

Case report

Familial giant hypertrophic gastritis (Ménétrier's disease)

B LARSEN, U TARP, AND E KRISTENSEN

From the Medical Department, The Silkeborg Hospital, Silkeborg, Denmark

SUMMARY Familial giant hypertrophic gastritis involving three generations is reported. A review of the literature, where approximately 200 cases are described, showed only few cases of familial occurrence of this disease, and only in siblings. Our findings suggest dominant heredity, but considering the sparsity of familial occurrence reported earlier, heredity seems to be of only minor pathogenetic significance.

Giant hypertrophic gastritis was originally described as a clinical entity by Ménétrier in 1888 (Ménétrier's disease). This rare condition is characterised by enlargement of the gastric mucosal folds primarily affecting the body of the stomach, whereas the gastric antrum is often saved. Histologically, there is proliferation of the gastric glands with preservation of nuclear polarity, and cystic dilatation of the basilar portion of the glands. In extensive cases, the mucous secreting cells are present in the glands deep in the mucosa replacing the normal chief and parietal cells. The number of lymphocytes in the lamina propria may be increased.¹

Some authors diagnose Ménétrier's disease on the basis of histopathological lesions and presence of hypochlorhydria and hypoproteinemia, while other authors do not include these deficiencies in the definition.¹⁻⁵ The most frequent clinical features are asthenia, weight loss, upper abdominal pain or discomfort, nausea, diarrhoea, oedema and anaemia. The disease is reported in infants, but occurs most often in adults. Thus, some 200 adult cases and 16 children cases have been published since 1888.^{1,6}

Information of the aetiology of Ménétrier's disease is inadequate, although a causative role of allergy and various infections and toxicants has been suggested.^{7,8} Hereditary disposition presumably plays a minor role as familial relationships have been reported in only a few cases, and only between siblings.⁹⁻¹¹ We here describe natural heredity of Ménétrier's disease in three generations.

Address for correspondence: Birgit Larsen, MD, Medical Department, The Silkeborg Hospital, DK - 8600 Silkeborg, Denmark.

Received for publication 9 April 1987.

Case 1

In July 1974, a 49 years old woman entered the hospital because of asthenia, hunger sensation and epigastric pain from which she had suffered since childhood. Physical examination revealed a well nourished woman in a good general condition. Epigastric palpation was painful. Laboratory tests showed normal values of haemoglobin, haematocrit, ESR, alkaline phosphatases, aspartate aminotransferases, serum calcium, serum creatinine and urine analysis, whereas serum total protein (61 g/l) and serum albumin (34.7 g/l) were slightly decreased. Analysis of gastric juice revealed hyposecretion (peak acid output 2.6 meqH⁺/hour). Barium meal revealed markedly enlarged gastric rugae of the fundus ventriculi (Fig. 1). Gastroscopy showed hypertrophic gastric rugae of corpus and fundus. Microscopic examination of the gastric biopsy specimen showed elongated foveolae gastricae and cystic dilatation of the deeper part of some foveolae. The findings were compatible with Ménétrier's disease. The patient's symptoms have since partially disappeared. No re-examination has been carried out. There was no family history of symptoms of gastric disease.

Case 2

In October 1973 at the age of 16, the son of case 1, was admitted to the hospital because of a prolonged, marked asthenia and epigastric pain. Physical examination revealed a pale, poorly nourished youth, appearing acutely and chronically ill. Laboratory analysis showed iron deficiency anaemia (haemo-

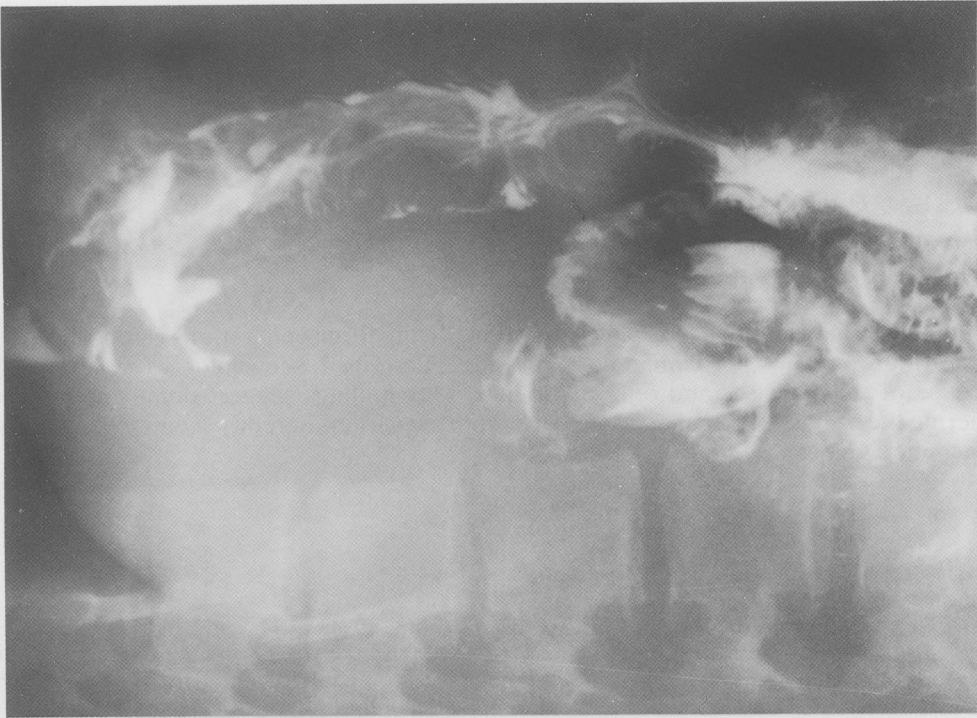


Fig. 2. Barium meal showing large gastric rugae all over the ventricle.

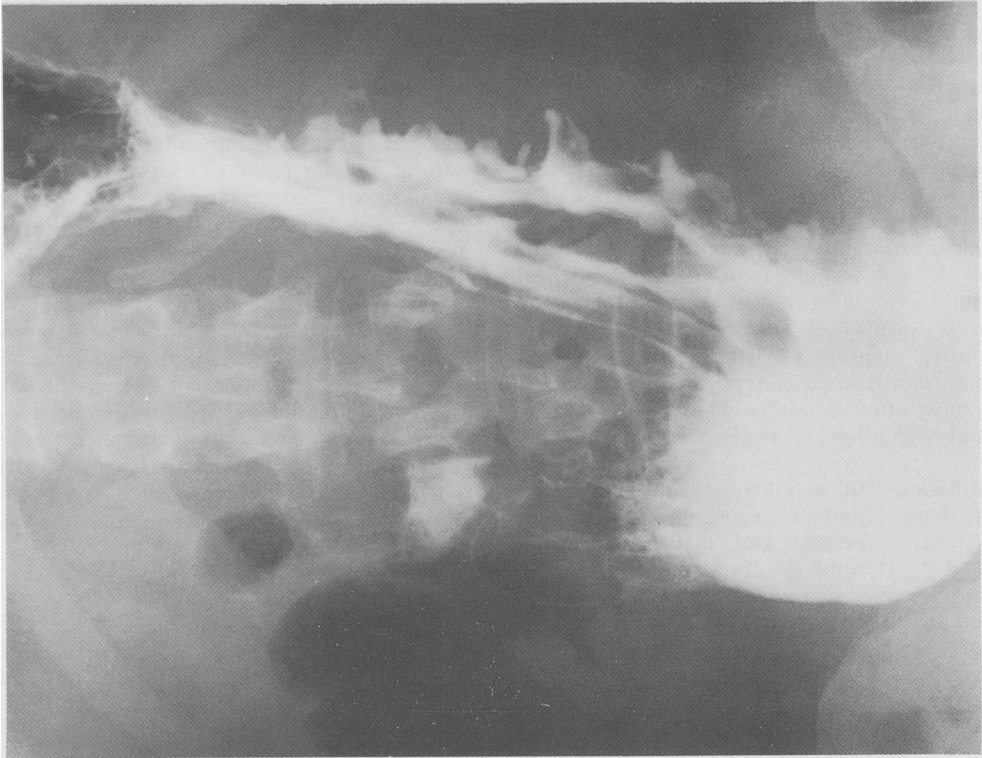


Fig. 1. Barium meal showing large gastric rugae especially in the fundic region.

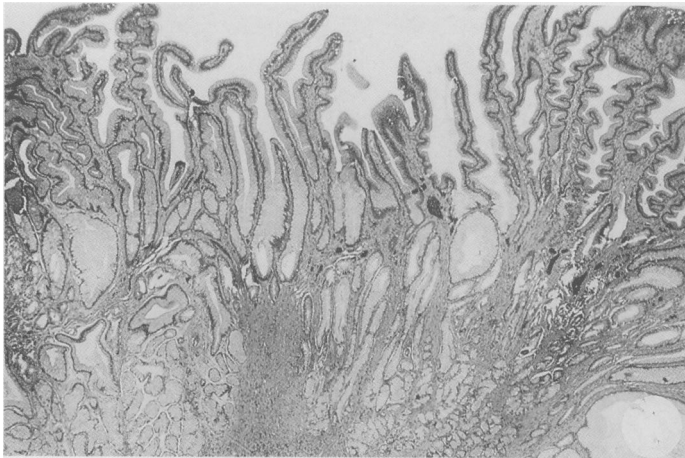


Fig. 3 Case 2. Marked thickening of the gastric mucosa with elongated and tortuous pits and cystic dilatations covered by surface type mucous cells (H+E).



Fig. 4 Case 2. Transition from Ménétrier-type mucosa (left) to adenoma with slight dysplasia (right). (H+E).

globin 6.4 mmol/l, serum iron 2 $\mu\text{mol/l}$, serum transferrin 38 $\mu\text{mol/l}$) and hypoproteinaemia (serum total protein 58 g/l). Other tests showed normal white blood cell count, thrombocyte count, and serum calcium and creatinine concentrations.

Analysis of gastric juice was not done. Barium meal showed enlargement of the gastric rugae (Fig. 2). Gastroscopy revealed marked hypertrophy of the fundus and corpus ventriculi, whereas the changes in antrum were minimal. The mucosa appeared oedematous and very vulnerable. The findings were compatible with Ménétrier's disease. The patient received iron substitution, which balanced the disease until April 1986, when he was readmitted, now 29 years old, presenting severe anaemia and hypoalbuminaemia. Laboratory data showed haemoglobin 1.7 mmol/l, haematocrit 0.12, erythrocytes $1.5 \cdot 10^{12}/\text{l}$, reticulocytes $155 \cdot 10^9/\text{l}$, serum iron 4 $\mu\text{mol/l}$, serum transferrin 65 $\mu\text{mol/l}$, white blood cell count $8.1 \cdot 10^9/\text{l}$, serum albumin 27 g/l and serum gastrin 120 pmol/l. Gastric juice analysis was not done. Bone marrow aspirate showed pronounced myelopoiesis and no other abnormalities.

Gastroscopy revealed significant hypertrophy of the gastric rugae in the corpus ventriculi, most prominent at the great curvature. Besides, a 1 cm polypoid projection in the corpus was removed by endoscopic polypectomy. Microscopic examination of the gastric biopsy specimens showed elongation of the gastric pits with cystic dilatation (Fig. 3). The polyp was a tubulo-villous adenoma with slight atypia (Fig. 4). There were no signs of invasive malignancy. The patient was given blood transfusion and iron substitution. The patient has no siblings, and his father is reported to be healthy.

Case 3

In April 1986 at the age of 5, the eldest daughter of case 2, the grandchild of case 1, was admitted because of severe anaemia. Two months before admission she developed abdominal pain, and at one occasion black stools were observed. Physical examination revealed a pale, but well nourished girl. Height and weight were normal for her age. Epigastric palpation produced slight pain. Laboratory values showed severe anaemia, haemoglobin 4.0 mmol/l, haematocrit 0.23, erythrocytes $3.7 \cdot 10^{12}/\text{l}$, reticulocytes $70 \cdot 10^9/\text{l}$, serum iron 4 $\mu\text{mol/l}$, serum transferrin 124 $\mu\text{mol/l}$, white blood cell count $10.5 \cdot 10^9/\text{l}$. Serum albumin was normal (40 g/l). Bone marrow aspirate showed hyperplastic bone marrow with strong erythropoiesis and signs of iron deficiency. Barium meal revealed marked enlargement of the gastric mucosal folds, especially in the fundic zone compatible with Ménétrier's disease (Fig. 5). Gastroscopy and gastric juice analysis were not done. The findings were compatible with Ménétrier's disease. The patient was given blood transfusions and iron substitution. The patient has a younger sister age 2½ year reported to be healthy as well as their mother.

Discussion

To establish a certain proof for the diagnosis of Ménétrier's disease, full thickness mucosal biopsy is necessary. The biopsies obtained with a conventional biopsy forceps are often inadequate, as the characteristic histological feature of cysts with replacement of the fundic glands are placed in the deep part of the thickened mucosa. However, the endoscopic biop-

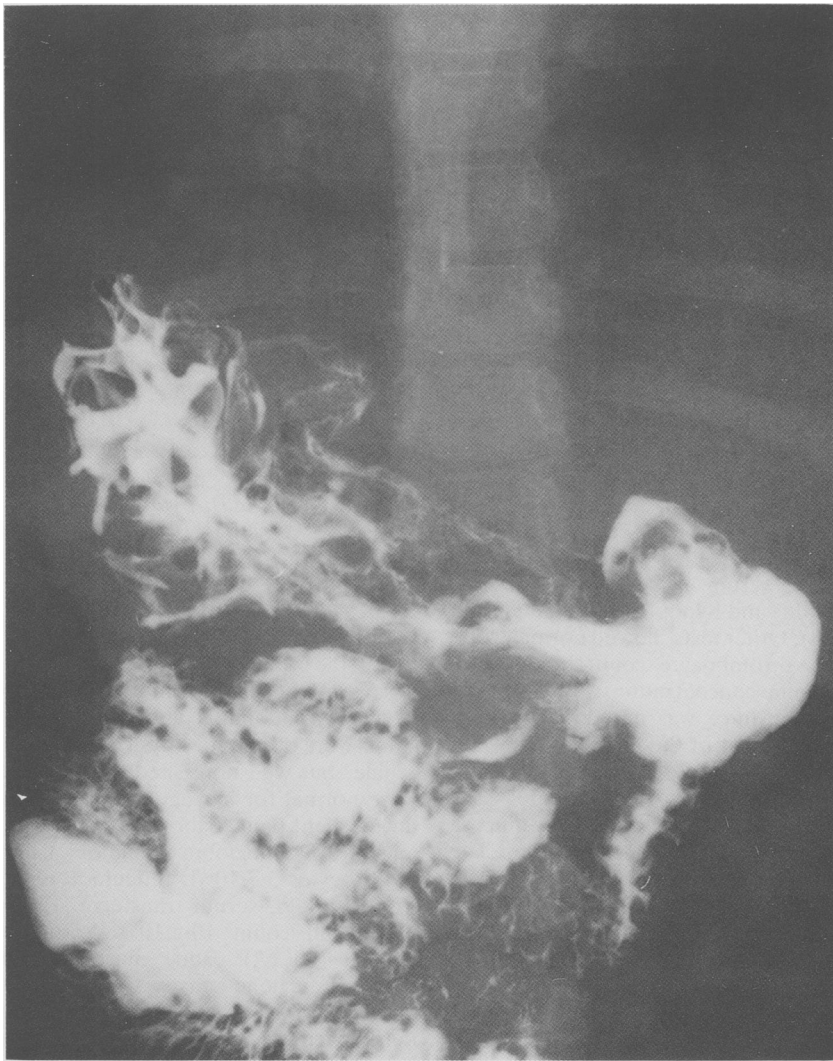


Fig. 5 Case 3. Barium meal showing large gastric rugae especially in the fundic zone (dorsal view).

sies might be suggestive for the diagnosis. Full thickness mucosal biopsies can often be obtained by means of a diathermic snare. This procedure is meanwhile not possible in all hospital units and laparotomy for diagnostic purposes is in most cases not acceptable. Therefore, the diagnosis may be based on radiography, endoscopy and endoscopic biopsies perhaps combined with hypoproteinaemia and hypochlorhydria. This practice has also been adopted in the vast majority of cases published in literature.^{12,12}

Ménétrier's disease has been considered as a precancerous condition.¹³ The finding of a tubulo-

villous adenoma with slight atypia in case 2 is in agreement with this point of view.

Among the earlier published cases of giant hypertrophic gastritis, only three cases of familial occurrence have been described, and all in siblings.⁹⁻¹¹ Catanzaro *et al* reported two cases in a 43 year old man and his 31 year old sister.⁹ Maimon *et al* found that a familial occurrence was pertinent because a sister to a patient with Ménétrier's disease had been operated for benign gastric polyposis 27 years earlier.¹⁰ Lam *et al* reported pachydermoperiostosis, an autosomal dominant syndrome, and Ménétrier's disease in two Chinese brothers aged 27 and 29 years.¹¹

The cases presented here involve three generations, which indicates a dominant pattern of heredity rather than coincidence. The few published reports taken into consideration genetic transmission seems to play only a minor role. Mild symptoms may result in subclinical cases, however, and the frequency of Ménétrier's disease may therefore be underestimated.^{7,13} This possibility further hampers an evaluation of the genetic impact based on the cases in the literature.

Peter K A Jensen, MD, Institute of Human Genetics, University of Aarhus, is acknowledged for valuable discussions, and N O Jacobsen, MD, Institute of Pathology, The Aarhus Kommunehospital for evaluation of the biopsies.

References

- 1 Scharschmidt BF. The natural history of hypertrophic gastropathy (Ménétrier's disease). *Am J Med* 1977; **63**: 644-52.
- 2 Searcy RM, Malagelada J-R. Ménétrier's disease and idiopathic hypertrophic gastropathy. *Ann Intern Med* 1984; **100**: 565-70.
- 3 Citrin Y, Sterling K, Halsted JA. The mechanisms of hypoproteinemia associated with giant hypertrophy of the gastric mucosa. *N Engl J Med* 1957; **257**: 906-12.
- 4 Chokas WV, Connor DH, Innes RC. Giant hypertrophy of the gastric mucosa, hypoproteinemia and edema (Ménétrier's disease). *Am J Med* 1959; **27**: 125-31.
- 5 Tan DTD, Stempien SJ, Dagradi AE. The clinical spectrum of hypertrophic hypersecretory gastropathy. *Gastrointest Endosc* 1971; **18**: 69-73.
- 6 Chouraqui JP, Roy CC, Brochu P, Gregoire H, Morin CL, Weber AM. Ménétrier's disease in children: report of a patient and review of sixteen other cases. *Gastroenterology* 1981; **80**: 1042-7.
- 7 Lesser PB, Falchuk KR, Singer M, Isselbacher KJ. Ménétrier's Disease: report of a case with transient and reversible findings. *Gastroenterology* 1975; **68**: 1598-601.
- 8 Lachman RS, Martin DJ, Vawter GF. Thick gastric folds in childhood. *A J R* 1971; **112**: 83-92.
- 9 Catanzaro C, Weeks CB, Kafka RM. Chronic hypertrophic gastritis: report of two cases in siblings. *Am J Gastroenterol* 1962; **37**: 525-36.
- 10 Maimon SN, Bartlett JP, Humphreys EM, Palmer WL. Giant hypertrophic gastritis. *Gastroenterology* 1947; **8**: 397-428.
- 11 Lam SK, Hui WKK, Ho J, Wong KP, Rotter JI, Samloff IM. Pachydermoperiostosis. Hypertrophic gastropathy and peptic ulcer. *Gastroenterology* 1983; **84**: 834-9.
- 12 Kraut JR, Powell R, Hruby MA, Lloyd-Still JD. Ménétrier's disease in childhood: report of two cases and a review of the literature. *J Pediatr Surg* 1981; **16**: 707-11.
- 13 Morson BC, Sobin LH, Grundmann E, Johansen A, Nagayo T, Serck-Hanssen, A. Precancerous conditions and epithelial dysplasia in the stomach. *J Clin Pathol* 1980; **33**: 711-21.