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Menetrier's Disease: a Surgical and Pathological Challenge

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Abstract | **Case Report**

Menetrier's disease (MD) is a rare hypertrophic gastropathy clinically characterized by digestive signs as epigastric pain, nausea, vomiting and diarrhea, with hypoalbuminemia and anemia, endoscopically by giant rugal folds and histologically by tortuous foveolar hyperplasia with dilated glands and hypertrophic muscularis mucosae. The current study presents a case of MD in 44 year-old-man admitted to the hospital of Hassan II in Fez, Morocco with epigastralgia, vomiting and weight loss. Physical examination fond a pale face and anemia in laboratory studies. A total gastrectomy was performed given the resistance to treatment and the persistence of symptoms, as well as the suspect endoscopic aspect. Macroscopic examination showed hypertrophic and polyploid gastric mucosa resembles cerebral convolutions. Histological examination showed a foveolar hyperplasia, tortuosity and dilatation of the glands. Hypertrophic muscularis mucosae with smooth muscle bundles extending into the lamina propria have also been observed. MD is considered as precancerous condition, and is associated with an increased risk of gastric cancer. This is a retrospective study of MD to describe his clinical, endoscopic and histological features, showing also the difficulty of the histological diagnosis.

Keywords: Menetrier's disease, stomash, precancerous condition.

INTRODUCTION

Menetrier's disease (MD), or hypertrophic gastropathy, was first described in 1888 by Pierre Ménétrier [1]. It is a rare clinical entity characterized by large gastric folds associated with epithelial hyperplasia of the gastric fundus and body. The etiology of MD remains unknown, although previous studies have demonstrated that MD is associated with infections. MD presents with variable symptoms and signs. Giant rugal edematous folds are seen on gastroscopy. Histologically, it can be mistaken for other disorders showing hypertrophic gastropathy. Considering its rarity, the incidence and mortality rate data remain undetermined. Notably, a number of patients with MD have presented gastric cancer, which may demonstrate that MD carries an increased risk of cancer [2, 3]. We report a case of menetrier's disease of the Stomach and we describe macroscopic and morphologic features of this very rare variant, diagnosis difficulties, prognosis and treatment

CASE PRESENTATION

44 year-old-man was admitted to the university hospital of Hassan II in Fez, Morocco with epigastralgia, vomiting and weight loss. The patient's medical history included gastritis since 2012, put on H2-blockers. In physical examination, the patient's face was pale and no peripheral edema was detected. Laboratory studies indicated irondeficiency anemia (hemoglobin=8g/dL; normal range=12, 50-15, 50), hypoalbuminemia (albumin= 30g/L, normal range=35-52) and hypoprotidemia (prot= 53g/L, normal range= 66-83).

The patient had undergone a first fibroscopy wich revealed a budding process extended to the antro-fundic junction. Biopsies were performed in the body of the stomach and the anatomopathologic examination was in favor of hamatomatous and hyperplastic polyps.

To exclude a familial adenomatous polyposis, a total colonoscopy was performed and was without anomalies.

A thoraco-abdomino-pelvic computed tomography (CT) scan was also performed and showed the presence of a diffuse gastric parietal thickening involving the entire gastric wall.

Given the negativity of the first biopsies, a second fibroscopy was requested showing a hypertrophy of the fundic folds. Given the persistence of symptoms under treatment, the diffuse aspect of the lesion and the suspicious appearance on the fibroscopy and CT, a total gastrectomy was performed (figure 1).

Macroscopic examination showed hypertrophic and polyploid gastric mucosa mimicking cerebral convolutions (figure 2.a). Those lesions were limited to the mucosa without infiltration (Figure 2.b).

Histological examinationas had showed a relative preservation of mucosal architecture with foveolar hyperplasia, tortuosity and dilatation of the glands (figure 3.a). Hypertrophic muscularis mucosae with smooth muscle bundles extending into the lamina propriahave also been observed (figure 3.b).

We should re-examined the specimen looking for malignant transformation areas, the result of which was negative. Based on these macroscopic and histological features, the diagnosis of Menetrier's disease was retained.

The patient was administered oral folic acid for his anemia after surgery and received follow-up by clinical surveillance. The patient had gained weight and reported no symptoms 3 months after surgery.

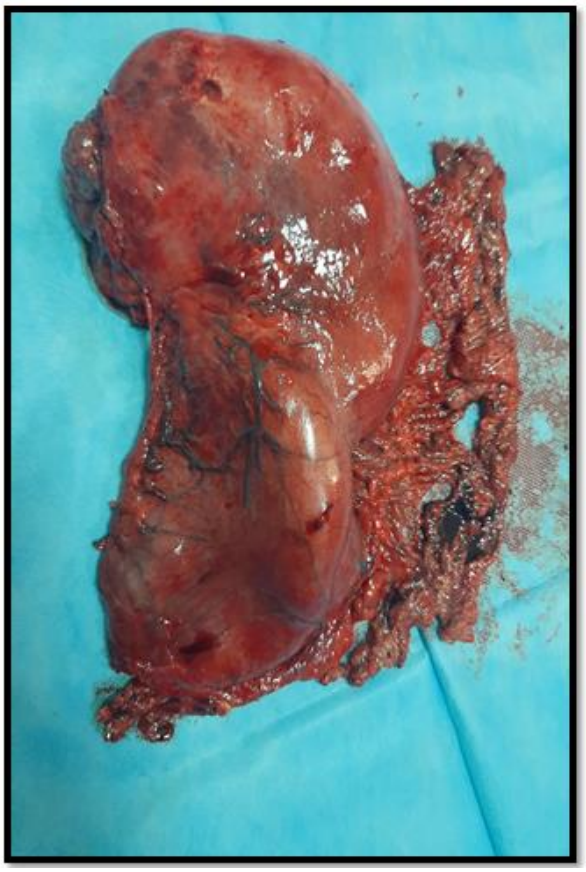

Fig-1: Total gastrectomy

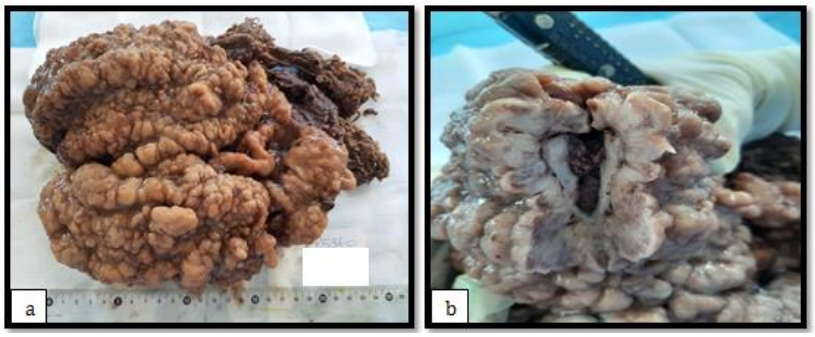

Fig-2

a: Total gastrectomy after fixation showing an hypertrophic and polyploid gastric mucosa mimicking cerebral convolutions.
b: polypoid, superficial and non-infiltrative aspect of the lesion

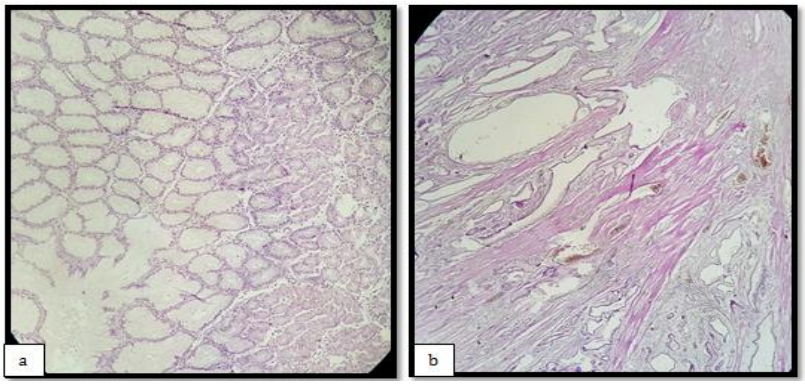

Fig-3

a: Preservation of mucosal architecture with foveolar hyperplasia, tortuosity and dilatation of the glands.
b: Hypertrophic muscularis mucosae with smooth muscle bundles extending into the lamina propriahave.

DISCUSSION

Menetrier's disease was first described by Pierre Menetrier in 1888 [4], a French pathologist who observed enlarged gastric folds during autopsies. He described two distinct varieties, one form which shows a diffuse appearance without cystic dilation of glands ("polyadenomes en nappe"), and a second form with cystic dilation of ducts and lobulated appearance ("polyadenomes polypeux").

It is a rare acquired disorder that occurred more often in men than in women, and the typical age at diagnosis is between 30 to 60 years [5].

The etiologies of Menetrie's disease are very poorly characterized. In the report published by Stolte. M and al [6], they found that hypertrophic gastropathy was associated with Helicobacter pylori in more than 90 percent of cases in a retrospective study of 138 patients with hypertrophic gastropathy. Many other studies have shown that the eradication of H. pylori may lead to complete remession [7-10]. However, in most adult cases of MD, an initial pathogenic agent cannot be determined like our case.

The research group of Robert Coffey [11] showed that patients with MD express TGFα, one of several ligands of the EGFR, significantly higher compared with the normal gastric mucosa. This overproduction of TGFα in the stomach has been suggested to explain several clinical features of MD, including increased hyperplasia of surface mucous cells and mucin production, decreased acid production and oxyntic atrophy.

MD has also been reported in patients with autoimmune diseases such as inflammatory bowel disease, ankylosing spondylitis and sclerosing cholangitis, suggesting an immunological component to its pathogenesis [12, 13].

Clinical presentations include epigastric pain, nausea, vomiting, diarrhea, weight loss, and peripheral edema due to hypoalbuminemia [14]. In addition, somes published cases of MD have also presented with severe irondeficiency anemia [15, 16] like our case, but no peripheral edema or hypoalbuminema were detected in physical and in biological examinations in our patient.

The presence or absence of hypoproteinemia in MD can only constitutes a distinction of two different stages of the disease, because, several cases of patients with documented spontaneous remission of hypoalbuminemia and edema have been reported [17-19], because excessive gastric protein leakage is only a temporary feature, usually seen in the early symptomatic stages of the disease. Noted that our patient has been on treatment for gastritis since 2012.

Endoscopic explorations like endoscopic ultrasonography can show diffuse thickening of the gastric wall [20-23]. Gastroscopy is the best mean of exploration showing giant rugal folds predominantly in the proximal stomach [24], but the diagnostic confirmation is based on the anatomopathological examination.

Histological examination shows a tortuous foveolar hyperplasia with often cystized and dilated glands, this is associated with hypertrophic muscularis mucosae with smooth muscle bundles extending into the lamina propria. In this lamina propria we note the presence of predominantly chronic inflammatory cell infiltration prominent eosinophils.

The histological aspect is not always obvious and several differential diagnoses are proposed, because some diseases share histologic characteristics with MD, correlation between microscopic findings, endoscopic and clinical features is important in order to establish the correct diagnosis, as well as accurate diagnosis of some of these diseases requires examination of a large biopsies that capture the entire thickness of the mucosa. In our case, the results of the performed biopsies were an hamartomatous and hyperplastic polyps.

Disease entities that share histological characteristics with MD include gastritis polyposa profunda, hypertrophic lymphocytic gastritis, hypertrophic hypersecretory gastropathy, Zollinger-Ellison syndrome (ZES), polyps and polyposis syndromes.

In the histological examination, the presence of diffuse thickening of the faveoli by the tourturous hyperplastic epithelium is the key to differentiated MD from the localized changes predominantly at the base of the glands in gastritis polyposa profunda [25, 26]. Hypertrophic lymphocytic gastritis is characterized in histological examination by the presence of diffuse and severe inflammation with prominent intraepithelial lymphocytes in the lamina propria. Foveolar hyperplasia is confined to areas with inflammation [27]. Hypertrophic hypersecretory gastropathy is a rare disease that characterized endoscopically by hypersecretion of mucin with hypertrophic gastric folds. Histologically, it is differentiated from MD in that hyperplasia is seen in both the foveolar epithelium and oxyntic glands [28, 29]. ZES is characterized by gastrinoma, augmentation of acid secretion with ulcer disease, and it shows diffusely thickened gastric folds. Histological examination shows parietal cell hyperplasia that can extend to the base of the glands and into the antrum, with a nodular or linear enterochromaffin-like cell hyperplasia that isassociated with multiple endocrine neoplasia type 1.

Polyps and polyposis syndromes can manifest as focal hypertrophic gastropathy and can be numerous

and diffusely distributed. The differential diagnostic between this polypes and MD in based on family history, manifestations outside the stomach, genetic testing, appearance at endoscopy and histological examination. Gastric hyperplastic polyps are the most common, accounting for 70% of gastric epithelial polyps [30], it usually develops in the background of other gastric pathology like chronic or atrophic gastritis. The histological examination shows foveolar hyperplasia with tortuous and dilated glands like in MD but this polyp show in addition a loss of parallelism of the glandular units with distortion of mucosal architecture. Additionally, lamina propria eosinophils were less visible and lamina propria smooth muscle fibres much less hyperplastic than in MD.

Juvenile polyposis syndrome (JPS) is characterized by hamartomatous polyps and mainly located in the colon [31]. Patients with JPS will typically have a history or presence of colonic polyps at the time of diagnosis and/or a family history of JPS. Histologically, gastric polyps in JPS are similar to other hyperplastic polyps and are characterized by foveolar hyperplasia similar to MD. But, in comparison with MD, gastric juvenile polyps show a loss of tissue architecture, edematous stroma with fewer glandular units and less smooth muscle fibers in the lamina propria. We note also the presence of a mixed inflammation with numerous small congested vessels. All these differential diagnoses remind that the diagnosis of MD is a challenge for the pathologist and requires a clinical, radiological, endoscopic and histological confrontation.

Various treatments have been reported to provide therapeutic benefit. In the report published by J. BURDICK [32], they have shown that systemic blockade of the epidermal growth factor receptor by a monoclonal antibody against the epidermal growth factor receptor (C225, ImClone Systems) improved the clinical and biochemical features of the disease. Helicobacter pylori eradication can be attempted for variants associated with Helicobacter pylori infection [33, 34]. Other than these approaches, several protocols like, antibiotics, non-steroidal anti-inflammatory drugs, prednisone and anticholinergic agents have been tried; however, they have yielded inconsistent benefits and none has been evaluated in a clinical trial.

A total gastrectomy is indicated in case of resistance to treatment and persistence of symptoms and it is often associated with considerable morbidity and even mortality related to surgical resection.

MD is considered as precancerous condition, and is associated with an increased risk of gastric cancer like carcinoma or gastric lymphoma [1, 2]. It is impossible to estimate the true incidence of malignant change from this pathology. However, in the report published by Scharschmidt BF [2], carcinoma developed in three of the 26 patients who were followed for more than one year. Therefore, patients should be followed up for a substantial period of time.

In conclusion, MD is a rare pathology. Its diagnosis is a challenge for the pathologist. Establishing a correct clinicopathological diagnosis requires close communication between the physician, endoscopist and pathologist as the disease is difficult to identify based on clinical symptomatology, imaging or histological appearance alone.

Competing interests

The authors declare that they have no competing of interest.

Authors' contributions

AMAL DOUIDA drafted the manuscript. All authors read and approved the final maniscrupt.

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Statement of Ethics

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Duplicated publication

I confirm that the manuscript is original, has not already been published in a journal and is not currently under consideration by another journal.

REFERENCES

1. Coffey, R.J., Jr., & Tanksley, J. (2012). Pierre Ménétrier's and his disease. Trans Am Clin Climatol Assoc, 123, 126-134.
2. Scharschmidt, B.F. (1977). The natural history of hypertrophic gastrophy (Menetrier's disease). Report of a case with 16 year followup and review of 120 cases from the literature, *Am J Med, 63*; 644652.
3. Mosnier, J.F., Flejou, J.F., Amouyal, G., Gayet, B., Molas, G., Henin, D., & Potet, F. (1991). Hypertrophic gastropathy with gastric adenocarcinoma: Menetrier's disease and lymphocytic gastritis? Gut 32: 15651567.
4. Ménétrier, P. (1888). Des polyadenomes gastriques et leur rapport avec le cancer de l'estomac. *Arch Physiol Norm Pathol, 1*; 236–62.
5. Won Jae Huh · Robert, J. (2016). Coffey Mary Kay Washington, Ménétrier's Disease: Its Mimickers and Pathogenesis - Journal of Pathology and Translational Medicine, 50; 10-16 http://dx.doi.org/10.4132/jptm.2015.09.15
6. Stolte, M., Batz, C., Eidt, S. Giant fold gastritis -- a special form of Helicobacter pylori associated gastritis. Z Gastroenterol.
7. Bayerdorffer, E., Ritter, M.M., Hatz, R. (1994). Healing of protein losing hypertrophic gastropathy by

eradication of Helicobacter pylori–is Helicobacter pylori a pathogenic factor in Menetrier's disease? Gut, 35; 701–4.
8. Yoshimura, M., Hirai, M., Tanaka, N., Kasahara, Y., & Hosokawa, O. (2003). Remission of severe anemia persisting for over 20 years after eradication of Helicobacter pylori in cases of Menetrier's disease and atrophic gastritis: Helicobacter pylori as a pathogenic factor in irondeficiency anemia. Intern Med 42: 971977.
9. Ménétrier's disease associated with Helicobacter pylori infection. (1977). Resolution of enlarged gastric folds and hypoproteinemia after antibacterial treatment. *Am J Gastroenterol*, 92.
10. Hejna, M., & Base, W. (1999). Successful symptomatic management of a patient with Ménétrier's disease with longterm antibiotic treatment. Digestion 60: 358362.
11. Dempsey, P.J., Goldenring, J.R., Soroka, C.J., Modlin, I.M., McClure, R.W., Lind, C.D., Ahlquist, D.A., Pittelkow, M.R., Lee, D.C., Sandgren, E.P. (1992). Possible role of transforming growth factor alpha in the pathogenesis of Ménétrier's disease: Supportive evidence form humans and transgenic mice. Gastroenterology 103: 19501963.
12. Fiske, W.H., Tanksley, J., Nam, K.T. (2009). Efficacy of cetuximab in the treatment of Ménétrier's disease. *Sci Transl Med, 1*; 8ra18.
13. Hatemi, I., Caglar, E., Aksoy, D., Goksel, S., & Dobrucali, A. (2008). Menetrier's disease coexisting with ulcerative colitis and sclerosing cholangitis. *Digestive and Liver Disease*, *40*(1), 78-79.
14. Rich, A., Toro, T. Z., Tanksley, J., Fiske, W. H., Lind, C. D., Ayers, G. D., ... & Coffey, R. J. (2010). Distinguishing Ménétrier's disease from its mimics. *Gut*, *59*(12), 1617-1624.
15. Singh, A. K., Cumaraswamy, R. C., & Corrin, B. (1969). Diffuse hypertrophy of gastric mucosa (Menetrier's disease) and iron-deficiency anaemia. *Gut*, *10*(9), 735-737.
16. Yoshimura, M., HlRAI, M., Tanaka, N., Kasahara, Y., & Hosokawa, O. (2003). Remission of severe anemia persisting for over 20 years after eradication of Helicobacter pylori in cases of Menetrier's disease and atrophic gastritis: Helicobacter pylori as a pathogenic factor in iron-deficiency anemia. *Internal medicine*, *42*(10), 971-977.
17. Frank, B.W., Kern, F. J.R. (1967). Menetrier's disease: spontaneous metamorphosis of giant hypertrophy of the gastric mucosa to atrophic gastritis. Gastroenterology, 53; 9 5 3 -60.
18. Berenson, M.M., Sannella, J., Freston, J.W. (1976). Menetrier's disease: serial morphological, secretory, and serological observations. *Gastroenterology*, *70*; 257-63.
19. Lesser, P.B., Falchuk, K.R., Singer, M., Isselbacher, K.J. (1975). Menetrier's disease: report of a case with transient and reversible findings. Gastroenterology, 68; 1598-601.
20. Friedman, J., Platnick, J., Farruggia, S. (2009). Menetrier disease. Radiographics, 29; 297–301.
21. Maffei, M., Piessevaux, H., Jouret-Mourin, A. Polypoid lesions in the stomach and proximal esophagus. Menetrier's disease of the stomach. *Gastroenterology*, 140:32, 369.
22. Oguri, A., Ohmiya, N., Taguchi, A. (2007). Rugal hyperplastic gastritis increases the risk of gastric carcinoma, especially diffuse and p53- independent subtypes. *Eur J Gastroenterol Hepatol*, 19; 561–6.
23. Ohyama, I., Ohmiya, N., Niwa, Y. (2004). The association between tumour necrosis factor-alpha gene polymorphism and the susceptibility to rugal hyperplastic gastritis and gastric carcinoma. *Eur J Gastroenterol Hepatol, 16*; 693–700.
24. Nils, W. G. (2011). Lambrecht, Ménétrier's Disease of the Stomach: A Clinical Challenge, Curr Gastroenterol Rep, 13; 513–517.
25. Lechago, J., Genta, R.M. (1996). Stomach and duodenum. In: Damjanov I, Linder J, editors. Anderson's pathology. *New York: Mosby*; 1684.
26. Turner, J.R., Odze, R.D. (2004). Polyps of the stomach. In: Odze RD, Goldblum JR, Crawford JM, editors. Surgical pathology of the GI tract, liver, biliary tract, and pancreas. New York: Saunders. 274–5.
27. Wolfsen, H.C., Carpenter, H.A., Talley, N.J. (1993). Ménétrier's disease: a form of hypertrophic gastropathy or gastritis? Gastroenterology, 104; 1310-9.
28. Stempien, S.J., Dagradi, A.E., Reingold, I.M. (1964). Hypertrophic hypersecretory gastropathy: analysis of 15 cases and a review of the pertinent literature. *Am J Dig Dis*, *9*; 471-93.
29. Tan, D.T., Stempien, S.J., Dagradi, A.E. (1971). The clinical spectrum of hypertrophic hypersecretory gastropathy: report of 50 patients. *Gastrointest Endosc*, *18*; 69-73.
30. Carmack, S.W., Genta, R.M., Schuler, C.M., Saboorian, M.H. (2009). The current spectrum of gastric polyps: a 1-year national study of over 120,000 patients. *Am J Gastroenterol, 104*; 1524-32.
31. Gammon, A., Jasperson, K., Kohlmann, W. (2009). Hamartomatous polyposis syndromes. Best Pract Res Clin Gastroenterol, 23; 219e3.
32. Burdick, J. S., Chung, E., Tanner, G., Sun, M., Paciga, J. E., Cheng, J. Q., ... & Coffey, R. J. (2000). Treatment of Menetrier's disease with a monoclonal antibody against the epidermal growth factor receptor. *New England Journal of Medicine*, *343*(23), 1697-1701.
33. Badov, D., Lambert, J. R., Finlay, M., & Balazs, N. D. (1998). Helicobacter pylori as a pathogenic factor in Ménétrier's disease. *The American journal of gastroenterology*, *93*(10), 1976-1979.
34. Yoshimura, M., HlRAI, M., Tanaka, N., Kasahara, Y., & Hosokawa, O. (2003). Remission of severe anemia persisting for over 20 years after eradication of Helicobacter pylori in cases of Menetrier's disease and atrophic gastritis: Helicobacter pylori as a pathogenic factor in iron-deficiency anemia. *Internal medicine*, *42*(10), 971-977.