Summary: A case of intestinal pseudo-obstruction in a 76-year-old man who presented with a six-year history of intermittent vomiting and abdominal pain and a 1½-year history of diarrhea is described. Investigation demonstrated aperistalsis of the lower esophagus and an unresponsive tonic small intestine. Marked malabsorption was present and appeared due to intestinal bacterial overgrowth consequent to the hypomotility. Autonomic nervous system testing failed to reveal any definite abnormality. Although this disorder is markedly similar to scleroderma involving the gastrointestinal tract, there was only minimal fibrosis of the bowel musculature evident at autopsy and the neural components appeared to be intact. These findings suggest that the basic disorder may be one of smooth muscle dysfunction. Other known causes of pseudo-obstruction could not be demonstrated.

Résumé: L’auteur présente un cas de pseudo-obstruction intestinale chez un homme de 76 ans qui souffrait depuis six ans de vomissements et de douleurs abdominales intermittents, et depuis 1½ ans, d’épisodes de diarrhée. L’examen permet de mettre en évidence l’absence de périaltalisme de l’œsophage inférieur et un grêle atonic qui ne réagissait pas. Une forte malabsorption coexistait et était probablement causée par une prolifération bactérienne dans l’intestin, secondaire à l’hypomotilité. L’examen du système nerveux autonome n’a pu mettre en lumière aucune anomalie précise. Bien que la présente pathologie semble très voisine de la sclérodermie affectant le tube digestif, l’autopsie n’a révélé qu’une fibrose minimale des muscles lisses de l’intestin et un aspect intact des cellules nerveuses. Ces diverses constatations permettent de conclure que cette pathologie fondamentale peut relever d’un dysfonctionnement de la musculature lisse. Aucune autre cause de pseudo-obstruction n’a pu être mise en évidence.

Chronic idiopathic intestinal pseudo-obstruction with malabsorption, a scleroderma-like disorder

Bryan E. Lukie, M.D., M.S.C., F.R.C.P.[C] and Michael G. Sanders, M.D., F.R.C.P.[C], Toronto

Idiopathic intestinal pseudo-obstruction represents a clinical entity characterized by recurring episodes of intestinal obstruction without evidence of mechanical occlusion or primary disease known to cause intestinal hypomotility. Known causes of pseudo-obstruction must be carefully excluded before this diagnosis can be accepted. It is often associated with steatorrhea; probably the first case to be reported (by Ingelfinger in 1943) was one described as “sprue” associated with recurrent clinical obstruction but in which no mechanical cause could be detected.

The present communication describes a case of chronic idiopathic intestinal pseudo-obstruction associated with malabsorption, and serves to illustrate the investigation necessary to establish this diagnosis. In addition, results of autonomic nervous system function testing not previously described in this disorder are presented.

Case report

J. R., a 76-year-old man, was first admitted to The Toronto Western Hospital on August 27, 1971. Because he proved to be an inaccurate historian much of the history was compiled from previous hospital records.

He had been well until 1966 when intermittent diarrhea began, together with episodes of postprandial abdominal pain accompanied by emesis of dark brown fluid. Because of these symptoms and some weight loss he was hospitalized in April 1969. A diagnosis of subacute intestinal obstruction of small bowel was made and at laparotomy a volvulus of the ileum without obvious mechanical cause was reduced.

He was well until May 1970 when intermittent diarrhea recurred and became constant by July 1970. He lost 5.5 kg. in weight, developed rectal prolapse and was admitted to hospital on September 18, 1970. Barium studies revealed abnormal dilatation of both the large and small bowel without evidence of mechanical obstruction. Levels of serum calcium, phosphorus, proteins, carotene and 72-hour fecal fat excretion were normal, and on examination the small bowel biopsy was normal. The rectal prolapse was treated by insertion of a Thiersch wire ring. Postoperatively, constipation alternated with periods of diarrhea. Two episodes of abdominal pain accompanied by intestinal dilatation occurred and responded well to nasogastric suction and intravenous fluids. A cystometrogram, performed because of urinary incontinence, revealed an atomic bladder. He was discharged on February 3, 1971.

On April 13, 1971 recurrence of abdominal pain and intestinal dilatation necessitated readmission to hospital. He again responded well to decompression.

On August 27, 1971 he was admitted to hospital because of severe periumbilical pain and vomiting. A questionable history of Raynaud’s phenomenon was obtained. Examination revealed an ischemic ulcer on the index finger of the right hand (Fig. 1). No other cutaneous abnormalities were present. The abdomen was distended and tympanitic. There were no bowel sounds or signs of peritoneal irritation. Abdominal films (Figs. 2 and 3) demonstrated marked distension of both large and small bowel. Serum electrolytes and amylase levels were normal and he improved rapidly following nasogastric suc-

FIG. 1—Ischemic ulcer of a digit involved by Raynaud’s phenomenon.

FIG. 2—KUB showing dilated small and large bowel (August 27, 1971).
tion and administration of intravenous fluids. A barium enema failed to demonstrate colonic obstruction and he was discharged on September 17, 1971.

He was readmitted five days later because of a recurrence of symptoms. In addition to the history outlined above, he complained of chronic diarrhea with the daily passage of up to 12 frothy, foul, greasy stools. His periumbilical pain was described as crampy, occurred immediately after meals, lasted two to three hours and was relieved somewhat by walking. When it was severe, only gastric decompression provided relief. There was no family history of a similar disorder. Physical examination revealed a distended, tympanic abdomen with hyperactive bowel sounds. Abdominal films (Figs. 4 and 5) again revealed distension of large and small bowel without free air. Levels of serum amylase and electrolytes were within normal limits and treatment as before resulted in satisfactory improvement. Results of pertinent laboratory studies are shown in Table I. A superior mesenteric arteriogram failed to demonstrate any evidence of vascular abnormality. Barium meal revealed a normal esophagus, stomach and duodenum accompanied by marked dilatation and hypomotility of the small intestine without evidence of localized obstruction.

Esophageal motility studies were performed by means of a three-lumen polyvinyl tube assembly continuously perfused with water. The mean between inspiratory and expiratory deflections was taken as the pressure reading. A sample tracing (Fig. 6) is shown. The lower esophageal sphincter had a normal pressure and relaxed normally. However, peristalsis was absent below the upper 5 cm. of esophagus. An intestinal motility study was performed following passage of a Miller-Abbott tube into the upper jejunum. The balloon was connected to a kymograph and pressures recorded for 2½ hours. During the 30-minute baseline tracing, marked hypomotility was evident with only very occasional weak spontaneous contractions occurring at 3- to 5-minute intervals. Attempts to stimulate motor activity by the intraluminal instillation of 100 ml. of tap water, 30 ml. 0.1 N HCl and 20 mg. acetylcholine were all without effect. Bethanechol, 2.5 mg. subcutaneously, produced flushing and the urge to urinate but did not alter motility.

Testing of the autonomic nervous system was performed. Locally applied 2% homatropine, cocaine or 2.5% methacholine chloride failed to alter pupil size appreciably. Intravenous administration of 1 mg. of atropine resulted in pupillary dilatation, an increase in pulse rate from 66 to 98/min. and an increase in peak expiratory flow rate from 200 to 260 l/min. Methacholine chloride, 15 mg. subcutaneously, resulted in slight sweating.

Table I—Laboratory investigations

<table>
<thead>
<tr>
<th>Estimation</th>
<th>Patient's results</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>11.6—14.1 g./100 ml.</td>
<td>16.0 ± 2.0 g./100 ml.</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td>8400—10,000/mm.³</td>
<td>5000—10,000/mm.³</td>
</tr>
<tr>
<td>Blood smear</td>
<td>few hypochromic cells</td>
<td>normal</td>
</tr>
<tr>
<td>Serum iron</td>
<td>52 μg./100 ml.</td>
<td>90-200 μg./100 ml.</td>
</tr>
<tr>
<td>Latent iron-binding capacity</td>
<td>143 μg./100 ml.</td>
<td>150-250 μg./100 ml.</td>
</tr>
<tr>
<td>Total iron-binding capacity</td>
<td>195 μg./100 ml.</td>
<td>250-400 μg./100 ml.</td>
</tr>
<tr>
<td>Iron saturation</td>
<td>27%</td>
<td>24-49%</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>12 secs.</td>
<td>11 secs.</td>
</tr>
<tr>
<td>Serum carotene</td>
<td>32.5 μg.</td>
<td>50-200 μg.</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>95 mg./100 ml.</td>
<td>140-260 mg./100 ml.</td>
</tr>
<tr>
<td>Serum folates</td>
<td>7.0 ng./ml.</td>
<td>5-25 ng./ml.</td>
</tr>
<tr>
<td>Serum B₁₂</td>
<td>230 pg./ml.</td>
<td>160-800 pg./ml.</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>7.8 mg./100 ml.</td>
<td>8.9-10.3 mg./100 ml.</td>
</tr>
<tr>
<td>Serum phosphorus</td>
<td>1.5 mg./100 ml.</td>
<td>2.8-4.5 mg./100 ml.</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>6.5 KA units</td>
<td>4-13 KA units</td>
</tr>
<tr>
<td>Fasting blood sugar</td>
<td>75 mg./100 ml.</td>
<td>65-100 ng./100 ml.</td>
</tr>
<tr>
<td>2-hour p.c. blood sugar</td>
<td>83 mg./100 ml.</td>
<td>&lt;110 mg./100 ml.</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>88 ml./min.</td>
<td>90-130 ml./min.</td>
</tr>
<tr>
<td>Serum thyroxine</td>
<td>8.6 μg./100 ml.</td>
<td>5.4-14.0 μg./100 ml.</td>
</tr>
<tr>
<td>T₃ resin uptake</td>
<td>34%</td>
<td>24-34%</td>
</tr>
<tr>
<td>Xylose tolerance test (x3)</td>
<td>0.74, 0.1, 3.3 g.</td>
<td>5-8 g.</td>
</tr>
<tr>
<td>Stool fat</td>
<td>7.1-38.5 g./day</td>
<td>&lt;5 g./day</td>
</tr>
<tr>
<td>Schilling test (x2)</td>
<td>0.3, 6.9%</td>
<td>&gt;11%</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>2.67 g./100 ml.</td>
<td>3.9-5.1 g./100 ml.</td>
</tr>
<tr>
<td>ɑ₁ globulin</td>
<td>0.25 g./100 ml.</td>
<td>0.10-0.30 g./100 ml.</td>
</tr>
<tr>
<td>ɑ₂ globulin</td>
<td>0.63 g./100 ml.</td>
<td>0.42-0.84 g./100 ml.</td>
</tr>
<tr>
<td>β globulin</td>
<td>0.89 g./100 ml.</td>
<td>0.66-1.17 g./100 ml.</td>
</tr>
<tr>
<td>γ globulin</td>
<td>1.06 g./100 ml.</td>
<td>0.56-1.24 g./100 ml.</td>
</tr>
</tbody>
</table>

FIG. 3—Lateral film showing distended large and small bowel elevating the diaphragm; there is no intraperitoneal air (August 27, 1971).

FIG. 4—Dramatic distension of entire bowel similar to that observed previously (September 22, 1971).

FIG. 5—Lateral abdominal film showing more marked bowel dilatation than seen previously (September 22, 1971).
The Valsalva maneuver increased blood pressure from 90/60 to 105/65. A cold pressor test raised the blood pressure from 90/60 to 105/75 after 10 seconds' immersion of an arm with return to pre-immersion level in 30 seconds.

Biopsy of the second part of the duodenum failed to reveal any evidence of the changes characteristic of scleroderma, while jejunal biopsy revealed normal villus architecture without evidence of amyloid. A rectal biopsy was normal. Pulmonary function studies demonstrated a moderate obstructive ventilatory defect consistent with a long history of cigarette smoking. Transfer factor for carbon monoxide was normal. A culture of duodenal contents produced a mixed growth of Klebsiella aerogenes and Escherichia coli with over 100,000 colonies/ml.

Treatment with tetracycline (1.0 g./day) for 10 days did not result in any clinical improvement. However, a repeat duodenal culture produced a growth of Candida albicans, Diphtheroid species and E. coli with a colony count of 60,000/ml. He was discharged on December 28, 1971.

He was readmitted on January 11, 1972 because of abdominal distension, edema of the lower extremities, and a weight loss of 6.9 kg, since discharge. Radiologic evidence of large and small bowel distension was present as before. Gastric decompression improved the abdominal distension only temporarily. His condition progressively deteriorated and he died on January 30, 1972.

At autopsy, a careful search failed to reveal any mechanical cause of bowel obstruction. The only areas in the gut that appeared abnormal were the esophagus (Fig. 7) and ileum, both of which demonstrated mural thickening due to small amounts of suberosal fibrosis and muscular hypertrophy. Ganglion cells were present in normal numbers. Special stains and electron microscopy failed to reveal amyloid or any other significant abnormality. Incidental findings were atrophy of the liver and spleen, which weighed 990 and 45 g. respectively. There was nonspecific fibrosis of the myocardium and pericardium. The skin was normal.

Discussion

The patient with intestinal pseudo-obstruction presents the clinician with a difficult diagnostic and therapeutic challenge, many aspects of which are illustrated by this case. The exclusion of mechanical obstruction is the initial and most pressing problem since laparotomy with its resultant ileus will be detrimental to the patient already suffering from intestinal hypomotility. The presence of high-pitched "tinkling" bowel sounds does not exclude a diagnosis of pseudo-obstruction as illustrated above. The presence of gas throughout small and large bowel in the presence of intestinal dilatation is helpful in suggesting the absence of a complete mechanical obstruction.9

With these findings and in the absence of signs of peritoneal irritation, laparotomy may be safely postponed and a barium enema performed to exclude mechanical obstruction of the colon. If the results are negative, a carefully observed barium small bowel follow-through may be safely performed9 to observe motility and exclude a partial small bowel obstruction. However, this must be carefully performed and follow-up films taken several hours after the barium has reached a point of apparent obstruction, since it will eventually pass beyond this point if hypomotility is the basic disorder, as in the present case.

Concomitant investigation should be undertaken to exclude known causes of acute ileus. Treatment is aimed at decompression of the bowel and parenteral correction of fluid, electrolyte and nutritional deficiencies. Complete decompression of the bowel may be difficult to attain because of the slow distal clearing of bowel contents due to hypomotility. However, once the patient is clinically improved the presence of intestinal hypomotility should be documented by proper manometric studies if available.

Following documentation of chronic intestinal hypomotility, the clinician's next task is to exclude known causes of this disorder and determine whether or not malabsorption is present. Scleroderma with intestinal involvement has been implicated as a cause of pseudo-obstruction since the first case report in 1931.8 Subsequent experience4-14 has amply verified this association. Small bowel involvement occurs in approximately 5% of cases16 and may occur in the absence of Raynaud's phenomenon or the characteristic skin changes of this disease.16 Peroral duodenal biopsy is helpful in establishing this diagnosis if the characteristic increase in collagen deposits with muscle fragmentation is seen,1,6 but absence of this finding does not exclude the diagnosis. In the present case, postmortem examination revealed only minor deposits of collagen in the musculature which were not of the degree evident in previously reported cases of pseudo-obstruction associated with scleroderma.4-16

The aperistalsis of the lower two-thirds of the esophagus seen in our

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FIG. 6—Esophageal motility tracing. SW = dry swallow, WSW = wet swallow. C = cough. Abscissa scale (mm. Hg) reflects intraluminal pressure in esophagus. Numbers across top on ordinate scale indicate distance (cm.) from nares to most proximal recording opening. Note the absence of peristalsis below proximal third of esophagus.

FIG. 7—Gross specimen showing thickened wall of lower esophagus. The overlying esophageal and gastric mucosa are somewhat hemorrhagic, an unexplained finding.
patient (Fig. 6) is a characteristic finding in scleroderma. It is not pathognomonic, however: recent reports have described a similar disorder in patients with pseudo-obstruction without the histopathologic characteristic of scleroderma.

The resting motor activity of the small intestine in the present case was markedly reduced and failed to respond to stimuli which normally produce frequent and powerful contractions, indicating a profound functional disturbance without morphologic counterpart. In order to implicate scleroderma as the cause of this disorder we would have to postulate a broad spectrum of disease in which pathologic criteria are few but clinical manifestations florid and vice versa. Clearly, if the above case represents the manifestations of gastrointestinal scleroderma, a major abnormality of bowel motility has resulted from minimal evidence of muscle hypertrophy and mural fibrosis.

Partial autonomic nervous system testing in the present case failed to discover any definite evidence of dysfunction. The failure of acetylcholine and betahistine to stimulate the atomic small bowel musculature, along with the postmortem finding of plentiful ganglion cells in the esophagus and jejunum, suggest that the primary disorder may very well reside in the bowel musculature itself rather than in the nervous system.

Of the other infiltrative disorders, amyloidosis of the bowel has been implicated in the etiology of intestinal pseudo-obstruction since 1933. Recently, Legge, Wollaeger and Carlson described eight cases of pseudo-obstruction occurring in this disorder and reviewed the existing literature. As in scleroderma, the clinical presentation of pseudo-obstruction appears to result from intestinal hypomotility produced by the infiltration of the bowel musculature. Intestinal amyloidosis was excluded in the present case by the absence of amyloid material in the small intestinal and rectal biopsies.

Gluten-sensitive enteropathy has been implicated as a cause of pseudo-obstruction since the report by Ingelfinger in 1943. Unfortunately, documentation of small bowel morphology was not provided in his report or in the report of McClelland, Lewis and Naish, which was said to support this association. Fone et al and Badenoch in large series of cases of gluten-sensitive enteropathy refer to an occasional case in which laparotomy has been performed because of a clinical presentation of intestinal obstruction, with negative findings. Unfortunately, these cases require additional documentation to support the occurrence of pseudo-obstruction in this disease. Although intestinal hypomotility does occur in active gluten-sensitive enteropathy, whether it is of sufficient degree to cause clinical pseudo-obstruction is undetermined. The presence of normal villus architecture in all peroral intestinal biopsies performed on our patient eliminated this diagnostic consideration.

Recently, Gleeson et al described a single case of malabsorption with intestinal dilatation and hypomotility due to a glucagon-secreting tumour of the kidney and cured by its removal. Other causes of intestinal pseudo-obstruction include myxedema, hypoparathyroidism and malignant infiltration of the celiac ganglion. These considerations were all eliminated by the investigation of the present case and confirmed by the findings at autopsy.

The failure to determine a cause for the chronic intestinal hypomotility exhibited by our patient indicates that at present he must be classified as a case of chronic idiopathic intestinal pseudo-obstruction. Such a classification, of course, merely reflects our ignorance of the cause of this disorder, which may in fact represent several diseases.

The characteristics of chronic idiopathic pseudo-obstruction have been recently described by Maldonado et al. The clinical presentation varies and includes combinations of diarrhea, steatorrhea, gross distension of small and sometimes large bowel, weight loss, abnormal sweating responses, lower esophageal hypomotility, hypothermia, failure of bowel motility to respond to cholinergics and sometimes a family history of a similar disorder. The case presented above exhibited many of these features.

Malabsorption in pseudo-obstruction was first described by Naish, Capper and Brown although the earlier report of Ingelfinger likely represents an example of this disorder. Subsequent experience has documented this association and implicated bacterial overgrowth within the bowel lumen resulting from the hypomotility in its production. The presence of steatorrhea, vitamin B12 malabsorption and the presence of large numbers of fecal organisms in the small-intestinal aspirate indicated that this was probably the mechanism of malabsorption in the above case. The occurrence of an abnormally low xylose excretion may occur in instances of small-intestinal bacterial overgrowth and therefore does not necessarily indicate the presence of mucosal disease. Malabsorption and abdominal distension in pseudo-obstruction may improve dramatically following antibiotic administration, but this did not occur in the present case.

The authors acknowledge the assistance of many of the attending and house staff members of The Toronto Western Hospital in the management and investigation of this case. We are also indebted to Drs. N. E. Diamant and C. L. Green for performing the esophageal and intestinal motility studies.

References
23. FINK S: The intraluminal pressures in the human intestine. Am J Physiol 56: 661, 1925