

Case Report

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Gastric plexiform fibromyxoma in children: A new case report and review of pediatric literature

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Abstract

Introduction: Plexiform Fibromyxoma (PF), also known as Plexiform Angiomyxoid Myofibroblastic Tumour (PAMT) is a rare mesenchymal myxoid tumour originating in different areas of the digestive system. Symptoms and signs are usually elusive: the most common are abdominal discomfort, dyspepsia, nausea and gastrointestinal bleeding with anemia and hematemesis. Imaging tests are useful to identify plexiform fibromyxoma, but only pathology provides the definitive diagnosis and differentiate it from other mesenchymal tumours. PF seems to display a benign behaviour and the only complete surgical removal of the mass represents the gold standard of treatment; no recurrence or metastasis has been described so far. A little more than 100 cases have been described in adulthood with only 14 cases reported up to now in pediatrics.

Case report and review: We report the case of a gastric plexiform fibromyxoma occurred in an 8-year old girl went to our observation with a story of dyspepsia, vomiting, weight loss and anemia. A 4 X 2.5 cm mass was found in the gastric antrum. The tumour was removed by laparoscopic antrectomy and the pathological exam was consistent with PF. A detailed review of PF pediatric literature is also provided.

Keywords: plexiform fibromyxoma; gastric tumour; pediatrics; laparoscopic gastric resection.

Introduction

Plexiform Fibromyxoma (PF), also known as Plexiform Angiomyxoid Myofibroblastic Tumour (PAMT), is a rare gastrointestinal mesenchymal myxoid tumour first reported by Takahashi et al. in 2007 [1]. Adopting the name of plexiform fibromyxoma, this tumour is described as a distinct entity among mesenchymal tumours in WHO Classification of Tumours of the Digestive System [2] as it displays peculiar multinodular plexiform patterns [3], bland spindle cells, myxoid or fibromyxoid stroma with an arborizing vasculature [4,5] and specific immunohistochemical characteristics. PF predominantly arises from the muscularis propria of the gastric antrum [6] with very few cases found in esophagus [7], duodenum [8], gallbladder [9] and colon [10]. The prevalence is similar in both genders with a male-to-female ratio approximately 1:1 [3] with a wide age range at diagnosis from childhood to elderly [5]. The most frequent symptoms are epigastric discomfort or abdominal pain, dyspepsia, nausea, vomiting, weight loss, hematemesis and anemia. Rarely, the tumour is incidentally found during endoscopy or at radiological images [5]. Plexiform fibromyxoma is considered to be a benign tumour, as it presents low proliferation index and poor mitotic activity; metastases and recurrence following complete excision have not been described so far. We report a new case of gastric antrum PF occurred in an 8-year-old female, operated with a laparoscopic technique, which can be added to the only 14 previous reported pediatric cases to improve our knowledge about this rare tumour. A detailed review of PF pediatric literature is also provided.

Case report

Symptoms and signs: An 8-year-old girl came to our emergency department because of lasting and bothersome nausea with occasional episodes of vomiting in the last past year. These symptoms have been increasing in the past five months with appearance of weight loss, blocking of height gain and constipation. Her past history was unremarkable. Physical examination of the abdomen was normal. Blood examination were normal, except for low haemoglobin values and low mean corpuscular volume (Hb 7.7 g/dL; MCV 70,4fL).

Diagnostic assessment: Abdominal Ultrasound (US) showed a 3,5 X 3 cm solid mass originating within the gastric wall. The tumour was well circumscribed, homogeneously hypoechoic, poorly vascularised at Color-Doppler evaluation and because of its proximity to the pylorus it caused a partial gastric outlet obstruction.

Upper gastrointestinal tract series showed a large, round filling defect of 3,3 cm in diameter, with regular shapes and located between the gastric antrum and pylorus (Figure 1).

MRI scans of the abdomen confirmed a solid oval mass of 4 X 2,5 cm, with regular profiles (Figure 2). The mass arose from the pyloric antrum with upstream stomach dilated by fluid. It showed an hyperintense signal in T2-weighted sequences with no diffusion restriction to the ADC map and homogenous post-contrast enhancement. Imaging was suggestive of mesenchymal tumour.

At Endoscopic Ultrasound (EUS) a large bulging lesion about 4 X 2,5 cm in size, located at the anterior wall of the antrum,

with a normal-appearing overlying mucosa was detected (Figure 3). The mass, arising from the third layer of the gastric wall, presented an isoechoic lesion, with small hypoechoic foci in the deeper part, without involvement of the muscularis propria of the stomach and with a weak Color-Doppler signal at the peripheral inner margin (Figure 4). A fine needle aspiration was performed. The tumor, with valve effect, almost completely obstructed the entrance to the pylorus.



Figure 1: Radiographic findings of upper gastrointestinal tract – A mass was protruding into the gastric lumen causing a stomach filling defect at the passage between antrum and pylorus.

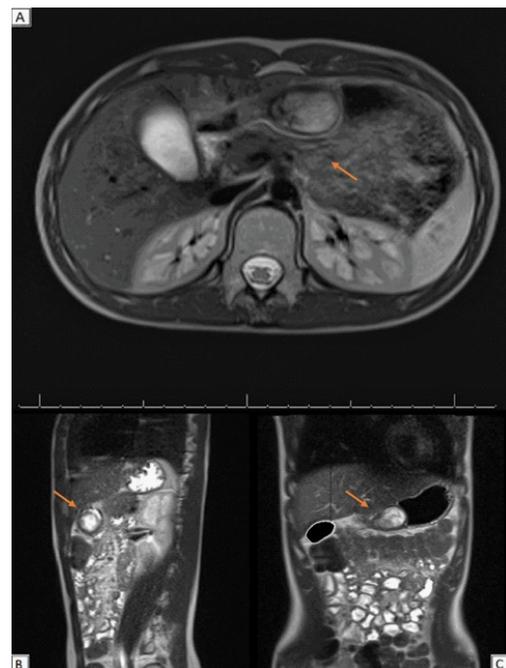


Figure 2: Magnetic resonance imaging findings of the abdomen – MRI showing a mass developing inside the wall of the antrum with well-defined profiles. The lumen of the stomach is partially obliterated by the lesion. (A): Axial scan; (B): Sagittal scan; (C): Coronal scan.

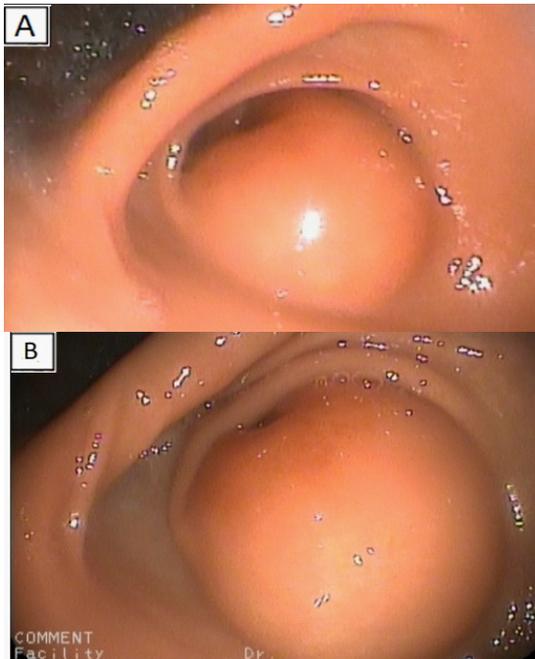


Figure 3: Upper gastrointestinal endoscopy – A and B: Submucosal bulge was observed at the anterior wall of the gastric antrum. No mucosal injury was evident.

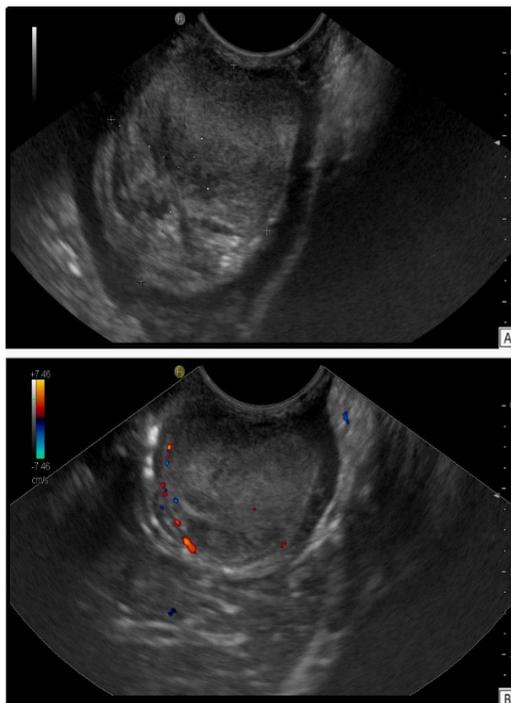


Figure 4: Endoscopic ultrasound – (A): Grayscale US image demonstrates an isoechoic mass involving the superficial layers of the gastric wall. (B): Color-Doppler function shows the presence of fine vessels around the lower part of the lesion.

Cytological features: Microscopic examination of the cytological specimen revealed aggregates of spindle cells without signs of atypia and no abnormal mitotic activity. The cytomorphological features suggested a spindle cells neoplasm of mesenchymal nature.

Surgery: Two days after the admission, the patient underwent to surgery. Laparoscopy confirmed the origin of the mass from the gastric antrum. As enucleation of the tumour was not feasible, a laparoscopic pylorus sparing antrectomy with a gastro-pyloric anastomosis was performed (Figure 5).

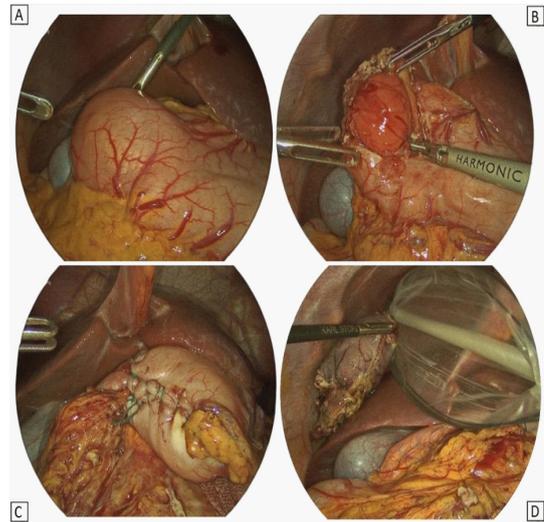


Figure 5: Shots from laparoscopic surgery – (A): Presence of a gastric mass located at the anterior wall of the gastric antrum was confirmed; (B): After opening the stomach wall, the mucosal-covered mass was shown; (C): Outcomes of gastro-pyloric anastomosis after antrectomy; (D): Removal of the mass using an endobag.

Histopathological features: Gross examination of the surgical specimen showed a nodular lesion of 4 X 2,5 cm, macroscopically limited to the submucosal layer, with greyish appearance on cut sections (Figure 6). Microscopically, the lesion showed a multilobulated and plexiform growth pattern. It was formed by spindle cells with no cyto-nuclear atypia, embedded in a myxoid matrix with fibrous features. In some areas, the tumour had poor cellularity while in others it was more abundant and disorganized with a vascular component. Focal inflammatory infiltrate was detected too. Immunostaining for muscle actin and desmin showed strong and diffuse positivity, while caldesmon staining was less intense (Figure 7). Tumour cells were negative for cytokeratins, CAM 5.2, S100, STAT6, MUC4, CD34, CD117, DOG1, p16, CD10. Proliferation index (percentage of Ki67 positive cells), was less than 5%. Fluorescence in situ hybridization (FISH) assay was negative for MDM2 amplification, These findings were consistent with PF.

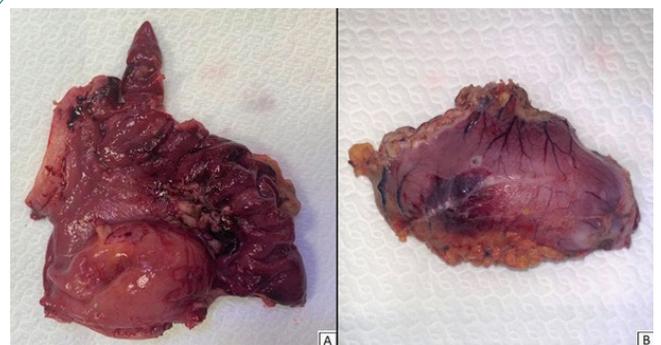


Figure 6: Gross appearance of the excised specimen – A and B: a reddish nodular mass of 4x2,5 cm is protruding from the gastric mucosa without necrosis. A portion of stomach was removed along with the lesion.

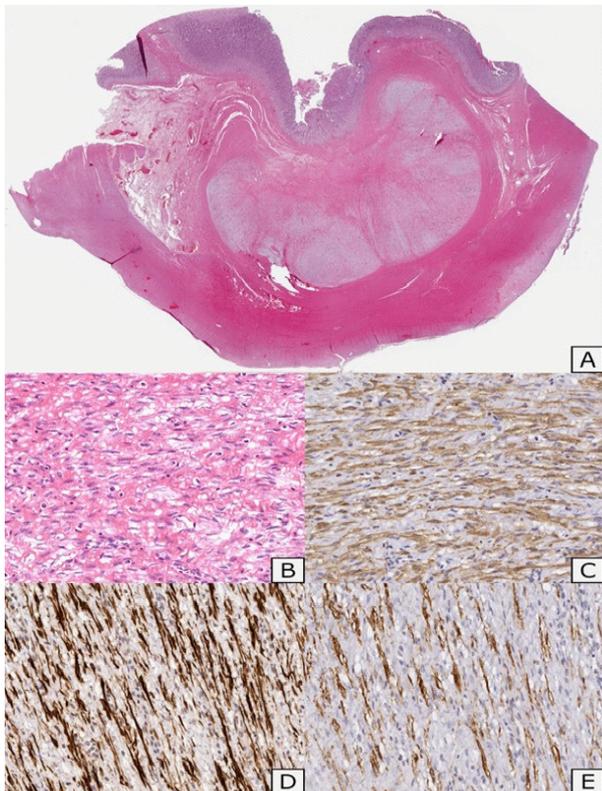


Figure 7: Histological and immunohistochemical examinations – (A) and (B): Low and high-power view of the lesion, Hematoxylin and Eosin; (C): Immunostain for Smooth Muscle Actin; (D): Immunostain for Desmin; (E): Immunostain for Caldesmon.

Follow-up

The post-operative course was uneventful. Three months after surgery a gastroduodenoscopy was performed. The exam showed hypo-continent cardias and normal gastric mucosa. The histological examination of the biopsies showed of mild es-

ophagitis and active chronic gastritis. At 1-year follow-up, the patient was well, normally growing and with normal abdominal US.

Literature review

The PubMed database was searched for original studies on PF published since 1990, involving patients younger than 18 years of age. Eligible study designs were case reports, case series and reviews. We omitted reports in which abstracts indicated an adult population (> 18 years) and improper reporting of the diagnosis and treatment methods. We then evaluated the full text of the selected articles and consider only where that diagnosis was confirmed by authors. The date of the last search was September 2021.

Results

The initial PubMed search yielded 89 potentially relevant studies. Eventually, 12 eligible articles met the inclusion criteria, involving 14 children with PF (Table 1) for a total of 15 pediatric cases including ours. All selected studies were case reports (class of evidence III and rating scale of evidence E). Baseline demographic, clinical characteristics and surgical treatment of the 15 patients are shown in Table 1. Median patient's age was 12 years (range 5 -18 years); 9 patients were female (60%). The most frequent reported symptoms were abdominal discomfort (36%) anemia (29%) and gastrointestinal bleeding (29%). Ulcerative lesions of the tumour were observed in 6 patients (55%) and 3 of them had contextual gastrointestinal bleeding. In 13 cases (87%) the location of the tumour was within the stomach, always involving the gastric antrum. In 1 patient presenting with thoracic pain, shortness of breath and numbness of fingers (Table 1, pts no. 4) the tumour was founded in the middle-third of the esophagus and caused tracheal compression. Median tumour size at diagnosis was 5,25 cm (range 3-15 cm). All patient underwent to surgical treatment, but only in 3 cases, including ours, a minimally invasive technique was used.

Table 1: Demographics, clinical characteristics and treatment of 15th PF pediatric patients.

No	Age	Sex	Symptoms	Tumor Location	Size (cm)	Ulceration	Treatment	tumour Recurrence	Ref
1	7	F	Vomiting, diarrhea and evident abdominal mass	Gastric antrum, pylorus and duodenal bulb	15 X 11 X 8	N	Tumour Resection	No	[3]
2	16	F	Hematemesis	Gastric antrum and pylorus	10 X 9 X 6	Y	Distal Gastrectomy	No	[3]
3	12	M	Gastrointestinal bleeding	Gastric Antrum	n.d.	n.d.	Partial Gastrectomy	No	[15]
4	11	F	Anemia	Gastric antrum and pylorus	3,5	Y	Laparoscopic distal Gastrectomy	No	[7]
5	16	F	Chest pain, shortness of breath and numbness of finger	Esophagus at the level of the carina	3,2	N	Thoracoscopic tumour Resection	No	[7]
6	9	F	Abdominal pain, nausea, vomiting and weight loss	Gastric antrum, posterior	5	Y	Laparotomic anterior gastrotomy with tumour resection	No	[16]
7	18	F	n.d.	n.d.	4,5 X 3,5 X 2,7	n.d.	n.d.	No	[17]
8	11	M	Abdominal pain	Gastric antrum	n.d.	n.d.	Partial Gastrectomy	No	[18]
9	11	M	Right epigastric discomfort with episodic pain	Gastric pylorus	17 X 10,5 X 5	N	Partial Gastrectomy	No	[19]

10	16	F	Anemia and nausea	Gastric antrum, anterior wall	6,5	Y	Distal Gastrectomy and retrocolic gastrojejunostomy (Billroth II)	No	[20]
11	14	M	Anemia, fatigue and gastric pain	Gastric antrum	5,0	N	Partial Gastrectomy	No	[21]
12	14	F	Abdominal pain, hematemesis	Gastric antrum	5,5	y	Partial Gastrectomy	No	[5]
13	5	M	Pale complexion	Gastric antrum	8,2 X 7,5 X 5,5	n.d.	Distal gastrectomy	No	[22]
14	16	M	Hematemesis, weight loss	Gastric cardia near gastroesophageal junction	5	Y	Laparotomic wedge resection	No	[23]
15	8	F	Vomiting, anemia, weight loss and constipation	Gastric antrum, anterior	4,0	N	Laparoscopic antrectomy	No	our case

Discussion

Plexiform fibromyxoma is a very rare mesenchymal tumour; in a recent review in 2019, Su et al. collected 121 cases of PF. In the past the prevalence was considered similar in both genders with a female-to-male ratio 1:1 [5], but in a recent review Su et al. found a female predominance (57% of patients) and a range ages from 5 to 81 years (mean age 43 years, median age 46 years) [11]. It is predominantly a tumour of adulthood with an adult-to-child ratio 8:1 according to reported cases and up to now only 14 pediatric cases have been reported.

Symptoms and signs vary from abdominal discomfort or pain, dyspepsia, weight-loss, nausea and vomiting (secondary to pyloric obstruction), to gastrointestinal bleeding with anemia and hematemesis (due to ulceration and invasion of the mucosa). PF is a lobulated submucosal or transmural mass, originating from the muscularis propria [12], usually localized in the gastric antrum, but it has been found in other gastric and extra-gastric areas. The size of the tumour at diagnosis can be very different from 1,5 cm up to 15 cm in longest axis (average size 4,8 cm, median size 4 cm).

As PF displays common clinical and radiological findings with other mesenchymal tumours like GISTs, neuronal tumours, smooth muscle tumours and fibroblastic tumours [3], pre-operative diagnosis is unreliable. Indeed, histological features are typical and show a plexiform growth pattern with multiple nodules with spindle-cells embedded in an abundant myxoid or fibromyxoid stroma [13]. Mitoses are rare and cells have no signs of atypia. Vascular invasion is reported in literature suggesting that intravascular tumour spread is possible [13]. Immunohistochemically, a diffuse positive reaction to vimentin, Smooth Muscle Actin (SMA) and Muscle Specific Actin (MSA) is founded, indicating the fibroblastic, myofibroblastic and smooth muscle cell natures of PF [11]. Focal expression of desmin and caldesmon has been found, suggesting PF is able to smooth muscle differentiation [14].

Regardless patients' age, PF displays a benign clinical behaviour and no recurrence, metastasis or tumour-related deaths have been reported in literature so far. The positive prognosis is also confirmed by the absence or low degree of atypia and low mitotic index (Ki67), with surgery being limited only to tumour excision with no regional lymphadenectomy performed [13]. However, due to scanty literature with short follow-up, it is not possible to exclude with certainty that the tumour could express malignant features in the long run. Analysing the pediatric literature, 15 cases including ours have been reported up to now. In 14 cases, PF was localized in the gastric antrum or

pylorus and the only case of tumour localized in the esophagus was detected in a 16 years old girl (Table 1, pts no. 5). Biological, clinical and radiological features of pediatric PF at diagnosis are similar to adult ones except for tumour size, which was larger in children. This difference is probably explained by age-related higher tumour cell proliferation and lower frequency of incidental diagnosis in childhood [5]. Ulceration of the mucosa was frequently reported and that was always associated with digestive symptoms. As in adults, for whom the mainstream treatment is the surgical removal of the tumor [11], all children underwent surgery, with a minimally invasive approach only in 3 cases (Pts no. 4, 5 and 15). Even in children, partial gastric resection was the most performed surgery, but differently from adults, none of the pediatric patients underwent to endoscopic PF removal, probably due to the size of the tumor at diagnosis. In our experience a safe and complete tumor resection has been accomplished laparoscopically, with the well-known advantages of this technique [4] and we suggest it might be considered the gold standard of the treatment, even in pediatrics. Eventually, as now data have been reported about long term follow-up and postoperative quality of life of the pediatric patients, a scheduled control throughout adulthood is mandatory.

Conclusion

Despite plexiform fibromyxoma is extremely uncommon in the pediatric settings, it should be included in the differential diagnosis of gastric tumours even in childhood and teen ages, here we have reported the 15th pediatric case. PF definitive diagnosis is exclusively histological due to the difficulty of distinguishing it from other mesenchymal tumours only by imaging assessment. The benign behaviour of the tumour justifies a surgical approach, limited only to tumour excision with no excessive free resection margins and no need of regional lymphadenectomy. Nevertheless, a long run follow-up is mandatory at least in pediatrics. In our experience a safe and complete resection has been accomplished laparoscopically, with the well-known advantages of the mini-invasive surgery.

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