Comorbidity of Menetrier’s disease and diabetes mellitus.  
A clinical case

Abstract. We present a case report describing the diagnosis and management of a patient who presents with a rare diagnosis of Menetrier’s disease. This condition poses a diagnostic challenge to clinicians due to its nonspecific clinical presentation and is oftentimes misdiagnosed for more common gastric disorders. Menetrier’s disease is characterized by gastric mucosal hypertrophy and subsequent protein loss, resulting in gastric symptoms and widespread edema. While the etiology remains unclear, notable associations have been observed with Helicobacter pylori infection and overexpression of transforming growth factor alpha. The management often involves supportive measures with medical and surgical interventions for refractory cases and when necessary. This report includes a comprehensive review of the literature on the clinical presentation, diagnostic approach, and management of this rare disease. By documenting such cases in the medical literature, we aim to enhance the clinician’s ability to recognize and manage this disorder, thereby preventing the development of more severe manifestations such as diabetes mellitus. Menetrier’s disease is a rare disorder that should be suspected in patients with upper gastrointestinal complaints and hypertrophied gastric mucosa. With a rather broad differential diagnosis consisting of Zollinger-Ellison syndrome, hypertrophic lymphocytic gastritis, hypertrophic hypersecretory gastropathy, gastric adenocarcinoma, gastric polyps, infections such as histoplasmosis and tuberculosis, autoimmune-like inflammatory conditions such as sarcoidosis, and more commonly, gastrointestinal disease, it is often overlooked in the diagnostic workup. Therefore, it is crucial for clinicians to conduct a thorough evaluation and maintain a high clinical suspicion when there is concurrent H. pylori infection and/or imaging findings suggestive of hypertrophied gastric mucosa to avoid missing this disease.

Keywords: Menetrier’s disease; diabetes mellitus; clinical case

Introduction
Menetrier’s disease is a rare acquired disorder of the stomach associated with giant rugal folds involving the body and fundus, hypochlorhydria or achlorhydria, excess gastric mucus production, and hypoaaluminemia resulting from gastric mucosal protein loss [1, 2]. Patients with Menetrier’s disease generally are men, diagnosed at a mean age of 55 years with progressive and insidious symptoms of abdominal pain, nausea, and vomiting, often with concomitant peripheral edema resulting from severe protein-losing enteropathy [3, 4]. In 1888, Pierre Ménétrier first described the disease that bears his name. Many of the findings he reported then remain accepted features of the disease [5, 6].

The disease is characterized by histologic features of massive foveolar hyperplasia, tortuosity and cystic dilation of glands, smooth muscle hyperplasia, and atrophy of oxyntic gland mucosa, with a marked reduction in the number of parietal and chief cells [7, 8].

Although decreased gastric acid production is frequently associated with this condition, serum gastrin levels remain relatively normal [9].

The clinical description of Menetrier’s disease in the current literature largely is limited to case reports and case series, and the today understanding of the etiology and epidemiology of this rare condition is unknown [3, 10, 11].
The differential diagnosis for a clinical presentation consistent with Menetrier’s disease includes signet ring cell carcinoma, lymphoma, sarcoidosis, and linitis plastica, but all of these can be excluded by clinicopathologic correlation. In 1993, H.C. Wolfsen et al. [12] reported the pathologic features of 23 cases of Menetrier’s disease diagnosed at Mayo Clinic. Since this time, very few publications have addressed the etiology or outcomes of this disease, with a lack of data about the demographic characteristics or long-term follow-up evaluation of patients with Menetrier’s disease. Currently, there have been less than 1,000 reported cases of this disease [1].

Its etiology is not known, although several childhood cases have been associated with cytomegalovirus, which has been characterized by an abrupt onset of symptoms, spontaneous and complete resolution, and evidence of acute and convalescent titers for cytomegalovirus [13].

The clinical presentation is often nonspecific and can resemble signs and symptoms of gastritis. However, the protein loss can cause widespread edema, providing a clearer picture of Menetrier’s disease. A detrimental complication of Menetrier’s disease is the evolution to gastric adenocarcinoma. Because of the rarity of the disease and the often vague clinical presentation, it is important for clinicians to conduct a comprehensive diagnostic workup to prevent further harm to the patient.

**Clinical case**

Patient D., 42 years old, complained about gnawing pains in the epigastric area that become stronger after eating, nausea, sometimes vomiting after eating, weight loss. He considered himself sick for 8 years. Almost annually, he was treated on both outpatient and in-patient basis in a district hospital for chronic gastritis with temporary improvements. Diabetes mellitus was diagnosed 2 years ago. The patient had a regular physique, height of 170 cm, body weight of 64 kg. The skin and visible mucous membranes were pale pink. Peripheral lymph nodes were not enlarged. The tongue was wet, with a slight white coating. Abdomen of the correct configuration, soft, moderately painful during palpation in the epigastric area. Blood pressure was 130/80 mm Hg.

**Laboratory data.** There were revealed: hypoalbuminemia — 28 g/l (normal 36.0–52.0), glucosuria — 5.2 mmol/l, hyperglycemia — 8.0–12.3 mmol/l, glycated hemoglobin 6.5 % (normal is up to 6.0 %), blood C-peptide — 3.2 ng/ml (normal 0.5–3.2 ng/ml). These results indicate the presence of type 2 diabetes mellitus.

**Instrumental data.** X-ray of the stomach with double contrast: accumulation of thick tortuous folds protruding into the lumen of the stomach (filling defects of irregular shape). CT scan of the abdominal cavity: diffuse thickening of the gastric walls without signs of lymphadenopathy. Esophagogastroscopy: the folds of the gastric mucosa are thickened mainly in the body of the organ, resembling cerebral convolutions. Biopsy microscopy: hyperplasia of surface mucous cells and glandular atrophy (reduction in the number of parietal and chief cells), cystic dilatation of gastric pits.

**Clinical diagnosis:** Menetrier’s disease, type 2 diabetes mellitus, mild form.

Since infection is considered as the main etiological factor of Menetrier’s disease [3], it can presumably be common to the development of DM, because viral infections can be among factors provoking its occurrence in case of genetic predisposition [9].

The optimal method for treatment of Menetrier’s disease is not defined. Surgery (gastric resection) is indicated for gastric bleeding. The use of cetuximab, which blocks the activity of transforming growth factor alpha whose production is increased in patients, gives encouraging results [10]. The patient is prescribed symptomatic drugs, metformin 500 mg after dinner. Since Menetrier’s disease refers to precancerous diseases, observation by a family doctor, an esophagoscopist and an endocrinologist is recommended.

**Discussion**

Menetrier’s disease is a rare gastric disorder that causes enlargement of gastric mucus-secreting cells with subsequent atrophy of the acid-secreting glands. It is not well-documented, with less than 1,000 cases currently reported in the literature [1]. The disease tends to affect males slightly more often than females and typically presents between 30 and 60 years with an average age of 55 [2].

The clinical presentation of Menetrier’s disease is often nonspecific and can be misdiagnosed as other more common abdominal diseases and disorders. Most individuals present with upper abdominal pain with and typically without nausea and vomiting. Often, the patients note early satiety, most likely attributed to the increased gastric surface area. The protein loss, specifically albumin, causes a state of fluid extravasation in peripheral tissues, leading to edema, most prominent in the lower extremities. Patients can also present with gastrointestinal bleeding [14].

There have been few reports of Menetrier’s presenting with intussusception, causing small bowel obstruction [15]. Although the disease is rarer in children, the presentation in this population often follows a transient viral illness [16].

The diagnostic workup for Menetrier’s disease often begins with a physical examination, medical history assessment, and basic laboratory tests such as complete blood count and comprehensive metabolic panel.

Imaging studies can be of many types, including a radiological swallow with either barium or water-soluble contrast, allowing the radiologist to visualize the gastrointestinal tract and detect any abnormalities in size and shape. An esophagogastroduodenoscopy is widely used in gastrointestinal practice to grasp a better and more direct view of the gastrointestinal lining in both the esophagus and the stomach. CT scans and magnetic resonance imaging can be used to evaluate gastric wall thickness as well as detect any associated complications that can arise with Menetrier’s such as gastric ulcers and even gastric carcinoma. These images can also identify lymphadenopathy, which can be a nonspecific finding or an early indication of carcinoma development.

Biopsies are also taken with esophagogastroduodenoscopy, allowing the pathologist to examine the tissue under the microscope, aiding in the diagnosis.
The management of Menetrier’s disease is largely supportive with a focus on nutritional replenishment. Patients are advised to follow a high-protein diet with frequent electrolyte monitoring and supplementation as needed. In patients whose disease is refractory to medical management or in patients with a risk of clinical deterioration, surgical intervention is utilized. If the disease is localized to the antrum, partial gastric resection can be done; however, if it is widespread, total gastrectomy is performed. Surgical intervention also reduces the risk of gastric cancer development.

Menetrier’s disease is a chronic condition with rare spontaneous regression and remission. Patient response to symptomatic and supportive treatment varies. Although this risk is low, frequent monitoring with annual endoscopies and biopsies is recommended. Unfortunately, there is no known cure for Menetrier’s disease, underscoring the importance of close patient follow-up to monitor the disease and prevent complications.

Conclusions
Menetrier’s disease (hyperplastic gastropathy) is a rare illness of stomach, belonging to the group of precancerous diseases. It should be suspected in patients with upper gastrointestinal complaints and hypertrophied gastric mucosa. With a rather broad differential diagnosis consisting of Zollinger–Ellison syndrome, hypertrophic lymphocytic gastritis, hypertrophic hypersecretory gastropathy, gastric adenocarcinoma, gastric polyps, infections such as histoplasmosis and tuberculosis, autoimmune-like inflammatory conditions such as sarcoidosis, and more commonly, gastrointestinal disease, it is often overlooked in the diagnostic workup. Consequently, such patients belong to the group of systematic dispensary (X-ray laboratory) observation. The combination with diabetes worsens the prognosis of this pathology.

References

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Information about authors
Ruslana Lyashuk, PhD, Associate Professor at the Department of Clinical Immunology, Allergology and Endocrinology, Bukovinian State Medical University, Chernivtsi, Ukraine; e-mail: office@bsmu.edu.ua; https://orcid.org/0000-0002-6121-6716

Yuliya Marchuk, PhD, Associate Professor at the Department of Clinical Immunology, Allergology and Endocrinology, Bukovinian State Medical University, Chernivtsi, Ukraine; e-mail: marchuk.yuliya@gmail.com; phone: +380(50)926277; http://orcid.org/0000-0002-3702-1994

Yulya Marchuk, PhD, Associate Professor at the Department of Clinical Immunology, Allergology and Endocrinology, Bukovinian State Medical University, Chernivtsi, Ukraine; e-mail: marchuk.yuliya@gmail.com; phone: +380(50)926277; http://orcid.org/0000-0002-3702-1994

Received 24.10.2023
Revised 29.12.2023
Accepted 11.01.2024

152
Międzynarodni endokrinologiczni Żurnal, ISSN 2224-0721 (print), ISSN 2307-1427 (online)
Vol. 20, No. 2. 2024
Коморбідність хвороби Менетріє і цукрового діабету. Клінічний випадок

Резюме. Представлено опис діагностики та лікування пацієнта з рідкісною хворобою Менетріє. Цей стан є діагностичною проблемою для клініцистів через неспецифічні клінічні прояви, його часто помилково приймають за більш поширені розлади шлунка. Хвороба Менетріє характеризується гіпертрофією слизової оболонки шлунка та подальшою втратою білка, що призводить до появи симптомів з боку шлунково-кишкового тракту і генералізованого набряку. Хоча етіологія хвороби залишається нез'ясованою, помітний зв'язок з інфекцією Helicobacter pylori і надмірною експресією трансформуючого фактора росту альфа. Лікування часто включає підтримуючі заходи з медичними й хірургічними втручаннями в рефрактерних випадках та за необхідності. У статті наведений огляд літератури щодо клінічних проявів, діагностичних підходів та лікування цього рідкісного захворювання. Документуючи такі випадки в медичній літературі, ми прагнемо покращити здатність клініциста розпізнавати та контролювати цей розлад, запобігаючи розвитку більш серйозних проявів, зокрема цукрового діабету. Хвороба Менетріє є рідкісним захворюванням, яке слід запідозрити в пацієнтів зі скаргами на розлади шлунково-кишкового тракту та при гіпертрофованій слизовій оболонці шлунка. Диференційну діагностику слід проводити із синдромом Золлінгера — Елікса, гіпертрофічним лімфоцитарним гастритом, гіпертрофічною гіперсекреторною гастритом, аденоакриномою шлунка, поліпами шлунка, інфекціями (гістоплазмоз і туберкульоз), автоімунними запальними станами (саркоїдоз). Тому для клініцистів важливо ретельно обстежити пацієнта за умов супутньої інфекції, що вказує на гіпертрофовану слизову оболонку шлунка, щоб не пропустити це захворювання. Такі хворі належать до групи систематичного диспансерного спостереження. Поєднання з цукровим діабетом погіршує прогноз цієї патології. Ключові слова: хвороба Менетріє; цукровий діабет; клінічний випадок.