucosa where they expand the gland and distort the crypts<sup>(1, 2, 5, 6, 8, 13, 17-19, 21, 22)</sup>. At microscope, the tumor is composed by a tortuous mass of expanded nerve branches, which are better seen in various planes of section. PN is composed of a growth of cells with oval to elongate normochromatic nuclei, which are loosely dispersed in a variably myxoid matrix intermingled with collagen fibers. Nuclei of neurofibroma cells are about one-third the size of schwannoma cell nuclei and their cell processes are indistinguishable from collagen fibers. The cells grow alongside nerve fibers of fascicle origin. The fascicle is expanded by the tumor but maintenance of original contour. Each nodule of PN is outlined by an evident perineurium. PN can show nuclear atypia and areas of heightened cellularity. Uncommon histologic findings in PN are pseudomeissnerian bodies, densely aggregated hyperchromatic nuclei, melanin pigmentation, discrete formation of neoplastic Schwann cells, and true epithelial cell differentiation. Electron microscopy of PN demonstrates that Schwann cell is the predominant cell type, and it is surrounded by basal lamina. A significant number of fibroblasts are also present. PN shows immunopositivity for vimentin and Leu7, and only a few cells can be highlighted for S100 protein. Positive immunostaining for glial fibrillary acidic protein (GFAP) and EMA can be found<sup>(1, 2, 5, 6, 8, 13, 17-19, 21, 22)</sup>.

Differential diagnosis includes schwannomas, plexiform schwannomas (PS), plexiform fibrohistiocytic tumors (PFT), and gastrointestinal stromal tumors (GIST). Schwannomas occur at all ages but are more common in persons between the ages of 20 and 50 years. Schwannomas affect more commonly the nerve roots of the head, neck, and flexor surfaces of upper and lower extremities. Most schwannomas are uninodular masses surrounded by fibrous capsule consisting of epineurium and residual nerve fibers. The tumor shows some areas composed by compact spindle cells with twisted nuclei arranged in short bundles (Antoni A areas, including nuclear palisading), and less cellular zones showing spindle or oval cells arranged haphazardly in a loosely textured matrix (Antoni B areas). PS are composed of uniform Schwann cells, can show Verocay bodies, lack of a diffuse extraneural component, exhibit large cells when compared to PN, and uniform S100 protein immunopositivity. PFT show female predilection. They are small and firm, do not demonstrate large expanded nerves, lack of an underlying nerve association, composed of myofibroblasts, epithelioid, and giant cells, and show anti-muscle specific actin (HHF35) immunoreactivity rather than S100 protein positivity. The stomach is the most common site of localization for GISTs, which are generally benign lesions, with well-defined borders. Gastric GIST usually exhibits two histologic patterns. One is a cellular spindle stromal tumor characterized by fascicles of spindle cells exhibiting monotonous and uniform nuclei. The epithelioid GIST contains round epithelioid cells with prominent clear cytoplasm and cytoplasmic perinuclear vacuolization, arranged in sheets or packets. Gastric GIST shows variable positive immunoexpression for CD117, CD34, smooth muscle actin, heavy caldesmon. GISTs strongly express the DOG-1 gene, and infrequently exhibit immunopositivity for desmin and S100<sup>(1, 2, 8, 13, 19, 20)</sup>.

## RESUMO

*Neurofibroma plexiforme (NP) gástrico solitário é um tumor muito raro originado a partir dos nervos periféricos. É uma causa rara de obstrução pilórica. Paciente masculino, 58 anos, relatava desconforto epigástrico, náuseas e vômitos durante dois meses. A endoscopia digestiva superior mostrou estenose moderada/acentuada do piloro. Tomografia computadorizada (TC)/ecoendoscopia revelaram nódulo no piloro. O paciente foi submetido a gastrectomia distal. À macroscopia, identificou-se nódulo cinzento medindo  $1.1 \times 1 \times 1$  cm. À microscopia, encontrou-se tumor benigno composto por fascículos nervosos dilatados/tortuosos, exibindo proliferação neurofibromatosa com atípicas leves e matriz mixoide. A lesão exibiu imunoe expressão positiva para S100, Leu7 e antígeno da membrana epitelial (EMA), e negatividade para CD117, DOG-1, desmina e actina de músculo liso. O diagnóstico de PN foi, então, determinado.*

*Unitermos: neurofibroma; piloro; neoplasias gástricas; trato gastrointestinal; patologia.*

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## Errata

O artigo "Solitary plexiform neurofibroma determining pyloric obstruction: a case report", publicado no volume 50, número 3, do Jornal Brasileiro de Patologia e Medicina Laboratorial [JBPM. 2014; 50(3): 238-41], sofreu as seguintes alterações nas Figuras 2 e 3:

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