

## Malignant Transformation of Ménétrier Disease: Case Report and Review of the Literature

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### Abstract

### Case Report

Ménétrier's disease is an infrequent hypertrophic disease of the stomach associated with hypoproteinemia of unknown etiology. This disease is considered to be premalignant since 10-15% of affected individuals develop gastric cancer. We report the case of a malignant degeneration of Ménétrier disease associated with gastric polyposis in a 60-year-old man who had received a diagnosis of Ménétrier's disease 4 years previously and who was found to have advanced antral gastric cancer during the follow-up. We provide an update on the optimal therapeutic approach, which has not been clearly defined to date.

**Keywords:** Hypertrophic gastritis – Ménétrier disease – Cancer – Stomach.

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## INTRODUCTION

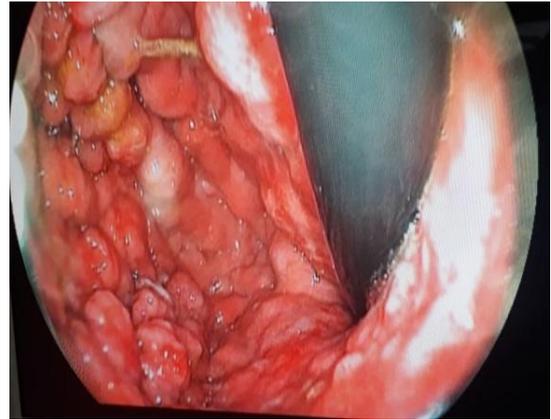
Menetrier's disease (MD) is a rare disease that was first described by the French pathologist Pierre Menetrier in 1888 [1]. It is a rare acquired hypertrophic gastropathy leading to dilatation of the mucus-secreting gastric pits (foveola) on the expense of the gastric glands containing the acid-producing parietal cells and pepsinogen-producing chief cells which undergoes atrophy. These changes gives the disease its characteristic features of the huge expansion of gastric mucosa, thick mucus secretion, protein loss and hypochlorhydria [2]. The disease is more dominant in middle-aged males [3] but several authors reported it in pediatric population [4]. The etiology is not well established. Some theories tried to link it to *Helicobacter pylori* (*H. pylori*) infection [5] and enhanced gastric epidermal growth factor receptor signaling by transforming growth factor-alpha [1]. The clinical picture includes epigastric pain and discomfort, nausea, vomiting and peripheral edema due to low serum albumin levels. MD has a recognized premalignant potential [6-8]. Also it can lead to severe uncontrollable protein loss or upper GIT bleeding [8]. Medical treatment of MD includes proton pump inhibitors, high-protein diet, eradication of *H. pylori* [5], cetuximab (monoclonal antibody) [6] and octreotide long-acting release [4]. Also total and partial gastrectomy are attempted in managing resistant cases. We describe a case of MD with an unusual

presentation that was recently managed in our hospital. We present a new case of Ménétrier disease (MD) associated with gastric cancer.

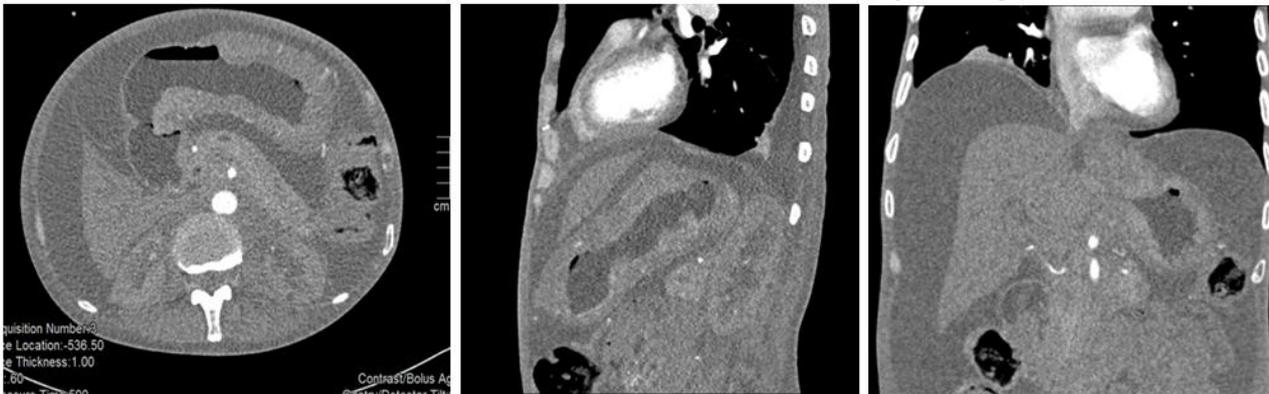
## CLINICAL CASE

A 60-year-old male with Ménétrier disease (MD) diagnosed 4 years earlier. In the endoscopy that was performed, a large area of thickened folds was observed in the greater curvature, compatible with MD. The biopsy confirmed the endoscopic suspicion. The patient refused surgical treatment and chose medical treatment and endoscopic follow-up, without having presented remarkable changes. He advanced his annual appointment, since he presented heaviness and epigastric pain, retrosternal heartburn, dark vomiting, hematemesis, ascites with a peripheral edema and weight loss. Endoscopy were performed, very thickened folds were observed in both curvatures and also the duodenal walls, with a very hyperemic mucosa and multiple ulcers, signs of recent bleeding, without any macroscopic mass or stenosis. Biopsies were released and the histological microscopy corresponds to an adenocarcinoma. Low protein ascites without any neoplastic cells, total proteins 4.1 g / dl, anemia hemoglobin 10,6 g/dl, hypokaliemia 2,8 mmol/l and lactate dehydrogenase 288 IU / l. Abdominal computed tomography was performed, and who objectified extensive gastric thickening of the cardia, large curvature and pylorus, stenosing and locally infiltrating.

Associated with a circumferential and irregular thickening of D2 and D3, stenosing and locally infiltrating and responsible for dilation of the pancreatic ducts. A peritoneal effusion of great abundance. Multiples lung nodules, without any hepatic nodules. And so it was decided to perform palliative surgery using gastroenteroanastomosis. And biopsies of the lung nodules. The gastric biopsies show the typical histological aspect of MD (hyperplastic gastropathy with hypertrophy foveolar), and the lung lesion is compatible with adenocarcinoma. In the postoperative follow-up he presented 3 episodes of low abundance hematemesis. He died 3 months after the intervention due to progression of the neoplasm.



**Fig-1: Endoscopic image reveals very thickened folds in both curvatures, with a very hyperemic mucosa and multiple ulcers, without any macroscopic mass or stenosis**



**Fig-2: CT in axial sections with sagittal and coronal reconstruction: Thickening of the large and the small curvature extended to the cardia**

## DISCUSSION

A condition described for the first time by Pierre Ménétrier in 1888, Ménétrier's disease, also called giant hypertrophic gastritis or hypertrophic hypoproteinemic gastropathy, is a precancerous condition. If the cause remains unknown, an expression of the epidermal growth factor has been demonstrated on the cells of the pathological gastric mucosa. The condition occurs readily in men in their forties. Exceptionally, it occurs in children where it is linked to cytomegalovirus infection [9]. The condition affects the fundus and the stomach body but most often spares the gastric antrum [10] as is the case in our observation. However, localized forms have been described [11].

The clinical signs are dominated by digestive symptoms (nausea, vomiting, hematemesis), weight loss, peripheral edema or even anasarca related to hypoprotidemia and hypoalbuminemia [12]. In our observation, epigastric pain, ascites and peripheral edema, and hematemesis were the warning signs, the diagnosis being made on the basis of a clinicopathological and biological correlation (hypoprotidemia is considered as a corner stone in the diagnosis) [2]. However, anemia is a sign frequently found in 70% of cases. In patients with MD there seems to be a higher incidence of serious infections and thromboembolic diseases.

On endoscopy, a thickening of the gastric folds or nodular thickening of the mucosa is observed macroscopically, and a biopsy of the entire thickness of the affected mucosa should be performed. Microscopically there is an increase in epithelial thickness, foveolar hyperplasia, glandular atrophy and a mild inflammatory infiltrate [13]. As for the malignant degeneration of MD, it would occur between 8 and 14% in one aid 1 to 5 years [7].

Abdominal computed tomography shows the thickened folds usually located in the fundus and the greater curvature [8, 14]. A differential diagnosis should be considered with other gastric diseases that can cause thickening of folds: Zollinger-Ellison syndrome, Stiempen syndrome, chronic lymphocytic gastritis, syphilis, sarcoidosis, lymphoma and diffuse infiltrating carcinoma (Bormann IV) [8, 15, 16].

The risk of malignancy of MD is controversial. As there are only isolated cases or short series, reliable epidemiological data cannot be obtained. The concurrence of gastric cancer and published MD ranges from 0-10%. But it is difficult to assess in the literature whether it really is a malignancy of MD or a coincident cancer [7, 8]. The treatment of MD is not clearly established.

Several drug treatments based on anti cholinergics, octreotide, antacids, prednisone, and the

eradication of *Helicobacter pylori* have been proposed for the treatment of MD with unsatisfactory results [4,5]. Relapse generally occurs when treatment is stopped, except in children where spontaneous regressions after a few weeks have been observed [1]. The use of monoclonal antibodies such as cetuximab which inhibits growth factor has made it possible to stop anemia in certain patients and constitutes an alternative when gastric resection is contraindicated [4, 6, 17, 16]. However, in cases with major symptomatology (uncontrollable loss of protein or bleeding) or a fortiori in case of degeneration, the surgical treatment is offered. Total gastrectomy, a radical gesture, allows better survival, especially in this superficial form of cancer associated with polyposis where polypectomy or even mucosectomy involves the risk of allowing a small cancer to develop. The feasibility of this laparoscopic gastrectomy has been demonstrated [18]. Supporters of total gastrectomy they defend its realization because the risk of malignization is eliminated, the usual location is fundic, and the performance of an anastomosis with a hypertrophied mucosa is avoided [8].

On the contrary, the defenders of a more economic surgery affirm that it allows to control the symptoms with less morbidity. Perhaps the most reasonable position is to adapt the technique to the location of MD and the degree of dysplasia. In diffuse cases, located near the heart, as usually occurs, or with dysplasia / neoplasia, total gastrectomy is the technique to be performed. In contrast, in antral lesions without signs of dysplasia, subtotal gastrectomy is sufficient.

## CONCLUSION

Ménétrier's disease is rare in Africa. Total gastrectomy remains the best gesture to propose in case of malignant transformation of this affection. It is necessary to monitor the gastric mucosa via routine endoscopy on the follow-up of patients who has been diagnosed with MD. Treatment with octreotide had little effect on the gastric mucosa, while antimicrobial combination therapy provided no benefit in *H. pylori*-negative and if the patient is concerned about the potential development of cancer, a partial or total gastrectomy is recommended.

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