The diagnosis of Ménétrier's disease

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Summary

Two cases of Ménétrier's disease are reported to illustrate the clinical presentation and diagnosis of this unusual condition. The literature has been reviewed of all the reported cases to establish the relative importance of the individual symptomatology, the value of the diagnostic methods, and to highlight the diagnostic pitfalls. Recognition of the barium meal appearances and snare biopsy at gastroscopy may avoid the necessity of diagnostic laparotomy.

Introduction

Ménétrier's disease is a condition affecting the stomach, in which there is gross hypertrophy of the gastric mucosa, hence its alternative name of giant hypertrophic gastritis. The many different clinical manifestations, of which abdominal pain and vomiting, oedema and anaemia are common, are all secondary to the hypertrophy. It is a rare condition, perhaps one or 2 patients would be seen every 5 years in any hospital. The condition was first described by Ménétrier in 1888 and since then some 200 cases have been reported in the literature. These reports have concerned the pathology (Butz, 1960), the protein turnover (Jarnum and Jensen, 1972; Jones *et al.*, 1972), the gastric protein loss (Citrin, Sterling and Halstead, 1957) and case reports of the various types of presentation, notably acute gastrointestinal (GI) bleeding (Williams, 1956), chronic GI bleeding (Singh, Cumaraswamy and Corrin, 1979), and oedema (Chokas, Connor and Innis, 1959). Diarrhoea has occasionally been reported. What is particularly prominent in the reports is that very frequently diagnosis is only made at laparotomy since, if the condition is not recognized on barium meal, endoscopy with standard biopsy is unlikely to be diagnostic. From the reported series, the majority of patients have been treated by gastrectomy of variable extent, but

reports of regression (Frank and Kern, 1967) and a transient form of the condition (Jarnum and Jensen, 1972) suggest that this is not always necessary. The well established tendency to malignancy (Chusid, Hirsch and Colcher, 1964; Scharschmidt, 1977) would mean, of course, that life-long follow-up is required.

Two patients have been seen in the Gastrointestinal Unit at University College Hospital over the last 4 years. Both were referred as diagnostic problems. The purpose of this report is to present the clinical features of these 2 patients and review those cases reported in the literature with adequate clinical details in order that the relative value of the various clinical and investigative findings may be assessed.

Case reports

Case 1

T.S. a 37-year-old man, 30-month history of nausea and vomiting and vague upper abdominal discomfort. Investigated 6 months after start of symptoms; normal haematology and serum proteins, normal barium meal and upper GI endoscopy. Seen by psychiatrist and given antidepressants, with improvement. Returned again 2 years later: vomiting more frequent and often blood-stained, more pain, weight loss of 6.3 kg. Investigations: Hb 10.6%, total serum proteins 45 g/l, albumin 27 g/l, globulins 18 g/l. Serum gastrin 132 pg/ml (range 25-75 pg/ml). Occult blood positive on 4 occasions. Barium meal (Fig. 1): mucosal hypertrophy. Endoscopic biopsy; superficial gastritis, no evidence of malignancy. A subtotal gastrectomy was performed.

Case 2

S.K. an 18-year-old man, referred for investigation of tiredness and weakness due to iron deficiency anaemia. There was no abdominal pain or nausea.

and no weight loss. Serum proteins at this time normal. Barium meal showed gross thickening of mucosal folds with large polypoidal masses protruding into stomach. Upper GI endoscopy confirmed the polypoidal protrusions into the stomach.

FIG. 1. Frequency of symptoms and signs in Ménétrier's disease.

Multiple gastric biopsies showed superficial gastritis. He was treated symptomatically for 2 years abroad but referred again with persistent symptoms and Hb of 6.8. Serum proteins again normal (total protein 77 g/l, albumin 45 g/l, globulins 32 g/l). A total gastrectomy was performed. Histology of the stomach showed a diffuse polypoid appearance of the mucosa with marked thickening of the mucosa, typical of Ménétrier's disease.

Discussion

The 2 patients reported presented with quite different but previously recognized symptom complexes of Ménétrier's disease. The second patient (S.K.) being diagnosed at the age of 16 years is the youngest yet reported, the age range in the literature being 20–75 years. There is a slight preponderance in the 4th and 5th decades. Both the patients are male and the sex distribution of reported cases shows a male to female ratio of 3.4 : 1. Fieber (1955) reviewed 50 pathologically verified cases up to 1955 and, since then, approximately 160 cases have been added to the literature.

The majority of patients have symptoms for between 6 months and one year, the range being 6 weeks to 6.5 years with one exception having symptoms for 17 years. The rather non-specific and mild nature of the pain in the early stages and the difficulties with diagnostic methods, accounts

for this delay in diagnosis. Figure 1 is a diagrammatic representation of the frequency of symptoms and signs in the studied reports and the 2 patients. One of the 2 patients had been fully investigated 2 years before the diagnosis was made, but the second patient was diagnosed at his initial presentation with iron deficiency anaemia.

The number of different case reports indicates the variety of ways in which Ménétrier's disease may present. The pain is usually epigastric and perhaps most mimics gastric ulceration, exacerbated by eating. It seems to be a discomfort more than a pain in most instances and rarely if ever the sole cause for laparotomy. It was present in 78% of patients. This compares with Fieber's (1955) figure of 74%. Vomiting, although present in only 40% is more troublesome. It occurs after meals and in one of the present patients (T.S.) was associated with fresh bleeding in the later stages. It has been said to be due to prolapsing of the mucosa through the pylorus. In 4 previously reported cases, severe haematemesis was the indication for emergency surgery (Dickinson and Axon, 1979; Singh *et al.*, 1979). Occult bleeding is more common and, in T.S. and S.K., occult bloods were positive on at least 4 occasions. Occult bleeding is recorded in 44% of patients.

Weight loss was present in one of the present cases (T.S.) and in 77% of the reported cases. This is always a symptom of sinister significance in evaluation of patients with upper abdominal symptoms and adds considerable weight to the need for full investigation of perhaps mild symptoms of upper abdominal discomfort.

One of the characteristic features described by Ménétrier is oedema. This is attributed to a protein-losing gastropathy and resultant hypoalbuminaemia, Ménétrier's disease being the first condition in which a protein-losing enteropathy was reported. Using ¹³¹I-labelled albumin in one patient (Citrin *et al.*, 1957), it was shown that there is a large loss of albumin into the stomach in company with all other plasma proteins. This was further studied in 5 patients with Ménétrier's disease without hypoalbuminaemia (Jones *et al.*, 1972). Abnormal albumin metabolism was found in all studied patients and it was suggested that the demonstration of increased fractional catabolic rate may be of assistance in the diagnosis of these patients. Oedema was not present in either of the present 2 cases despite a low albumin (27 g/l) in one (T.S.). Oedema is recorded in 29% of the cases reported with corresponding low albumin value in 60%.

In one of the patients the serum gastrin was slightly elevated at twice the normal. This is noted in 2 other reports (Dickson and Axon, 1979; Overholt and Jeffries, 1970). This is probably no

FIG. 2. Barium meals showing stomachs of cases T.S. (a) and S.K. (b).

more than a reflection of the hypochlorhydria but is of some diagnostic value and may suggest the need for acid secretion studies. It has been established that Ménétrier's disease is associated with a reduction in acid output, although there are 2 reports of a hypersecretory type (Brooks, Isenberg and Goldstein, 1970; Overholt and Jeffries, 1970). In case T.S., a very viscous secretion with low acidity

was produced (1.76 mmol/hr). This would appear to be similar in appearance and content to those reported results. Acid measurement may not be possible owing to the very viscous nature of the secretion.

It is difficult to ascertain from several of the reports at what stage the diagnosis was actually made, and the relative contribution of endoscopic

FIG. 3. Gross appearance of resected stomach of case T.S.

or barium meal. In S.K., the diagnosis was made on gastroscopy and barium meal. In T.S., the endoscopic appearances were of a lymphosarcoma but superficial biopsy showed only the changes of gastritis. The barium meal showed gross mucosal folds, consistent with the endoscopic diagnosis although they are the typical appearance of Ménétrier's disease. The barium meal appearances of the 2 patients are shown in Fig. 2. The follow-through appearance of the small bowel was normal in both patients, but thickening has been reported as extending into the upper small bowel in some patients. The gross appearances of the surgical specimen (T.S.) are shown in Fig. 3 for comparison with the barium meal. If the appearances are not recognized on endoscopy and barium meal, the endoscopic biopsy techniques will simply show superficial gastritis. Scharschmidt (1977) in his review suggested that a full thickness open biopsy is necessary. It may be that endoscopic snare biopsy is sufficient for histological diagnosis, since the folds of mucosa may vary from 1 to 3 cm in depth.

It is difficult to extract information concerning follow-up from the many published reports. Scharschmidt (1977) gave a 16-year follow-up on one patient with ultimate development of adenocarcinoma, and reviewed the follow-up available from reported cases. The majority of patients have required laparotomy for diagnosis and usually partial or total gastrectomy for relief of their symptoms. The gross mucosal thickening may be confined to part of the stomach only in some patients. A total gastrectomy was performed in S.K. after 2 years' observation, and a sub-total gastrectomy was performed in T.S. Follow-up periods of 6 months and 2 years have shown the symptoms thus to have been relieved. The reports of a transient form of the disease in 3 cases (Jarnum and Jensen, 1972) and the spontaneous regression after 5 years in another case (Frank and Kern, 1967) indicate that surgical resection is not inevitable. Quite clearly, however, follow-up must be maintained in the light of well established potential for adenocarcinoma formation (Strode, 1957; Scharschmidt, 1977). Both patients reported are very well after periods of follow-up of 4 years and 18 months.

Conclusion

Ménétrier's disease, although rare, should be considered in all patients with otherwise unexplained symptoms of vague abdominal pain, vomiting and occult gastrointestinal bleeding, especially in the presence of weight loss. The presence of oedema, or panhypoproteinaemia should further suggest the diagnosis. A slightly elevated serum

gastrin concentration with acid secretion studies showing thick viscid aspirates of low acidity is highly suggestive of Ménétrier's disease. If the appearances are recognized on endoscopy or barium meal examination, a histological diagnosis can only be made by full thickness snare biopsy of the mucosa. A superficial biopsy showing normal mucosa or mild superficial gastritis is to be expected and may well be misleading. If the diagnosis is made histologically before laparotomy an initial period of supervised medical management is indicated.

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