



Chronic Ménétrier disease leading to gastric cancer in youth

Bruno Salomão Hirsch¹, Silvia R. Cardoso², Elisa R. Baba¹, Diogo T. H. de Moura¹, Manoel Ernesto P. Gonçalves², Rodrigo S. de P. Rocha¹, Eduardo G. H. de Moura¹

¹Gastrointestinal Endoscopy Unit, Department of Gastroenterology, ²Instituto da Criança, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Ménétrier disease (MD) is a rare, acquired gastric hyperproliferative disorder characterized by enlarged gastric folds, hypoalbuminemia, and reduced acid production.¹ Histological hallmarks include a massive expansion of surface mucous cells (foveolar hyperplasia) and glandular atrophy.² Adults and children have different etiologies, clinical manifestations, and outcomes. It is a chronic condition in adulthood with a risk of neoplastic transformation of up to 9% after 10 years of diagnosis.³ During childhood, it is considered an acute, self-limiting condition, with an average disease duration of 2 weeks.⁴ Pathogenesis is still unclear, which might limit the management of patients suffering from this condition.

This article reports the first case in the literature of chronic pediatric MD leading to gastric cancer. A previously healthy 10-year-old girl presented with vomiting, sporadic melena, and weight loss (10% of body weight) over one month. A physical examination revealed pallor and mild edema. Laboratory studies demonstrated anemia (hemoglobin [Hb], 5.0 g/dL), hypoalbuminemia (3.4 mg/dL), and an elevated serum gastrin level (350 pg/mL). Esophagogastroduodenoscopy (EGD) revealed

decreased gastric distensibility and hypertrophic gastric folds in the corpus and fundus with thick mucus, sparing the antrum (Figs. 1A, B). Gastric biopsies were inconclusive; therefore, repeat EGD with deep snare biopsy was performed. The histopathological assessment revealed massive foveolar hyperplasia, tortuous gland ducts with cystic dilatation, and atrophy of chief and parietal cells, confirming MD (Fig. 1C). Immunohistochemistry testing for cytomegalovirus (CMV) and histopathological and urease tests for *Helicobacter pylori* demonstrated negative results.

The patient was managed with supportive treatment, oral iron supplementation, and a high-protein diet. She presented with slow progressive improvement after 4 months with weight gain and resolution of vomiting, and normalization of Hb and serum albumin levels. However, the endoscopic findings were not resolved.

She maintained close clinical, laboratory, and endoscopic follow-up. After 8 years, biochemical studies revealed hypoalbuminemia (3.0 mg/dL) and mild anemia (Hb 11.8 g/dL). EGD demonstrated a protruding lesion (Paris Classification type 0–Is) located at the greater curvature of the corpus with friability, loss of glandular pattern, and altered vascular pattern (Figs. 2A, B). Biopsies confirmed the presence of moderately differentiated tubular adenocarcinomas (Fig. 2C). A computed tomography scan showed a large mass protruding from the greater curvature measuring 7.2×5.5×5.0 cm and diffuse parietal thickening of the gastric background mucosa with no signs of metastatic disease (Fig. 3).

The patient underwent laparoscopic total gastrectomy with D2 lymphadenectomy (Fig. 4A). Histopathological analysis

Received: January 10, 2022 Revised: March 15, 2022

Accepted: March 15, 2022

Correspondence: Bruno Salomão Hirsch

Gastrointestinal Endoscopy Unit, Department of Gastroenterology, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Av. Dr. Eneas de Carvalho Aguiar, 225, 6o andar, bloco 3, Cerqueira Cesar, São Paulo 05403-010, Brazil

E-mail: brunosalomah@hotmail.com

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

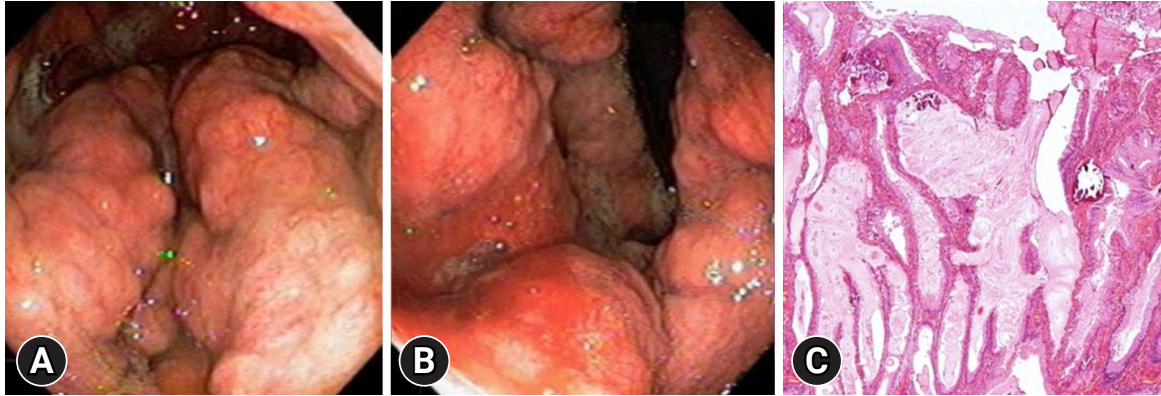


Fig. 1. Ménétrier disease. (A) Endoscopic findings in forward view. (B) Endoscopic findings in retroflexed view. (C) Histopathological features (hematoxylin and eosin stain, $\times 10$).

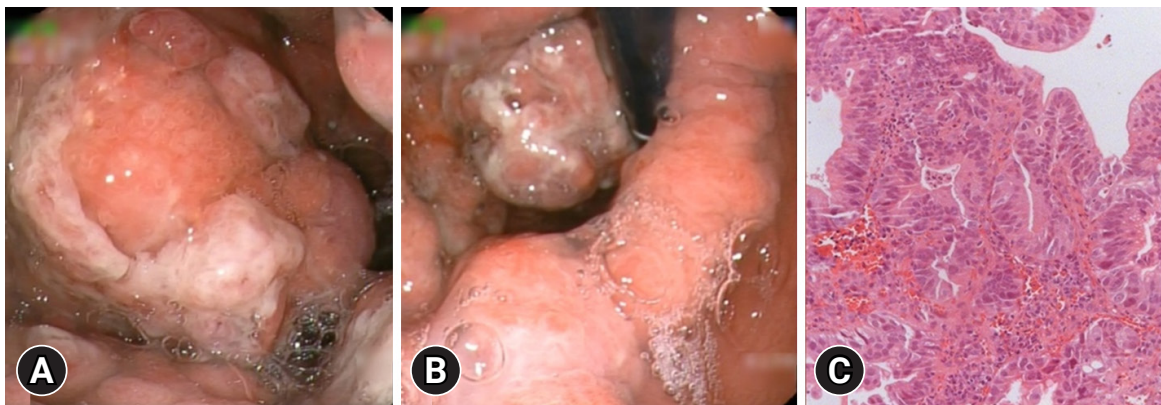


Fig. 2. Gastric cancer in a Ménétrier disease background. (A) Endoscopic findings in forward view. (B) Endoscopic findings in retroflexed view. (C) The endoscopic biopsy specimen showing gastric adenocarcinoma (hematoxylin and eosin stain, $\times 250$).



Fig. 3. Computed tomography of the patient showing gastric cancer in Ménétrier disease.

confirmed an intramucosal adenocarcinoma (T1a) with free margins and no lymphovascular invasion (Fig. 4B). The post-operative course was successful without any complications, and the patient was discharged on the 14th postoperative day with well-tolerated oral feeding. Adjuvant therapy was not required, and there was no recurrence of the disease after eight years of follow-up.

MD is considered a self-limiting disease in children. There are approximately 150 reported cases of pediatric MD, and the only prolonged case was described by Faure et al.,⁵ in which a 7-year-old girl with MD maintained endoscopic gastric alterations at her 26-month follow-up. However, this patient was asymptomatic with a progressive histological improvement of the gastric lesions. To our knowledge, this is the first case in the literature of chronic MD in a child with gastric cancer.

The present case modifies the clinical rationale for treatment of a case of MD in a young patient. As opposed to previous

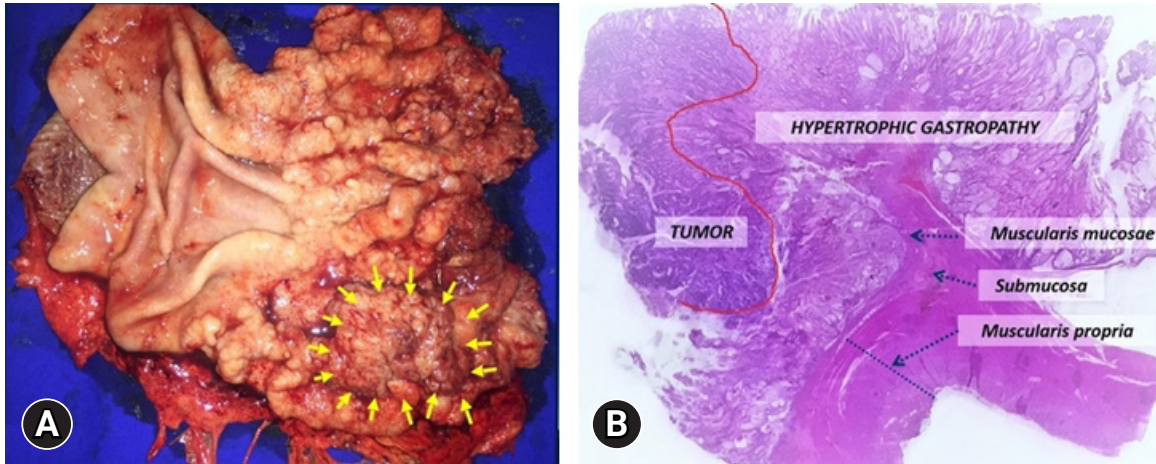


Fig. 4. (A) Gross pathological appearance with gastric adenocarcinoma (arrows). (B) The specimen showing gastric adenocarcinoma (hematoxylin and eosin stain, $\times 5$).

findings,^{3,4} we believe that endoscopic follow-up is indicated until normalization of the gastric alterations since the disease may become chronic. If the disease does not resolve, the patient should undergo close gastric cancer screening. Depending on the clinical symptoms and laboratory studies, total gastrectomy might be considered, similar to the management of adult MD.

Interestingly, the reported case did not present any known triggers associated with MD. CMV is the most commonly described agent in children, with a prevalence of approximately 60% among patients with pediatric MD.⁴ Furthermore, CMV infection has also been reported in adults.^{6,7} *H. pylori* is another frequently associated agent.⁸ However, as both CMV and *H. pylori* can often be detected in asymptomatic patients, it is difficult to confirm the cause-and-effect relationship. Immune-mediated disorders, such as ulcerative colitis and sclerosing cholangitis, have also been reported in patients with MD, suggesting an immune component in its pathogenesis.¹ Genetic predisposition probably plays a role in the development of the disease.^{9,10}

The etiology and pathogenesis of MD have not yet been fully elucidated. Current knowledge suggests that triggers induce local overproduction of transforming growth factor- α in the stomach, leading to increased tyrosine kinase epidermal growth factor receptor signaling.¹ It results in a shift in the gastric progenitor cell differentiation, leading to a marked increase in mucosal surface cells and consequent reduction in parietal and chief cells.³ Gastrin levels remain normal to moderately elevated despite the hypochlorhydria.² Increased mucin synthesis and the widening of tight junctions result in gastric protein loss.

Children usually present with an abrupt onset of nausea,

vomiting, abdominal pain, anorexia, weight loss, diarrhea, and edema,⁸ whereas adults usually present with insidious onset. Diagnosis is suggested by EGD findings, such as giant rugal folds in the corpus and fundus, with relative sparing of the antrum, occasionally with erosions, decreased distensibility, and a large amount of thick mucus. Routine biopsies may not confirm the disease because superficial samples assess only the foveolar compartment. Therefore, total mucosal samples with deep snare biopsies are necessary to evaluate mucosal architecture and pit-to-gland ratio.⁶

In conclusion, this case report raises concerns regarding the management of MD in children and may change the clinical rationale for pediatric patients with such a disease. We suggest endoscopic surveillance until normalization of gastric changes, even if clinical and laboratory remission is achieved. Additionally, gastrectomy should be considered in severe chronic cases, similar to that in the adult population. Written informed consent was obtained from all patients.

Conflicts of Interest

The authors have no potential conflicts of interest.

Author Contributions

Conceptualization: BSH, SRC, ERB, RSPR; Data curation: BSH; Formal analysis: BSH, SRC, ERB, RSPR; Investigation: BSH, SRC, ERB, RSPR; Supervision: MEPG, EGHM; Writing-original draft: BSH, ERB; Writing-review & editing: SRC, DTHM, MEPG, RSPR, EGHM.

ORCID

Bruno Salomão Hirsch <https://orcid.org/0000-0002-0777-0150>
Sílvia R. Cardoso <https://orcid.org/0000-0001-8760-0727>
Elisa R. Baba <https://orcid.org/0000-0001-7261-9054>
Diogo T. H. de Moura <https://orcid.org/0000-0002-7446-0355>
Manoel Ernesto P. Gonçalves <https://orcid.org/0000-0002-1154-405X>
Rodrigo S. de P. Rocha <https://orcid.org/0000-0002-0326-4998>
Eduardo G. H. de Moura <https://orcid.org/0000-0002-8023-3722>

REFERENCES

1. Huh WJ, Coffey RJ, Washington MK. Ménétrier's disease: its mimickers and pathogenesis. *J Pathol Transl Med* 2016;50:10–16.
2. Coffey RJ, Washington MK, Corless CL, et al. Ménétrier disease and gastrointestinal stromal tumors: hyperproliferative disorders of the stomach. *J Clin Invest* 2007;117:70–80.
3. Almazar AE, Penfield JD, Saito YA, et al. Survival times of patients with Ménétrier's disease and risk of gastric cancer. *Clin Gastroenterol Hepatol* 2021;19:707–712.
4. Barbati F, Marrani E, Indolfi G, et al. Ménétrier disease and cytomegalovirus infection in paediatric age: report of three cases and a review of the literature. *Eur J Pediatr* 2021;180:679–688.
5. Faure C, Besnard M, Hirsch A, et al. Chronic hypertrophic gastropathy in a child resembling adult Ménétrier's disease. *J Pediatr Gastroenterol Nutr* 1996;23:419–421.
6. Rich A, Toro TZ, Tanksley J, et al. Distinguishing Ménétrier's disease from its mimics. *Gut* 2010;59:1617–1624.
7. Xiao SY, Hart J. Marked gastric foveolar hyperplasia associated with active cytomegalovirus infection. *Am J Gastroenterol* 2001;96:223–226.
8. Krikilion J, Levy EI, Vandenplas Y. Diagnosis and management of Ménétrier disease in children: a case series review. *Pediatr Gastroenterol Hepatol Nutr* 2021;24:109–117.
9. Tard C, Madhi F, Verlhac S, et al. Protein-losing gastropathy associated with cytomegalovirus in two sisters: case reports and review of the literature. *Arch Pediatr* 2019;26:232–235.
10. Burmester JK, Bell LN, Cross D, et al. A SMAD4 mutation indicative of juvenile polyposis syndrome in a family previously diagnosed with Ménétrier's disease. *Dig Liver Dis* 2016;48:1255–1259.