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**J. Estêvão-Costa · J. Correia-Pinto · F. C. Rodrigues
J. L. Carvalho · M. Campos · J. A. Dias · F. Carneiro
N. T. Santos**

Gastric inflammatory myofibroblastic proliferation in children

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Abstract Gastric inflammatory myofibroblastic proliferation (IMP) is an extremely rare entity in children, which to our knowledge has only been mentioned in case reports. We describe the ninth pediatric case and review the literature concerning the etiology, clinical and laboratory features, pathology, treatment, and outcome. There has been a predominance in preschool females. Abdominal pain, upper gastrointestinal hemorrhage, and an abdominal mass, either isolated or associated, have been the main clinical features. Iron-deficiency anemia has been a constant finding. Lesions are elevated and involve the full thickness of the gastric wall, usually with ulceration of the luminal surface; extragastric extension suggesting malignancy is frequent. Diagnosis is made by histology after surgical excision. There was no mortality directly related to gastric IMP, and only one case recurred after surgical excision. The pathogenesis is controversial, but the finding of *Helicobacter pylori* in our case may indicate an inflammatory origin. Awareness of this benign lesion and its mimicry of malignancy is important so that inappropriately aggressive therapy can be avoided.

J. Estêvão-Costa (✉)[1] · J. Correia-Pinto ·
J.L. Carvalho · M. Campos
Division of Pediatric Surgery, Department of Pediatrics,
Faculty of Medicine and São João Hospital,
University of Porto, Porto, Portugal

F.C. Rodrigues · J.A. Dias · N.T. Santos
Division of Pediatrics, Department of Pediatrics,
Faculty of Medicine and São João Hospital,
University of Porto, Porto, Portugal

F. Carneiro
Department of Pathology, IPATIMUP,
Faculty of Medicine and São João Hospital,
University of Porto, Porto, Portugal

Present address:
[1]Serviço de Cirurgia Pediátrica, Departamento de Pediatria,
Faculdade de Medicina do Porto, Hospital de São João
Alameda Prof. Hernâni Monteiro,
4200 Porto, Portugal

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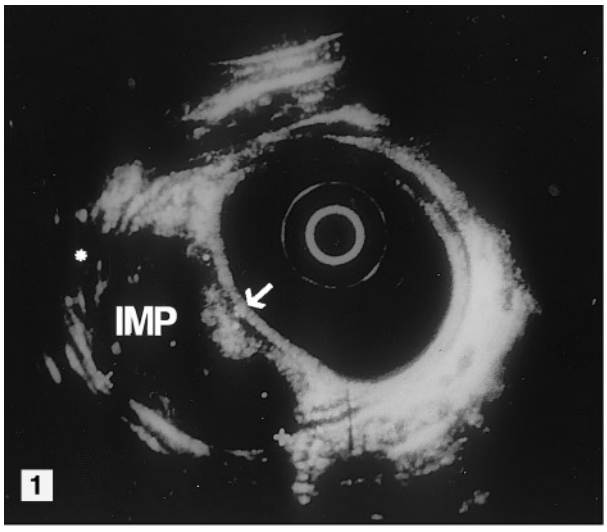
Introduction

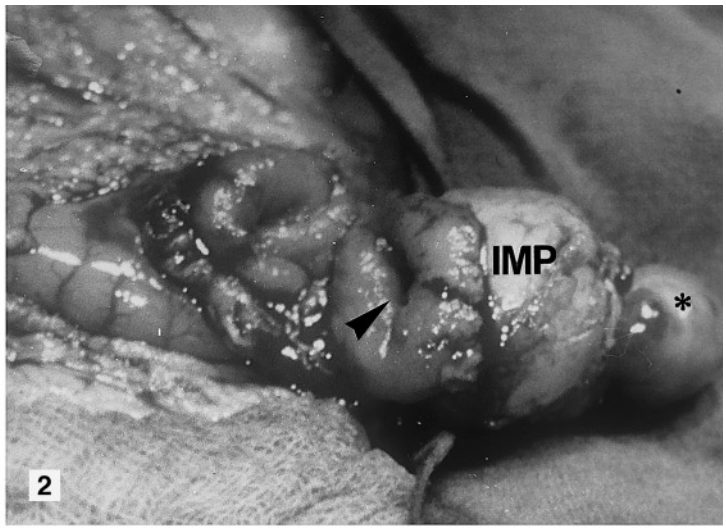
Inflammatory myofibroblastic proliferation (IMP) occurs frequently in the lungs [1], but is extremely rare in the stomach, and only eight pediatric cases have been reported to date [2–8]. The literature on gastric IMP in children is scattered in short case studies. We describe a child with gastric IMP and review the reported cases to assess the main features regarding clinical and laboratory features, pathology, treatment, and outcome. The pathogenesis of this lesion is also addressed.

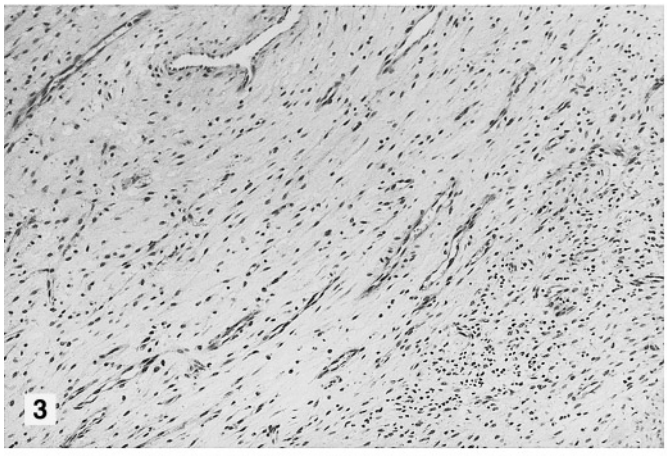
Case report

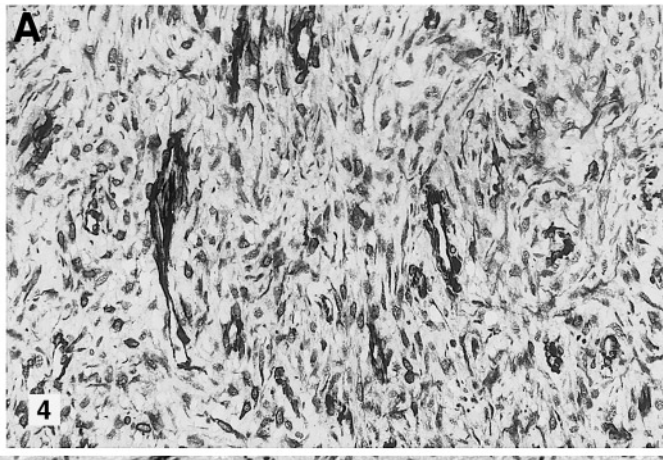
A 10-year-old girl was referred to our emergency room due to hematemesis and epigastric pain. She had been healthy until 2 months prior to admission, when she developed anorexia and weakness and noticed melena. Investigation for iron-deficiency (ID) anemia had been done elsewhere. She denied diarrhea, vomiting, dysphagia, constipation, or fever. There was no history of analgesic ingestion, trauma, neoplasm, or previous surgery. Physical examination revealed a pale but alert girl; vital signs were within the normal range except for tachycardia; there were no signs of a hemorrhagic diathesis. Anthropometry was between the 50th and 75th percentile. Her abdomen was nontender with no palpable masses or organomegaly. At admission laboratory evaluation revealed anemia (hemoglobin 5.5 g/dl; hematocrit 18.5%) and normal platelet and leucocyte counts; the erythrocyte sedimentation rate (ESR) was 14 mm. Electrolytes, urinalysis, and liver and renal function tests were normal. Upper gastrointestinal (UG) endoscopy revealed an elevated lesion in the prepyloric region with a large, deep central ulceration; biopsy suggested a benign lesion. On endoscopic ultrasonography (US) (Fig. 1) an intramural mass could be seen located in the muscularis propria with adjacent "lymph nodes", suggesting a leiomyosarcoma. A barium meal and abdominal US showed similar features.

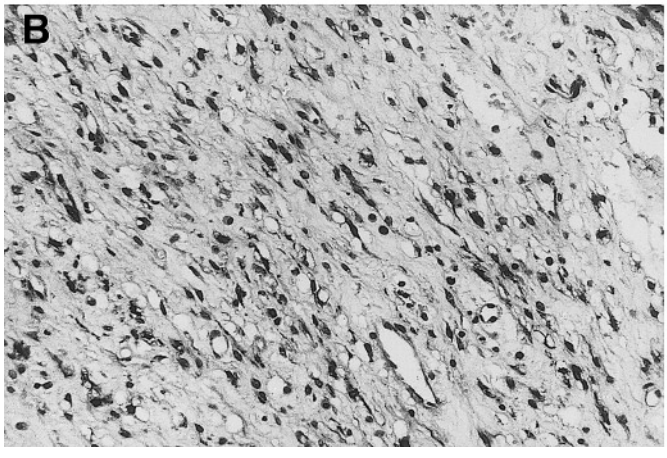
At laparotomy, a round, rubbery mass 3 cm in diameter with an extra-gastric component was excised (Fig. 2); a definite diagnosis could not be made on frozen-section biopsies, and so a partial gastrectomy (Billroth I) was performed. Histology revealed a

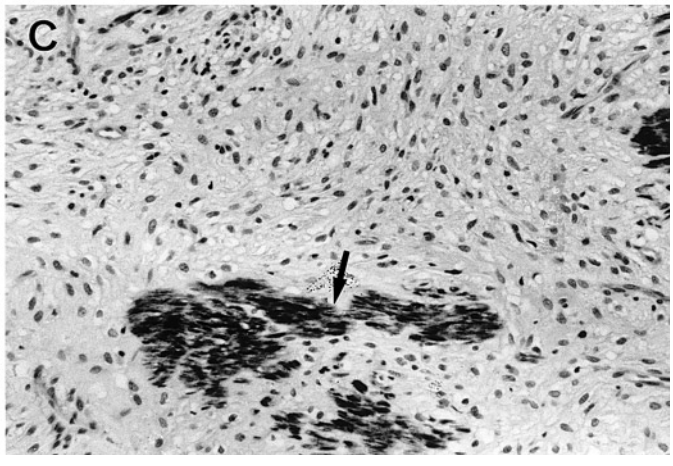












proliferation of spindle-shaped, fibroblast-like cells arranged in a fascicular pattern with scattered lymphocytes and plasma cells (Fig. 3). Most of the proliferating cells were elongated, with plump oval nuclei and without cytologic atypia. Mitoses were not observed and there was no necrosis. The pattern of growth was infiltrative, the whole thickness of the gastric wall being infiltrated by the proliferating spindle cells, leading to nodular growths in the sub-serosa. The gastric mucosa overlying the lesion showed signs of chronic gastritis associated with the presence of *Helicobacter pylori*. Immunocytochemistry (Fig. 4) revealed cytoplasmatic staining of spindle cells for vimentin and α-actin, while staining for desmin and S-100 protein was negative. These features are typical of IMP.

Fig. 1 Endoscopic ultrasonogram showing ulcerated (*arrow*) gastric mass (*IMP*) with extragastric extension (*asterisk*)

Fig. 2 Resected specimen: ulcerated (*arrow*) gastric mass (*IMP*) with extragastric extension (*asterisk*)

Fig. 3 Photomicrograph showing plump spindle cells arranged in fascicles with scattered inflammatory cells (H&E, ×160)

Fig. 4A–C Proliferating spindle cells showing diffuse cytoplasmic reactivity for **A** vimentin and **B** α-actin but not for **C** desmin, contrasting with strong immunoreactivity of smooth-muscle cells of gastric wall (*arrow*) (Immunoperoxidase, ×320)

Table 1 Review of cases of gastric inflammatory myofibroblastic proliferation (IMP) in children (*UG* upper gastrointestinal, *ID* iron deficiency, *ESR* erythrocyte sedimentation rate)

References	Age Sex	Clinical presentation	Laboratory abnormalities	Designation	Pathology	Treatment	Outcome
Schroeder et al. [7]	5 years Female	Abdominal pain, weakness, vomiting	ID anemia	Inflammatory fibroid polyp	Fundus, extragastric extension	Subtotal gastrectomy	?
Maves et al. [2]	5 years Female	UG hemorrhage, signs of liver disease	ID anemia Hypergamma-globulinemia	Inflammatory pseudotumor	Fundus	Resection	Died of sclerosing cholangitis, without recurrence
Maves et al. [2]	18 months Female	Abdominal mass, fever, weight loss	ID anemia Thrombocytosis	Inflammatory pseudotumor	Great curvature, 6 × 7 cm, extragastric extension, ulcerated	Surgical	11 months follow-up; no recurrence
Tang et al. [3]	5 years Female	Abdominal pain, abdominal mass, anorexia, constipation	ID anemia Elevated ESR	Inflammatory myofibrohistiocytic proliferation	Fundus and body, 10 cm	Partial gastrectomy	3 years follow-up; no recurrence
Lin and Hsueh [4]	2 years Female	Abdominal mass, fever, weight loss, ascitis	ID anemia	Inflammatory pseudotumor	Pylorus, extragastric extension, ulcerated	Radical gastrectomy	Died of ''nephrotic syndromes,'' without recurrence
Marn and Hsu [5]	5 years Male	Weakness, pallor, growth retardation	ID anemia Elevated ESR	Inflammatory myofibrohistiocytic proliferation	9 cm, ulcerated	Partial gastrectomy	?
Murphy et al. [13]	6 years Male	Weakness	ID anemia	Plasma cell granuloma	6 × 7 cm	Partial gastrectomy; total gastrectomy after recurrence	Recurrence 16 months later
Riedel et al. [6]	4 months Female	UG hemorrhage, gastroesophageal reflux	ID anemia Elevated ESR	IMP	4 cm, extragastric extension, ulcerated	Partial gastrectomy with splenectomy and excision of a peritoneal implant	3 years follow-up; no recurrence
Estêvão-Costa et al. (present case)	10 years Female	Abdominal pain, UG hemorrhage, weakness, anorexia	ID anemia Elevated ESR	IMP	Prepyloric, 3 cm, extragastric extension, ulcerated	Partial gastrectomy	3 years follow-up no recurrence

The postoperative course was uneventful and she was discharged with no further treatment. Three years after surgery she is doing well with no evidence of recurrence.

Discussion

Gastric IMP is a very rare entity in children, with a controversial etiopathogenesis. Since this lesion was first reported in 1953 [9], many designations such as inflammatory fibroid polyp [9], plasma cell granuloma [10], inflammatory pseudotumor [2], and inflammatory myofibrohistiocytic proliferation [3] have been used. To the best of our knowledge, the present case is the ninth reported in a child. Cases of secondary gastric involvement have not been included in this review.

Features of known cases of IMP are shown in Table 1. There has been a predominance of females (78%) and pre-school age (78%). The main clinical presentations were abdominal pain (33%), UG bleeding (33%), and an abdominal mass (33%), either isolated or in combination. Nonspecific symptoms such as fever and/or weakness occurred in almost all patients, being the sole symptoms in two (22%). Laboratory features of severe microcytic, hypochromic anemia refractory to iron therapy were always present. An elevated ESR was reported in about one-half of the cases (44%). Thrombocytosis and hypergammaglobulinemia were infrequently seen.

Further diagnostic evaluation depends upon the mode of presentation. There are some distinctive but nonspecific features of gastric IMP [11]. In cases of UG hemorrhage, endoscopy was the preferred method for initial evaluation. Macroscopically, these tumors appeared as elevated lesions measuring 3 to 10 cm, usually with ulceration at the top (56%) [2, 4–6], and no preferential localization. Once a tumor is discovered, computed tomography or, preferably, endoscopic US, as our case illustrates, may help to define the extragastric extension prior to surgery. Nevertheless, in all the reviewed cases the diagnosis was only made after surgical resection.

The cut surface shows a lesion that infiltrates the full thickness and frequently extends beyond the gastric wall (56%) [2, 4, 6, 7]. Histology usually reveals organized, interlacing fascicles of elongated spindle cells without nuclear atypia or mitoses; there is a chronic inflammatory-cell infiltrate of lymphocytes and plasma cells in a stroma of granulation tissue. Ultrastructural study, which was performed in only one case [6], may confirm the myofibroblastic nature of the spindle cells [8, 12]. Immunocytochemistry, performed in two cases [5, 6] as well as ours, was useful in demonstrating the polyclonal nature of the plasma cells and revealing the myofibroblastic markers of the spindle cells.

Complete surgical resection of the lesion was the treatment chosen for all gastric IMPs described in children. The prognosis appears to be good, as the outcomes of the known cases revealed only one recurrence 16 months after surgery [13]. There was no mortality directly related to IMP. Although chemotherapy and/or radiotherapy have been used in IMP of other organs, this has not been reported in gastric IMP in children.

The etiology and pathogenesis are still unclear. In spite of a confirmed myofibroblastic origin of the proliferating cells in lung and gastric IMP in adults [8, 14, 15] and demonstration that these cells are derived from fibroblasts [16], it is unclear whether this entity is inflammatory or neoplastic [17]. We describe for the first time the association of gastric IMP with chronic antral gastritis and *H. pylori* in a child; this feature and the high frequency of ulceration found in the other patients favor the assumption sustained by many authors [2, 12] that gastric IMP may result from an inflammatory reaction.

In conclusion, gastric IMP is a rare lesion in children that, although benign, may present features that simulate malignancy, such as infiltrative involvement of the gastric wall and extragastric extension. In order to avoid inappropriately aggressive therapy, IMP should be kept in mind as the possible cause for a gastric mass in a child presenting with ID anemia refractory to iron therapy. An associated ulceration further suggests this diagnosis.

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