Case report

Gastric signet ring cell adenocarcinoma associated with Menetrier's disease: a rare North African female case report

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ABSTRACT

Background

Case report

Menetrier's disease is an uncommon disease characterized by diffuse hypertrophy of gastric mucosa and giant gastric rugae with an increased risk of gastric cancer. Only a few reports supporting its association with gastric cancer have been found.

Material and methods

We present the case of signet ring cell adenocarcinoma associated with Menetrier's disease. The patient is a 54-year-old Algerian female.

Results

A 54-year-old woman was admitted to our hospital with a history of anemia, anorexia, and 10 kg weight loss. During her hospitalization, the patient presented an extradural hematoma. A biopsy was performed, which revealed a bone metastasis of the carcinomatous process. Abdominal computed tomography demonstrated diffuse thickening of the gastric wall. A gastric biopsy specimen showed thickened gastric mucosa and cystic dilatation of glands compatible with Menetrier's disease and diffuse infiltration by signet ring cell adenocarcinoma. A total gastrectomy was performed.

Conclusion

A patient with signet ring cell adenocarcinoma associated with Menetrier's disease is reported in our case study.

Keywords*: Menetrier's disease, signet ring cell adenocarcinoma, gastrectomy, gastric cancer, woman.*

Introduction

Menetrier's disease is uncommonly characterized by diffuse hypertrophy of gastric mucosa and giant gastric rugae with diminished acid secretory capacity, a protein-losing state, and hypoalbuminemia [1]. Fewer than 1000 cases have been reported [1,2], and a dozen reports support its association with gastric adenocarcinoma [2]. We present the signet ring cell adenocarcinoma case associated with Menetrier's disease.

Case report

A 54-year-old woman was admitted to the Hematology department for further investigations in March 2018 with a 2-month history of anemia, anorexia vomiting, nausea, epigastric abdominal pain, generalized edema, and 10 kg weight loss, upper gastrointestinal bleeding and melena, requiring transfusions of blood concentrates. Physical examination revealed a moderately tender abdomen. Total protein and albumin were 6.4 g/dL and 4.2 g/dL, respectively. All other laboratory data, including liver function tests, hemoglobin, and electrolytes, were average. Serological tests were negative for human immunodeficiency virus. Mild normocytic anemia was noted (hematocrit 38%). Tumor markers, such as carcinoembryonic antigen and cancer antigen 19-9, were also standard. The erythrocyte sedimentation rate was 100 mm in the 1st hour. During her hospitalization, the patient presented an extradural hematoma. Biopsy revealed a bone metastasis of carcinomatous process. Abdominal computed tomography demonstrated diffuse thickening of the gastric wall. Upper endoscopy showed a copious amount of mucus in the stomach with enlarged and hypertrophic gastric folds.

The signet ring cell adenocarcinoma was identified in the biopsy material, whereas Menetrier's disease was confirmed two weeks later in the total gastrostomy specimen.

Macroscopically, the mucosa was diffusely edematous with diffuse thickening of the gastric wall and gastric folds with a cerebroid appearance in the body and the fundus, a tumor localized on the border of the body and the fundus of the stomach, which was of 7 cm at the greatest diameter and was characterized by exophytic growth (fig.1).

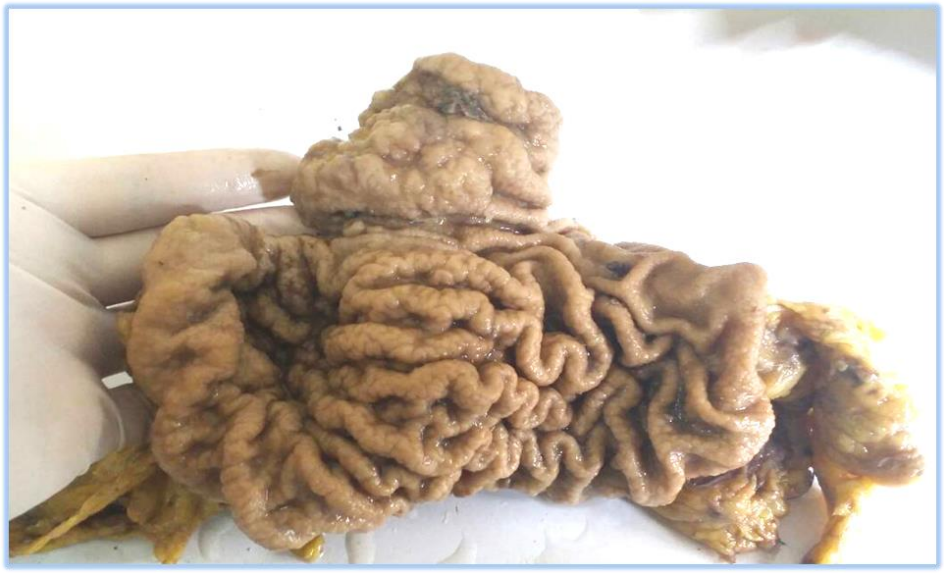

Fig 1. ***Gross postoperative specimen. An exophytic tumor localized on the border of the body and the fundus of the stomach, which was 7 cm at the greatest diameter. Presence of giant, thickened, and tortuous gastric folds resembling cerebral convolutions.***

A resected specimen was serially sectioned. Histopathology showed thickened gastric mucosa and cystic dilatation with tortuosity of the glands localized in the upper and middle third of the mucosa (Fig.2).

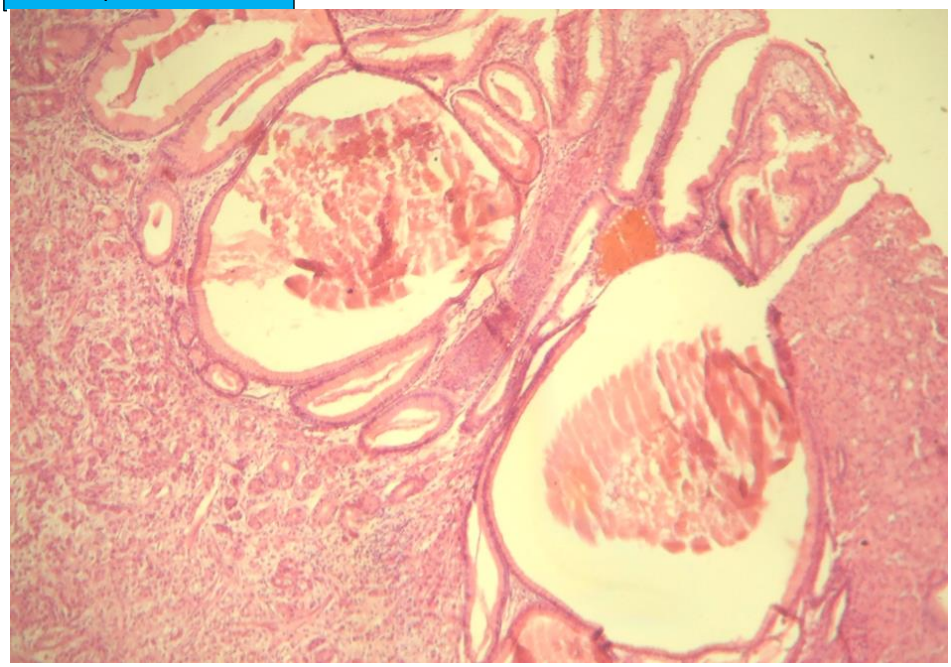

Fig 2. ***The glands show marked foveolar hyperplasia, elongated and tortuous appearance, and cystic dilatation(HE X20).***

The number of parietal cells increased, and inflammatory infiltration predominantly consisted of numerous eosinophils and plasma cells compatible with Menetrier's disease complicated by signet ring cell adenocarcinoma (Fig.3a,b) with a poorly differentiated malignancy (G3).

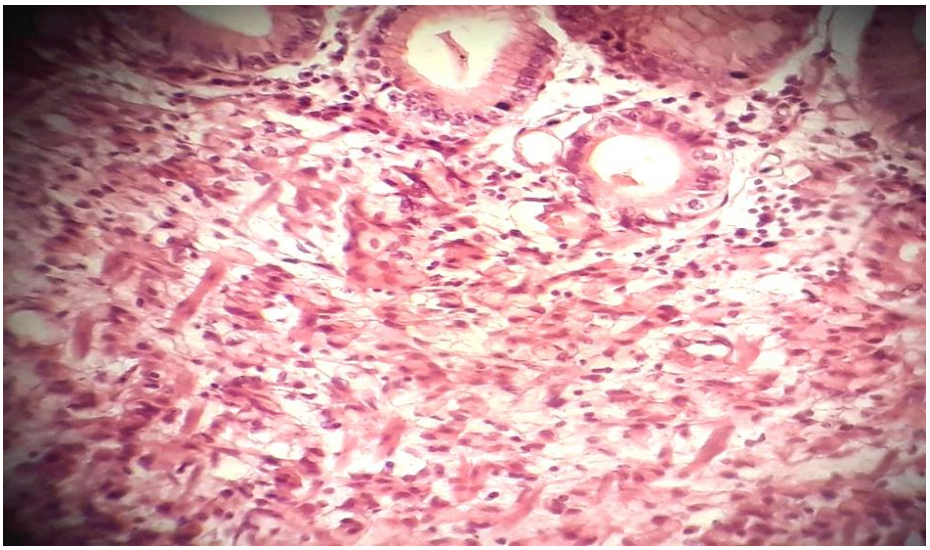

*Fig 3.****a: Signet ring cells show a mucin vacuole that pushes the nucleus to the periphery of the cell cytoplasm(HE X 20).***

It was classified histologically using the 8th edition of the Union for International Cancer Control classification (UICC) as extending to the serosal mucosa (pT3), metastases to 21/78 lymph nodes(N3b), brain metastasis (M1), and stage IV according to the 5th TNM staging stomach carcinoma. According to Lauren's classification, the tumor was classified as a diffuse type. The H. pylori infection was not detected.

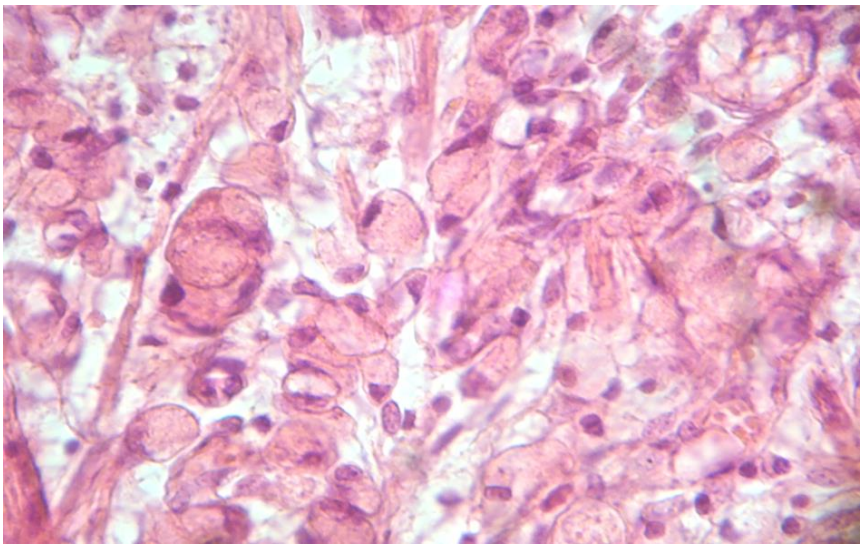

*Fig 3. b: **Signet ring cells show a mucin vacuole that pushes the nucleus to the periphery of the cell cytoplasm(HE X 40).***

Discussion

Menetrier's disease is a scarce type of hypertrophic gastropathy; the etiology, clinical features, and epidemiology of this disorder, including the risk of gastric cancer, are largely unknown. The disease was first described in 1888 by Pierre Ménétrier [1, 3-11] with an incidence of less than 1 in 200,000 individuals [4,6]. The link between Menetrier's disease and cancer remains controversial. It is known that Ménétrier's disease increases the risk of gastric cancer by around 2 to 15% over a lifetime. Still, this risk's magnitude is not entirely elucidated because of the rarity of cases [3,4,12]. In some instances, gastric cancer has been detected several years after the diagnosis of Menetrier's disease [12]. There has been little research on the incidence of

concurrent Menetrier's disease and signet ring cell adenocarcinoma [6], as reported in our study. The pathogenesis remains unclear, but recent experimental animal models have shown an overexpression of tumor growth factor α, a ligand for the tyrosinase epidermal growth factor receptor (EGFR), resulting in a selective expansion of surface mucous cells in the body and fundus of the stomach. The long-term may predispose to a malignant hyperproliferative disorder [2,3,8,12]. Only a couple of cases of familial clusters in the literature have been reported [8]

Menetrier's disease affects primarily adults but can also occur in children. A male predilection is often reported [2,3,6,8,10,12]. It usually occurs in patients between 50 and 70 years, with an average age of 55 years at diagnosis [2-4,8,11,13], consistent with our findings. The four classic symptoms of Menetrier's disease include abdominal pain, nausea, vomiting, and peripheral edema [1,3,4,6-8,12,13]. Our case showed all of these characteristics. Protein-loss gastropathy anemia, hypoalbuminemia, and diminished gastric acid secretion (hypochlorhydria) due to glandular atrophy[1,3,7,12]. Similar to other studies, our case had albumin levels within normal ranges despite having generalized edema. Menetrier's disease has been associated with some gastric diseases, including bacterial and viral infections such as CMV, H. pylori [1,4,6-8,11-14], herpes simplex [4,6,7,11,12], human immunodeficiency virus HIV, as well as ulcerative colitis [7] Our patient did not have a coexistent with an H. pylori infection. For some authors, Menetrier's disease is described as hypertrophy of gastric mucosa without gastritis, and for others, Menetrier's disease is considered hypertrophic gastropathy with hypoproteinaemia, regardless of histology [14]. Another issue related to the disease is thrombophilia. There are reported cases of unprovoked venous thrombosis associated with protein-losing diseases [1], as our patient presented an extradural hematoma.

On CT scans or MRIs, the thickened folds protrude into the gastric lumen and distort the mucosal surface. The serosal surface remains smooth, and the gastric wall between folds remains normal or slightly thickened [2,4,8].

Endoscopically, the gastric mucosa is characterized by giant, thickened, and tortuous gastric folds resembling cerebral convolutions [3,4,12]. The folds are usually less than 1.0 cm thick in the fundus and 0.5 cm in the antrum. Sometimes, large and irregular folds can mimic polyps [4].

Endoscopic ultrasound shows that only the second layer (muscularis mucosa) is thickened. The mucosa also shows increased echogenicity, while the submucosa and the muscularis propria remain normal [4]. The lesions are mainly seen in the body of the stomach, which can be localized or diffuse and are less involved in the gastric antrum [8, 12, 14]. There is frequently a poor correlation between endoscopic and or radiological findings and the histological features [14]. Histopathological analysis demonstrated mucosal hypertrophy due to foveolar hyperplasia and the development of tortuous glandular cysts [3,5,6,7,9] with a reduction in parietal and chief cells, causing reduction of acid secretion [1,4,7,12], infiltration of eosinophils and plasma cells, [7] All of these features were seen in our patient as well. For some authors, mild or no inflammatory cells [1, 3, 4, 9]. in Menetrier's disease may be distinguished from other gastropathies with thickening of the gastric folds such as the Zollinger–Ellison syndrome, lymphocytic gastritis, Cronkhite-Canada syndrome, carcinoma, lymphoma [2,3,5,6,9,12,14], stomach stromal tumor, Gastric mucosal prolapse [8].

Prognosis depends heavily on the timing of diagnosis, depth of tumor invasion, and lymph node metastasis of signet ring cell adenocarcinoma according to the WHO classification of gastric tumors 8th edition of the Union for International Cancer Control classification (UICC) [6,15].

Owing to its premalignant potential, annual endoscopy surveillance would be a helpful recommendation [3], but there is no consensus regarding screening [4, 12]. There is no specific treatment for Menetrier's disease. First-line treatment usually includes a high-protein diet, proton pump inhibitors, helicobacter pylori or CMV eradication, and long-acting octreotide release. Several studies reported disease regression after treatment with the monoclonal antibody against the EGFR receptor [1, 2, 9, 12]. A total or partial gastrectomy for refractory or complicated cases could be suggested [2, 3, 6-9, 12].

CONCLUSION

The present study describes a case of concurrent signet ring cell adenocarcinoma associated with Menetrier's disease and reviews the literature.

Footnotes.

Ahmed Elagrodey (Assistant professor of internal medicine) and Hayam Rashed (professor of pathology) were the peer reviewers.

E- Editor: Salem Youssef Mohamed, Osama Ahmed Khalil, Amany Mohammed.

Ethics Approval and Consent to Participate: The Institutional Review Board Committee approved the experimental protocol.

Consent for publication: the patient in this research gave written informed permission to publish the data in this study.

Data and materials availability: The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions

Houria Belkralladi and Zakaria Merad were responsible for conception and revision. Feriel Sellam and Abdelnacer Tou were responsible for interpreting and analyzing data. Houria Belkralladi, Zakaria Merad, and Feriel Sellam wrote the manuscript, which was revised and approved by all co-authors.

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This work was done according to the CARE guidelines.

Ethical approval: All procedures involving human participants followed the institutional and national research committee's moral standards, the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards. All authors declare that consent was obtained from the patient (or other approved parties) to publish this case report and accompanying images.

References

[1] Parianos. C, Aggeli. C, Sourla. A, Zografos. G.N. Total gastrectomy for treating Menetrier's disease persistent to medical therapy: A case report. International Journal of Surgery Case Reports 73 (2020) 95–99

[2] Bhate. P.A, Patel. J.A, Parikh. P, Ingle. M.A., Phadke. A, Sawant.P.Menetrier's Disease with Early.Gastric Cancer.Tropical Gastroenterology 2016;37(1): 53–76

[3] Remes-Troche,JM, Zapata-Colindres. JC, Starkman .I, De Anda. J, Arista-Nasr, J, Valdovinos-Diaz, MA. Early gastric cancer in Menetrier's disease. BMJ Case Reports. 2009; bcr07.2008.0453. doi: 10.1136/bcr.07.2008.0453.

[4] Quintino da Silva. P.H.R, Rigo. P, Batista. P.B, Katsuya Toma. R, Nunes de OliveiraL.A, Suzuki.L. Ménétrier's disease associated with gastric adenocarcinoma in a child-imaging aspect.RevAssocMedBras2016;62(6):485-489.

[5]Mosnier. J., Flejou. J., Amouyal. G., Gayet. B., Molas. G., Henin. D., Potet.F. Hypertrophic gastropathy with gastric adenocarcinoma: Menetrier's disease and lymphocytic gastritis?Gut1991;32:1565-1567.

[6] Kuo. A-H, Martinez. N, Rosenkranz.L. A Concurrent Case of Ménétrier's Disease and Signet Ring Carcinoma. ACG CaseRep J 2016;3(4):e176. doi:10.14309/crj.2016.149.

[7] Pryczynicz. A, Bandurski. R, Guzinska-Ustymowicz. K, Niewiarowska. K, Kemona. A, Kedra.B. Ménétrier's disease, a premalignant condition, with coexisting advanced gastric cancer: A case report and review of the literature. Oncology Letters 2014; 8: 441-445.

[8] Wang HH, Zhao CC, Wang XL, Cheng ZN, Xie ZY. Menetrier's disease and differential diagnosis: A case report. World J Clin Cases 2021; 9(23): 6943-6949.

[9] Thapa.S, Ghosh. A, Pun. G, Ghartimagar.D, O. P. Talwar. O.P.A Misdiagnosed Case of Hypertrophic Gastropathy—Hindawi Case Reports in Pathology 2020, Article ID4562531,4pageshttps://doi.org/10.1155/2020/4562531.

[10] Prokopchuk.O, Moreno-Ordaz .S , Hüser.N, Bachmann. J, Konukiewitz. B, Delgado-Picolomini. A Friess. H, and Martignoni M. E. Unusual coexistence of Ménétrier disease with adenocarcinoma of the esophagogastric junction: A case report and review of the literature.Integr Cancer Sci Therap, 2018 doi: 10.15761/ICST.1000277.

[11] Xiong. L.S., Gong. Y.Y . Natural history of adult-onset Ménétrier's disease: Report of a case with 9-year follow-up Experimental and therapeutic medicine 11: 2462-2466, 2016

[12] Genevay, M, Lauwers, G.Y. Polyps and tumor-like lesions of the stomach. In Shepherd N . A., Warren, B.F, Williams, G.T., Greenson, J.K, G.Y.Lauwers, Novelli. M.R. Morson and Dawson's Gastrointestinal Pathology 5th ed. 2013; 174-175.

[13] Munday. J.S, Aberdein.D., Cullen G. D, French. A. F. Mené trier Disease and Gastric Adenocarcinoma in 3 Cairn Terrier Littermates. Veterinary Pathology 2012; 49(6): 1028-1031.

[14] El-Zimaity.H, Riddell.RH.Inflammatory disorders of the stomach. In Shephered N . A, Warren. B.F, Williams G.T, Greenson. J.K, G.Y.Lauwers, Novelli. M.R., M, Lauwers, G.Y. Polyps and tumor-like lesions of the stomach. In Shepherd N . A., Warren, B.F, Williams, G.T., Greenson, J.K, G.Y.Lauwers, Novelli. M.R. Morson and Dawson's Gastrointestinal Pathology 5th ed.Morson and Dawson's Gastrointestinal Pathology 5th ed 2013; 148.

[15] Carneiro.F,Fukayama.M,Grabsch.HI, Yasui.W. Gastric adenocarcinoma in digestive system tumors, edited by the WHO Classification of Tumors Editorial Board 2019: 85-95.