Oesophago-colonic fistula in *ulcerative colitis* in a patient who previously underwent gastrectomy due to Ménétrier's disease. A case report and review of the literature

Przetoka przełykowo-okrężnicza u pacjentki z wrzodziejącym zapaleniem jelita grubego po przebytej gastrektomii z powodu choroby Ménétriera. Opis przypadku oraz przegląd literatury

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Słowa kluczowe: choroba Ménétriera, wrzodziejące zapalenie jelita grubego, przetoka przełykowo-okrężnicza.

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Abstract

Ménétrier's disease (MD) is a hypertrophic gastropathy with histological features such as foveolar hyperplasia of the gastric mucosa accompanied by mucus hypersecretion and glandular hypertrophy. In adults, the course of the disease in adults is complex and may lead to the necessity of gastrectomy. The aetiology of *ulcerative colitis* (UC) remains unknown and is probably multi-factorial. Apart from abdominal pain, diarrhoea and anaemia, progression of the disease can involve toxic megacolon, perforations, strictures and even intestinal tumours; therefore, after several years may lead to total colectomy. The combination of MD and UC is very rare. We report an unusual case of MD and UC coexistence. Surgical treatment was applied and the patient underwent total gastrectomy due to MD, and after several years proctocolectomy due to severe UC complicated by descending colon strictures and oesophago-colonic fistula.

Streszczenie

Choroba Ménétriera (CM) jest chorobą charakteryzującą się pogrubieniem fałdów błony śluzowej żołądka w następstwie hiperplazji komórek nabłonkowych z towarzyszącym przerostem komórek gruczołów żołądkowych i zwiększonym wydzielaniem śluzu. Ciężki przebieg tej choroby u osób dorosłych może prowadzić do konieczności leczenia operacyjnego, w tym całkowitego wycięcia żołądka. Objawy wrzodziejącego zapalenia jelita grubego (CU) obejmują dolegliwości bólowe, biegunki i niedokrwistość, a w zaawansowanych postaciach choroby toksyczne, rozszerzenie okrężnicy, perforacje i zwężenia. Powikłania są często wskazaniem do całkowitego wycięcia jelita grubego. Jednoczesne występowanie CM i CU jest bardzo rzadkie. W pracy przedstawiono wyjątkowy przypadek współwystępowania CM i CU. Pacjentce z powodu CM całkowicie wycięto żołądek, a po kilku latach jelito grube z powodu ciężkiego przebiegu CU powikłanego zwężeniem okrężnicy zstępującej z towarzyszącą przetoką przełykowo-okrężniczą.

Background

Ménétrier's disease (MD) is a hypertrophic gastropathy with histological features such as foveolar hyperplasia of the gastric mucosa accompanied by mucus hypersecretion and glandular hypertrophy [1-3]. In general, paediatric MD is considered an infectious condition usually resolving within 5 months. In adults, the course of the disease is more complex and may lead to the necessity of gastrectomy [1, 2]. Cytomegalovirus (CMV) infection has been implicated in the pathogenesis of MD in infants and children, whereas in adults *Helicobacter pylori* (HP) infection is of considerable interest [4-6]. Clinical manifestations, which include abdominal pain, hypoproteinaemia with hypoalbuminaemia accompanied by peripheral oedema, hypochlorhydria and vomiting, are the same for both adult and paediatric patients. Diagnostic means include upper gastrointestinal (UGI) endoscopy,

UGI series, computed tomography (CT) as well as abdominal sonography.

The aetiology of *ulcerative colitis* (UC) remains unknown and is probably multi-factorial. It is believed that genetically predisposed individuals interact with environmental factors, because the aetiopathogenesis of IBD is thought to be caused by mutual reactions among host susceptibility genes (CARD15/NOD2, HLA DRB1*0103, DRB1*1502, DRB1*0103), environmental factors, including enteric flora and food antigens, accompanied by impaired immunological balance [7, 8]. It is also accepted that several cytokines with proinflammatory activities, including interleukin IL-1, IL-6, IL-8, IL-12, and tumour necrosis factor TNF-α are upregulated in UC and play a key role in the clinical and immunopathological manifestations of the disease [9, 10]. Apart from abdominal pain, diarrhoea and anaemia, progression of the disease can involve toxic megacolon, perforations, strictures and even intestinal tumours; therefore, after several years it may lead to total colectomy [11].

Only five cases of UC coexisting with MD have been reported in the literature to date [12-16]. However, an unusual case of a patient who underwent gastrectomy due to MD, and after several years proctocolectomy due to advanced UC complicated by oesophago-colonic fistula and multifocal colon strictures, would appear to be the first such case reported in the literature.

Case presentation

History of UC and MD

A diagnosis of UC in a 29-year-old woman was established in 1994, based on clinical features and colonoscopic appearances which at that time were: frank friability, marked erythema, absent vascular pattern, erosions and ulcerations. Treatment with 5-aminosalicylic acid (5-ASA) was initiated in 1994. In 1995 she also underwent 6-month prednisolone therapy (20 mg/day) due to exacerbation of the disease.

In November 1996, the patient was admitted to the hospital due to upper-abdominal pain accompanied by nausea and vomiting and moderate anaemia. In gastroscopy, a multiple polypoid mass throughout the stomach was visible (mainly in the pylorus). Histopathological biopsies raised the suspicion of gastric adenocarcinoma (G1). Because of progressive weight loss due to gastric outlet obstruction with vomiting and malnutrition, the patient was elected to proceed for gastrectomy and Schlatter (omega) reconstruction of the alimentary tract. Pre-operatively, her total serum protein was modestly depressed at 5.9 g/dl; no significant peripheral blood eosinophilia (4%) was noticeable. The diagnosis of MD was established intraoperatively based on typical gross and histological features of the gastric wall.

After 10 years, at the age of 41, the woman received consultation in the local hospital in December 2006, with 1-month of exacerbation of UC. On admission, the main symptoms were abdominal pain, frequent diarrhoea (up to 6 stools per day) and subfebrile body temperature. The new, surprising symptoms claimed by the patient were recurring episodes of halitosis and belches, which were described as having a stool-like smell.

On admission, the skin and conjunctiva were pale. Cachexia and slight lower abdominal tenderness were observed. The rest of the physical examination was unremarkable. Laboratory data, except for moderate anaemia indices in blood morphology, were normal. Sigmoidoscopy revealed mildly friable, oedematous mucosa with marked erythema and decreased vascular pattern (Mayo UC Endoscopic Score 2). 40 cm from the rectal sphincter, a tight sigmoid stricture was visible. Upper gastrointestinal endoscopy showed moderate inflammatory changes in the lower oesophagus and within the anastomosis. Both afferent and efferent loops were normal in appearance. Although upper and lower GI endoscopy did not demonstrate a fistula, probably because of the existing sigmoid stricture and limitation of the one-sided endoscopic view, the unclear anatomical relationships gave rise to such a suspicion (fig. 1). Hence, double-contrast lower intestine radiography was performed which showed multiple strictures within the sigmoid colon and left part of transverse colon, and the fistula that had formed between the oesophagus (stump) and left part of the transverse colon (fig. 2).

Surgical treatment

The mild malnutrition was corrected by enteral feeding with a naso-jejunal tube placed endoscopically. The regimen of 25 kcal/kg b.w./day of polymeric complete diet (Peptisorb, Nutricia) was administered for 6 days before elective surgery. Open proctocolectomy and end-ileostomy were performed. The oesophago-colonic fistula was closed using simple suture and covering the suture line by mobilizing the blind end of the ascending jejunal loop and the creation of a Roux-en-Y type reconstruction of the alimentary tract. The naso-jejunal feeding tube was placed on the table about 30 cm below the distal entero-enterostomy. A non-complicated postoperative course provided the possibility of per os feeding on the 4th day after surgery, and the gastrojejunal tube was removed three days later.

Macroscopic examination showed massive pericolic inflammation and multiple colonic strictures, and microscopically advanced ulcerative pancolitis with the formation of cryptal abscesses.

Discussion and conclusions

UC is a chronic inflammatory bowel disease stemming from abnormal immune responses of unknown aetiology.

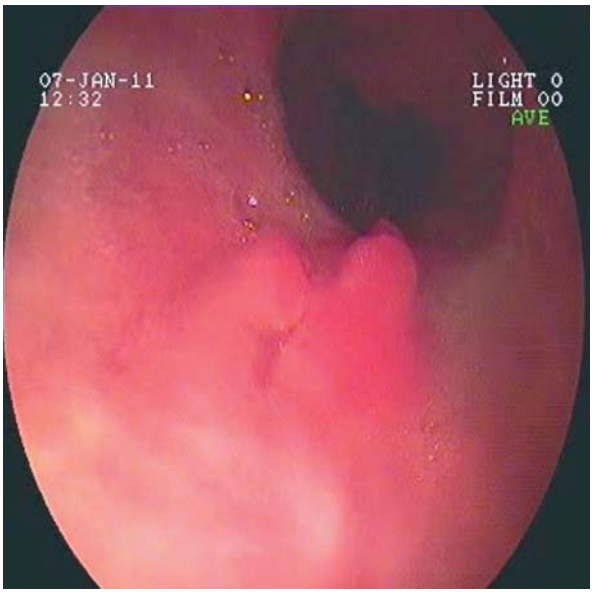

Fig. 1. Endoscopic examination showing probable esophageal localization of the fistula (a, c) and anastomosis followed by both ascending and descending loops

Ryc. 1. *Endoskopowy obraz prawdopodobnej lokalizacji przetoki (przełyk), dalej pętla doprowadzająca i odprowadzająca*

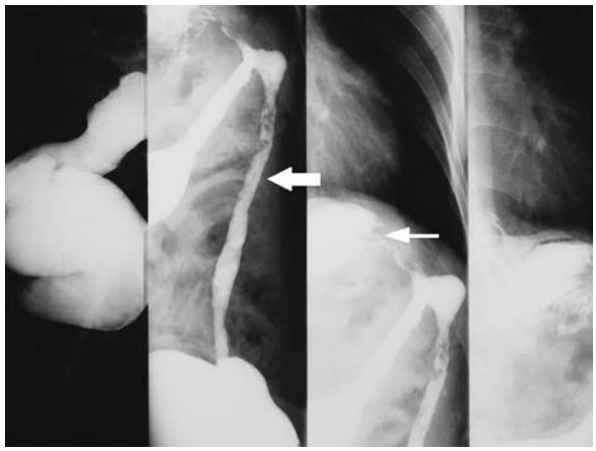

Fig. 2. Lower intestine radiography showing the stricture (thick arrow) within the sigmoid colon and left part of transverse colon and the fistula that had formed between esophagus and left part of the transverse colon (thin arrow)

Ryc. 2. *Obraz radiologiczny (wlew odbytniczy) pokazujący zwężony fragment esicy i lewej połowy poprzecznicy (cienka strzałka) oraz przetokę wytworzoną między przełykiem a poprzecznicą (gruba strzałka)*

Regarding the pathogenesis of MD, it appears that a variety of factors (infectious, immunological, or pharmacological) induce a constellation of specific changes through specific mediators, such as TGF-α [17]. UC and MD, however, are under the strong influence of and can be modified by genetic factors. Moreover, in both diseases, age appears to be important in determining patient susceptibility and response to different causative agents. It remains unclear whether the same factors could have a causal role in the pathogenesis of both MD and UC. There was no obvious aetiological agent to account for the MD or UC in the presented case (e.g. CMV or HP infection). Diagnostic criteria of MD are poorly defined in the literature. Some authors allow the presence of chronic inflammation, whilst others require the absence of inflammation. This might be just as important when considering the differentiation with Crohn's disease, especially after finding the fistula. However, in this patient, differential diagnosis, including a combination of clinical, laboratory, histopathological, radiographic and therapeutic observations, was conducted several times starting from 1994. The most relevant for UC were repeated bloody diarrhoeas and colonoscopies showing diffuse inflammation, loss of vascular pattern, friability (contact bleeding), abundant mucus and granular appearance, multiple erosions or ulcers, loss of haustration (lead-pipe pattern) and lumen narrowing. The results of the colorectal biopsies also showed histological features characteristic even for active (active inflammatory cell infiltration, crypt abscess, goblet cell depletion) or inactive UC (crypt architectural abnormalities, atrophic crypts). The diagnosis of UC was also confirmed by postoperative histopathological examination, which showed advanced ulcerative pancolitis with the formation of cryptal abscesses. Consequently, we suggest that MD should not be linked to the subsequent appearance of UC.

The coexistence of MD and UC is very rare. Only a few cases have been reported in the Serbian [12], Spanish [13], Australian [14], French [15] and Japanese [16] literature. What differentiates the presented case and makes it both unique and particularly interesting is the presence of oesophago-colic fistula.

Gastrointestinal fistulae represent an extremely complicated clinical problem and are associated with a great deal of morbidity. Mortality rates accounted for over 40% before the era of intensive care supported by nutritional therapy. Post-operative iatrogenic fistulae constitute approximately 80% of recognized cases, while spontaneous intestinal fistulae occur as complications of a wide variety of pathological processes. The aetiology of acquired gastrointestinal fistulas is extremely broad [18]. Inflammation is the most important of the spontaneous disease processes which may result in fistulisation, and Crohn's disease

and colonic diverticulitis are most frequent [19, 20]. Spontaneous internal gastrocolic fistulae may also occur as a late consequence of benign or malignant gastric ulcers [21], whereas gastrojejunocolic fistulae may arise as a result of stomal ulcers after incomplete gastric resection or vagotomy for peptic ulcer disease [22]. A characteristic secondary manifestation of upper GI tract fistulas is acid loss followed by hypokalaemic metabolic alkalosis; on the other hand, fistulas from the small intestine are usually associated with considerable deficiency in vitamin B_{12}, folic acid, zinc and copper [22]. However, internal fistulas are likely to be subtle, with symptoms of sepsis, diarrhoea, bleeding, weight loss and exacerbation of underlying disease; therefore, occasionally extensive diagnosis results in the finding of an otherwise unexpected fistula. However, in the presented case characteristic symptoms were limited to recurring episodes of halitosis and belches with a stool-like smell. But increasing diarrhoea followed by significant weight loss, instead of existing conditions of post-gastrectomy and UC, might also be attributed to the presence of an oesophago-colonic fistula. Due to inflammatory aetiology, the likelihood of spontaneous closure of the fistula, even supported by pharmacotherapy, was very doubtful. Therefore, definitive surgery was the treatment of choice.

In summary, we have reported an unusual case of MD and UC coexistence. Surgical treatment was applied and the patient underwent total gastrectomy due to MD, and after several years colectomy due to severe UC complicated by descending colon strictures and oesophago-colonic fistula. The occurrence of UC is much more common than MD; therefore, one might suspect Ménétrier's disease more frequently in patients with UC. However, based on this case, it is also interesting to speculate on a possible link between the two diseases or atypical gastric mucosa response to 5-ASA treatment in the early stage of UC.

Non-financial competing interests

Rafał Filip: contributed ideas to review, discussion, strategies, contributed work as physician – internal diseases/gastroenterology (preservative treatment), primary writer of the review.

Piotr Paluszkiewicz: contributed ideas to review, contributed work as surgeon (surgical treatment and post-operative treatment), secondary writer of the review.

References

1. Fenoglio-Preiser CM, Noffsinger AE, Stemmermann GN, et al. Hypertrophic hyperplastic gastropathies. In: Gastrointestinal Pathology. An Atlas and Text. 2nd ed. Lippincott-Raven, Philadelphia 1999; 209-13.
2. Lewin KJ, Appelman HD. Tumors of the esophagus and stomach. In: Atlas of Tumor Pathology. 3rd Series. Armed Forces Institute of Pathology, Washington 1996; 218-21.
3. Fieber SS, Rickert RR. Hyperplastic Gastropathy. Analysis of 50 selected cases from 1955-1980. Am J Gastroenterol 1981; 76: 321-9.
4. Eisenstat DD, Griffiths AM, Cutz E, et al. Acute cytomegalovirus infection in a child with Menetrier's disease. Gastroenterology 1995; 109: 592-5.
5. Bayerdörffer E, Ritter MM, Hatz R, et al. Healing of protein losing hypertrophic gastropathy by eradication of Helicobacter pylori: is Helicobacter pylori a pathogenic factor in Menetrier's disease? Gut 1994; 35: 701-4.
6. Axon AT. Treatment of Helicobacter pylori: an overview. Aliment Pharmacol Ther 2000; 14 (Suppl 3): 1-6.
7. Gleeson MH, Walker JS, Wentzel J, et al. Human leucocyte antigens in Crohn's disease and ulcerative colitis. Gut 1972; 13: 438-40.
8. Ma Y, Ohmen JD, Li Z, et al. A genomewide search dentifies potential new susceptibility loci for Crohn's disease. Inflamm Bowel Dis 1999; 5: 271-8.
9. Katz JA, Itoh J, Fiocchi C. Pathogenesis of inflammatory bowel disease. Curr Opin Gastroenterol 1999; 15: 291-7.
10. Isaacs KL, Sartor RB, Haskill S. Cytokine messenger RNA profiles in inflammatory bowel disease mucosa detected by polymerase chain reaction amplification. Gastroenterology 1992; 103: 1587-95.
11. Höie O, Wolters F, Riis L, et al. Ulcerative colitis: patient characteristics may predict 10-yr disease recurrence in a European-wide population-based cohort. European Collaborative Study Group of Inflammatory Bowel Disease (EC-IBD). Am J Gastroenterol 2007; 102: 1692-701.
12. Mirković D, Doder R, Ilić S, et al. Menetrier's disease associated with ulcerative colitis. Vojnosanit Pregl 2003; 60: 747-51.
13. Ojeda E, Ruiz J, Cosme A, Lobo C. Menetrier disease associated with ulcerative colitis. Response to the treatment with octreotide. Review of the diagnostic criteria and etiopathogenesis. Gastroenterol Hepatol 1997; 20: 175-9.
14. Hemmings CT. Menetrier's disease in patient with ulcerative colitis: a case report and review of the literature. Pathology 2007; 39: 282-3.
15. Belhocine K, Chaoui F. Menetrier disease and ulcerative colitis – an unusual association. Gastroenterol Clin Biol 2006; 30: 1105-7.
16. Sasaki E, Toyonaga A, Murayama S, et al. A case report of Menetrier's disease developed in a patient with ulcerative colitis. Nippon Shokakibyo Gakkai Zasshi 1991; 88: 96-9.
17. van der Berg M, Stokkers P, Rings E, et al. Transforming growth factor alpha in Menetriers disease. J Pediatr Gastroenterol Nutr 1993; 17: 230-2.
18. Pickhardt PJ, Bhalla S, Balfe DM. Acquired gastrointestinal fistulas: classification, etiologies, and imaging evaluation. Radiology 2002; 224: 9-23.
19. Ikeuchi H, Shoji Y, Yamamura T. Management of fistulas in Crohn's disease. Dig Surg 2002; 19: 36-9.
20. Laurent SR, Detroz B, Detry O, et al. Laparoscopic sigmoidectomy for fistulized divetriculitis. Dis Colon Rectum 2005; 48: 148-52.
21. Marschall J, Bigsby R, Nechala P. Gastrocolic fistulae as a consequence of benign gastric ulcer disease. Can J Gastroenterol 2003; 17: 441-3.
22. Chung DP, Li RS, Leong HT. Diagnosis and current management of gastojejunocolic fistula. Hong Kong Med J 2001; 7: 439-41.