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CASE REPORTS

Bezoar: An Unusual Cause of Protein-Losing Gastroenteropathy

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PATIENTS with gastric bezoars usually present with anorexia, a sense of oppression in the epigastrium, weakness, loss of weight and, less commonly, vomiting and hematemesis. On physical examination pallor, wasting, foul breath and an abdominal mass are often present. Complications such as gastric ulceration, perforation, peritonitis and intestinal obstruction have been reported,[1-3] but edema has rarely been described. In 1921 Davies[4] reported the case of a 34-year-old woman with a massive hair-ball in her stomach who gave a history of swelling of the limbs for six months. No cardiac or renal disease was found to account for edema. The bezoar was removed but the patient collapsed and died an hour after operation. More recently Wine[5] described a 15-year-old girl with a trichobezoar who had had edema of her legs for three months. The total plasma protein was 6.9 g. % but the albumin level was only 2.6 g. %. The bezoar was removed, the girl made a speedy recovery with rapid disappearance of the edema, and 10 days after operation the albumin had increased to 4.0 g. %. Wine regarded the edema as "nutritional" in origin.

Two cases of large gastric bezoars associated with edema are reported in which investigation showed that the edema was due to a diminution in plasma albumin and that this was associated with the loss of albumin into the alimentary tract.

METHODS

Protein loss into the gastrointestinal tract was measured with I^{131}-labelled human serum albumin (RISA, Abbott Laboratories, Montreal) and with I^{125}-labelled polyvinylpyrrolidone (PVP, Radiochemical Centre, Amersham, Bucks, England). Thirty microcuries (μc.) was injected intravenously and individual stool specimens were collected in disposable diapers. These were placed in plastic containers and the radioactivity in them was measured with a large well-type scintillation counter.[6] In certain studies where both I^{125} activity and I^{131} activity were present in a stool specimen the activity of each isotope was determined by counting the samples at intervals until the I^{131} activity had decreased to minimal levels.[7] Lugol's iodine, 10 drops by mouth every two hours, was given throughout the period of study. An estimate of the amount of albumin lost into the gastrointestinal tract was made from the total radioactivity excreted in the feces in the first five days after injection of the labelled compound and the results were expressed as a percentage of the injected dose of radioactivity. Measurements were also made of the disappearance of radioactivity from the plasma after the injection of labelled albumin. The results were expressed as a percentage of the mean radioactivity in the plasma 20 and 30 minutes after injection.

CASE REPORTS

The two patients were long-term residents of a hospital school for the mentally retarded and they both performed at the idiot level. They were largely bedridden and both were known to eat all manner of material such as bedding, mattress stuffing, clothing, surgical dressings, soap, string and so on.

CASE 1.—C.W., a male aged 27 years, was admitted to the hospital school at Smiths Falls, Ontario, at the age of 6 years. He was reported to have had the unpleasant habit of smearing feces on himself and other people. At the age of 19 years it was noted that he would eat almost anything he could lay his hands upon. One month prior to admission to the Kingston General Hospital he suffered an episode of vomiting and marked abdominal distension which was managed conservatively by gastric suction and intravenous fluids. At this time edema of the limbs and scrotum was noted and he was given digitalis and mercaptomerin (Thiomerin). Several hemoglobin estimations ranged from 11.9 to 13.3 g. % and the urinalysis was normal. On admission to the Kingston General Hospital one month later, the most striking clinical features were gross mental retardation, marked abdominal distension due to ascites and a hard mass occupying most of the upper abdomen, and extensive pitting edema of the legs and genitalia.

The results of investigation were as follows: hemoglobin 8.5 g./100 ml., hematocrit 26%, white blood cell count 9700/c.mm. with a normal differential count, erythrocyte sedimentation rate 18 mm. in one hour. The specific gravity of the urine was 1.016 and albumin was absent. The plasma urea nitrogen value was 20 mg. %. Total serum protein was 3.4 g./100 ml. and the electrophoretic strip showed albumin 42%, α_1-globulin 9.2%, α_2-globulin 13.9%, β-globulin 17% and γ-

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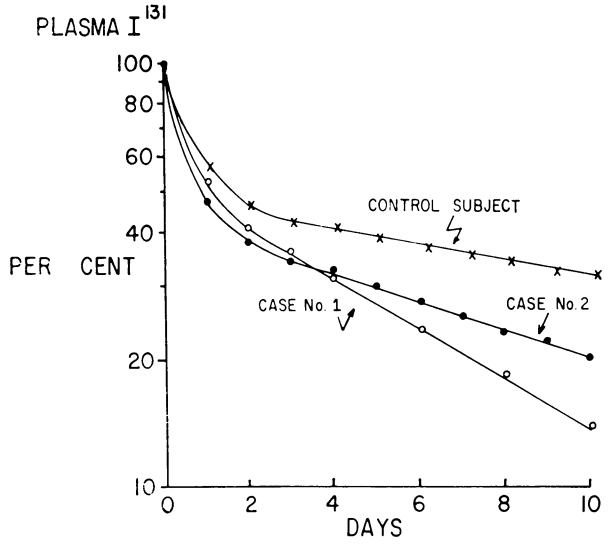

Fig. 1.—Plasma disappearance curves of I^{131}-labelled human serum albumin.

globulin 17.9%. Liver function tests were as follows: serum bilirubin 0.3 mg./100 ml., alkaline phosphatase 1.6 Bodansky units, thymol turbidity 10.2 units, prothrombin time 14 seconds (normal), bromsulphalein retention 1% in 60 minutes. The serum sodium was 135 mEq./l. and the serum potassium 3.2 mEq./l. Stool specimens contained 3+ and 4+ occult blood. A barium meal x-ray examination demonstrated a large bezoar in the stomach.

Investigation of albumin metabolism with I^{131}-labelled albumin was made prior to operation. The plasma disappearance curve of I^{131} albumin showed an accelerated rate of clearance of radioactivity from the plasma (Fig. 1). Measurement of the radioactivity in the feces was unsuccessful because of failure of the patient to co-operate.

After this study was completed, the patient was given 1600 ml. of blood and three weeks later 1200 ml. was given just before laparotomy. At operation a large bezoar consisting of cloth, rags, mucus and altered blood was removed from the stomach. The gastric mucosa was thickened; the rugae were large and prominent and in places their irregularity produced a nodular appearance (Fig. 2). No ulceration was apparent. Microscopic examination of the gastric mucosa showed hyperplasia of the surface epithelium which resulted in elongation and tortuosity of the foveolar pits, and in some areas there was infolding of the mucosa, giving a polypoid appearance. The parietal cells were normal in appearance, but in some areas cystic dilatation of the glands with replacement of the functioning elements by mucin-secreting cells was present. The lamina propria was infiltrated with a few chronic inflammatory cells and dilated capillaries were noted at the tips of the villi. The muscularis mucosae was hypertrophied. Biopsies of the jejunum and liver were normal.

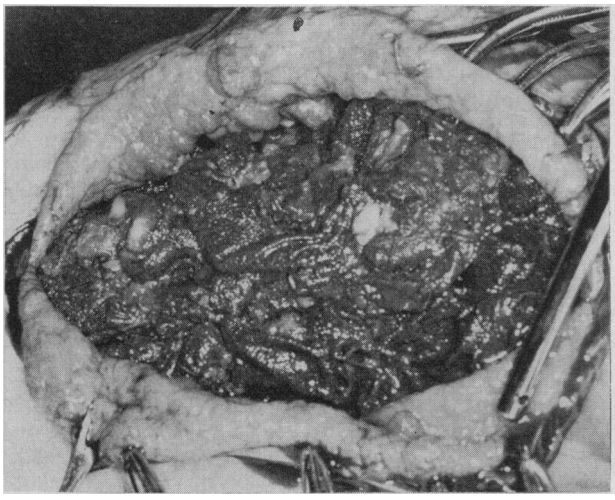

Fig. 2.—Appearance of thickened gastric mucosa in Case 1 at the time of laparotomy. The rugae are large and prominent, and in places they have a nodular appearance. The bezoar is seen lying in the markedly enlarged stomach.

Two weeks after operation the hemoglobin was 12.7 g./100 ml., the total serum protein was 4.0 g./100 ml., albumin 2.4 g./100 ml., and globulin 1.6 g./100 ml. The overnight gastric secretion of hydrochloric acid was 33 mEq. The patient returned to the hospital school, where he died eight days later from what appeared to be intestinal obstruction. No autopsy was performed.

CASE 2.—J.R., aged 21 years, had been mentally retarded since very early life, owing possibly to a severe attack of whooping cough suffered in the neonatal period. He was admitted to the hospital school at the age of 7 years. A year later it was noted that he ruminated excessively and at the age of 12 years he began to tear up his bedsheets and chew them. Indiscriminate eating of all available materials continued thereafter. At the age of 21 years he was found to have extensive widespread pitting edema of the face, chest wall, sacrum and legs together with pallor, abdominal distension and a hard mass in the right upper quadrant of the abdomen. The heart size and heart sounds were normal, and no abnormality was found on urinalysis. The hemoglobin was 5 g./100 ml., total serum protein 2.9 g./100 ml. with albumin 1.2 g./100 ml. and globulin 0.72 g./100 ml. A barium meal examination showed a large gastric bezoar (Fig. 3). The patient was transfused with 800 ml. of blood, given a high protein diet and a week later transferred to the Kingston General Hospital. On examination he appeared pale and emaciated and he was extremely retarded mentally and bedridden. He weighed only 70 lb. There was gross pitting edema over the lower limbs and trunk, marked abdominal distension was present and a hard mass was palpable in the epigastrium.

The results of investigations showed a hemoglobin value of 6.3 g./100 ml., hematocrit 24%, red blood cell count 2,360,000/c.mm., white blood cell count 5200/c.mm. with a normal differential count, platelets 429,000/c.mm. and reticulocytes 7.6%. The bone marrow aspiration revealed erythroid hyperplasia and there was an absence of stainable iron. The specific gravity of the urine was 1.026; a 24-hour sample contained 120 mg. albumin. The plasma urea nitrogen was 26 mg./100 ml. The total plasma protein was 3.6 g./100 ml. and on electrophoresis the serum albumin was 25%, α_1-globulin 8.8%, α_2-globulin 23%, β-globulin 18.2%, and γ-globulin 25%. Liver function tests were normal, serum bilirubin 0.1 mg./100 ml., alkaline phosphatase 5.5 Bodansky units, bromsulphalein retention at 60 minutes 0.4%. The stool repeatedly contained either 2+ or 3+ occult blood.

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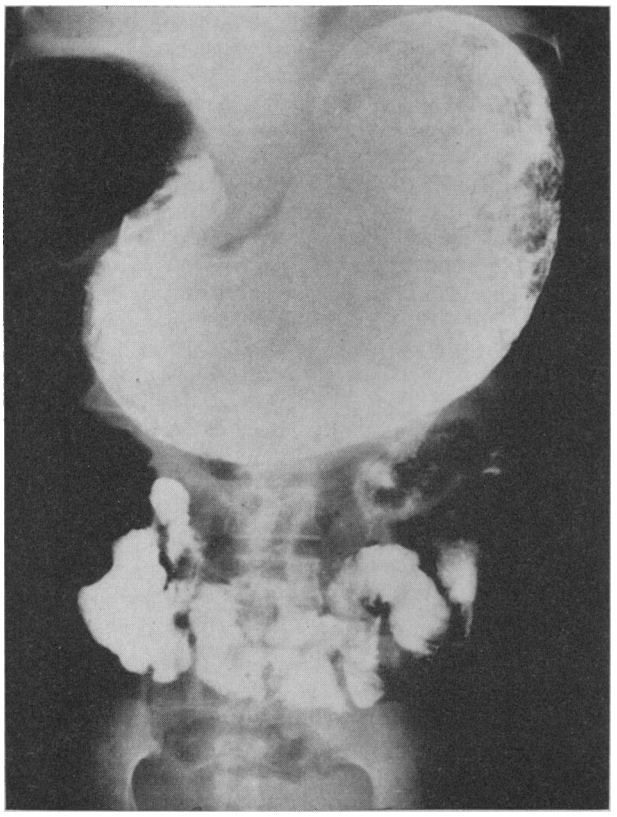

Fig. 3.—Barium meal in Case 2, showing marked enlargement of the stomach due to a bezoar.

The results of studies with labelled albumin, shown in Fig. 1 and Table I, demonstrate that tagged albumin disappeared rapidly from the plasma and excessive amounts of radioactivity were excreted in the stool. The result was confirmed with I^{125}-PVP which, after intravenous administration, also appeared in the feces in excessive amounts (Table I).

TABLE I.—FECAL EXCRETION OF RADIOACTIVITY IN CASE 2

	Case 2		*Normal subjects*[8]	
	I^{125}-PVP	*I^{131}-albumin*	*I^{125}-PVP*	*I^{131}-albumin*
Before operation	2.4	4.1	0–1	0–0.40
After operation	0.01	0.33	—	—

The patient was treated with a high protein diet containing 3 g. of protein/kg. body weight/day and this was gradually increased in stepwise fashion to 6 g. of protein/kg. body weight/day (Fig. 4). The iron deficiency was treated with parenteral iron. After two weeks of the high protein diet a marked diuresis occurred with the loss of 15 lb. in weight (Fig. 4). Concomitant with the diuresis the plasma albumin rose from 1 g./100 ml. to 2 g./100 ml., where it remained until operation. A reticulocytosis followed the administration of iron and the hemoglobin rose to 9 g./100 ml., where it remained until operation.

Laparotomy was performed, and a bezoar about the size of a football consisting of electrician's tape, rope, rubber and fibre-like material was removed from the stomach. The muscle layers of the stomach were thickened and the gastric rugae were enlarged. No

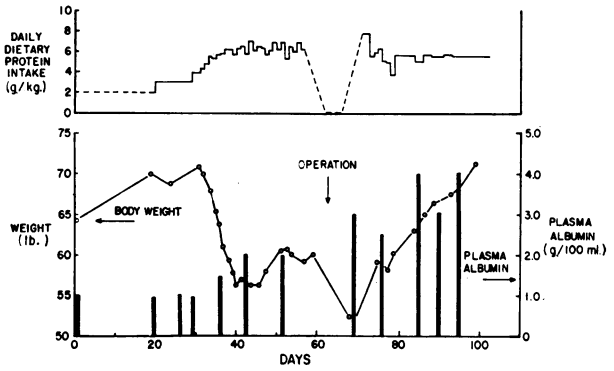

Fig. 4.—Clinical course of Case 2.

ulceration was present. Biopsies taken from the liver and jejunum showed no histological abnormality. Biopsy of the stomach was inadvertently misplaced. Postoperatively, he continued to take 6 g. of protein/kg. body weight/day and his weight increased from 52 lb. to 72 lb. over a period of 35 days. The serum albumin level rose from 2.0 g./100 ml. to 3.6 g./100 ml. Occult bleeding from the gastrointestinal tract continued three weeks after operation, and the hemoglobin level remained between 9.0 and 11.0 g./100 ml. during this period.

Measurements of plasma protein loss into the gastrointestinal tract with I^{131}-labelled human serum albumin and I^{125}-PVP made three and four weeks, respectively, after operation revealed normal values (Table I). The patient was returned to the hospital school in good physical health but with no alteration in his strange eating habits.

DISCUSSION

The results of investigation in the second patient (Case 2) provide convincing evidence of excessive loss of albumin into the gastrointestinal tract (Table I). Although direct evidence for this was not obtained in the first patient (Case 1), owing to our inability to obtain stool collections, the similarity of the clinical features, plasma albumin disappearance curve (Fig. 1) and operative findings in the two patients suggests that protein-losing gastroenteropathy was present in this patient. The gastrointestinal protein loss cannot be explained solely on the basis of bleeding from the gastric mucosa, because there was insufficient blood loss to account for the marked loss of albumin.

The finding of a marked increase in radioactivity in the feces in Case 2 (Table I) suggests that the albumin which was lost into the stomach was not completely reabsorbed. Ordinarily, in patients with excessive loss of plasma albumin from the gastric mucosa or upper small intestine, the albumin is degraded by proteolytic enzymes, the amino acids are reabsorbed and the loss of nitrogen from the body is negligible. The reason for the excessive loss of albumin and/or its degradation products from the body is not clear. One possibility is that there was a factor in the bezoar, possibly bacterial activity, which rendered a portion of the albumin nonabsorbable. A second possibility is an absorptive

defect in the small intestine but the absence of hypoprothrombinemia, hypokalemia and folic acid deficiency, the normal histological structure of the jejunal mucosa and the rapid gain in weight following the removal of the bezoar suggest that the absorptive capacity of the small intestine was normal. Studies of intestinal absorption were not practical owing to the prolonged retention of test substances in the stomach and the difficulty in collecting stool specimens.

Inadequate dietary intake of protein did not appear to be a factor in the development of the hypoalbuminemia. The dietary intake of both of these patients at the hospital school was adequate, and in the Kingston General Hospital a diet containing 6 g. of protein/kg. body weight failed to correct the hypoproteinemia in Case 2. The diuresis that followed the introduction of a high protein diet in this patient was probably due to the osmotic effect of an increased renal excretion of urea, and it was facilitated by the subsequent increase in the concentration of plasma protein.

The similarity of both the gross and microscopic appearances of the gastric mucosa in these two patients to those of patients with chronic hypertrophic gastritis associated with protein-losing gastroenteropathy[8, 9] suggests that the protein loss was secondary to the hyperplastic disorder of the gastric mucosa. Ulceration of the stomach was not present and the leakage of albumin from non-epithelialized surfaces did not appear to be a causative factor. Correction of the protein loss by removal of the bezoar indicates that this disorder is reversible and this finding supports the earlier observation of Wine,[5] who reported the rapid disappearance of edema in a patient after the removal of a gastric bezoar. It is not known whether reversal of the protein-losing disorder is accompanied by any change in the hypertrophic gastritis.

Hypertrophy and polyposis of the gastric mucosa is a common finding in patients with bezoars,[1, 2, 10] and it is probable that excessive protein loss, which is known to occur in association with hypertrophic disorders of the gastric mucosa, may be more frequent in this disorder than previously suspected.

CONCLUSION

Two mentally retarded adolescents with large gastric bezoars are described. Generalized edema due to marked hypoalbuminemia was present in both patients, and investigation revealed that this was due to excessive loss of plasma albumin into the gastrointestinal tract. Removal of the bezoar corrected the protein-losing disorder in each instance.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE ROOT OF IGNORANCE

Experience has shown that, whether we are physicians trying to diagnose a disease or understand a patient, or historians or philosophers investigating phases of human life, or laboratory workers observing a reaction in a test-tube, or looking at a slide under a microscope, there is only one method which leads to our goal, only one method which leads to truth, as far as we human beings may approach it, and that is the scientific method.

Unless its principles are accurately followed, we are plunged into a sea of individual ideas and speculations which possess no objective or lasting value to anyone.

What is the scientific method? A definition of the scientific method is best given by naming its parts. These are: 1. Observation and determination of facts. 2. Criticism and application of these facts. The latter again consists of three components. A. Appreciation of facts. B. Marshalling of facts. C. Interpretation of facts. All of these constantly interact, but for convenience's sake let us look at them independently.

1. Observation and determination of facts.

Nothing seems, at first sight, easier than to see, but to see and observe correctly are two very different things, and rarely met with without careful training.

Everyone of us is familiar with that. One of the most difficult things to do is to describe an object in full view without naming it. I may put an organ on the table, say for instance a liver or a kidney, and ask an untrained student what it is, and he will name it, but when I ask him to describe it, he not only hesitates, but then furnishes a description which is incomplete, often lacks in appreciation of the essential characteristics, and overestimates insignificant details, so that it may be impossible to recognize the organ from the description.

The untrained mind forms few superficial impressions of an object or occurrence, then without troubling any further, adds by memory associations the rest, and hastens to form a complete conception, that is, to name it. But it is a difficult matter, requiring thought, self restraint and time, first to observe carefully and completely, and then finally catalogue matters under a name.

How often do we find that we are wrong because we failed in our observations, because of a time saving device of our mind, or sheer laziness, or a wish, we depended upon parts of observation, instead of the whole? We all are guilty of this many times. And we all have experienced the disappointment at a bad result because we were negligent in our observations.

This is not by any means confined to the average mind or person. The history of medicine abounds with examples which illustrate that, either entire lack of, or deficient observation are often the root of ignorance.—H. Oertel, *Canad. Med. Ass. J.*, 6: 204, 1916.