THREE CASES OF SMALL-INTESTINAL NEOPLASM WITH UNUSUAL CLINICAL FEATURES

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New growths of the small intestine occur infrequently. Ewing (1940) states that the comparative incidence of malignancy in the large and small intestines is 97.5% and 2.5% respectively. Neoplasms of the small intestine may first produce symptoms because of (a) intestinal obstruction, (b) an associated anaemia (see Cases 1 and 2), or (c) rarely because of malabsorption (see Case 3). In the absence of obstructive symptoms the diagnosis may be most difficult to make.

The first two cases are presented because of the long latent period (17 months and four years respectively) between the recognition of an obscure anaemia and the ultimate discovery of its cause in spite of the most thorough investigations. The third case is described because of its initial clinical manifestations as idiopathic steatorrhoea.

Case 1

In January, 1948, a 59-year-old woman began to have symptoms of general loss of strength, diarrhoea, and some colicky abdominal pain. She had lost 21 lb. (9.5 kg.) in weight in the preceding year. She was first seen at the blood clinic in April, 1948, when physical examination was negative, except for slight pallor. The haemoglobin was 66% (14.8 g.=100%), red-cell count 3,800,000, and colour index 0.86. The possibility of an alimentary tumour was considered, but an investigation with barium meal and enema was negative. Ferrous sulphate failed to raise the haemoglobin level, and in September she was admitted to hospital. The haemoglobin was 44%, red-cell count 3,420,000, and colour index 0.65. The blood Wassermann reaction was negative and the E.S.R. was 75 mm. in one hour. The stool benzidine test was carried out on six occasions and was strongly positive on three. Fat-balance studies were negative. Gastric analysis revealed a histamine-fast achlorhydria. Sternal puncture showed a normoblastic reaction. A barium meal and follow-through was negative.

On October 25 the first of two injections (200 mg. and 80 mg. respectively) of intravenous iron was given. These were not continued because of unpleasant side-reactions. At the time of discharge (November 24) the haemoglobin had risen to 64%, and 30 gr. (2 g.) of iron and ammonium citrate was given three times a day. This was followed by a rise in haemoglobin to 90% on January 20, 1949, and iron therapy was discontinued. In April the patient was feeling well, but her haemoglobin had fallen to 64%. Iron was started again, but produced no significant rise in the haemoglobin level. On September 8 she complained of loss of appetite and a dull ache on the left side of the abdomen. There was no history of vomiting or melaena. The haemoglobin had fallen to 56%. Manual examination of the abdomen revealed for the first time the presence of a firm, slightly tender mass in the left hypochondrium. It was not fixed to skin and was about the size of an orange. Sigmoidoscopic examination and barium enema were negative.

In November laparotomy was carried out. In the left hypochondrium a tumour of the jejunum was discovered. It was not obstructing the lumen, but was adherent to the descending colon and had spread to the adjacent mesenteric lymph nodes. Microscopical examination revealed a carcinoid tumour with more cellular irregularity than usual and frequent mitotic figures. The tumour was resected, and the patient made an excellent post-operative recovery. She remained well for eleven months, but in September, 1950, the occurrence of upper abdominal pain and tenderness suggested recurrence of the tumour. Her condition gradually deteriorated and she died in April, 1951. The post-mortem examination showed recurrence of the tumour in lymph nodes adjacent to the anastomosis, with further involvement of the bowel wall and metastases in the lungs.

Case 2

A woman aged 58 reported to the blood clinic in January, 1948. She gave a history of general malaise, dyspnoea, palpitations, and precordial pain on exertion of one year's duration. Her appetite was good and her diet satisfactory. There was no history of dyspepsia, change in bowel habit, or melaena, or previous illness. On physical examination no abnormalities were detected apart from a moderate degree of pallor. The blood count showed: haemoglobin, 34%; red cells, 3,440,000; colour index, 0.5. The cause of the anaemia was not apparent and the possibility of a silent alimentary tumour was considered.

The patient was admitted to hospital for further investigation. The stool benzidine test was repeatedly strongly positive. There was free acid in the gastric juice, the E.S.R. was 25 mm. in one hour, and the blood Wassermann reaction was negative. A barium meal and enema were also negative. A total of 1,525 mg. of iron was given intravenously over a period of seven weeks, and on discharge on March 20 her haemoglobin was 70% and red-cell count 3,700,000. In April her haemoglobin was 68% and red-cell count 4,280,000, and she was given molybdenized ferrous sulphate, with no beneficial effects. During the following month she received 600 mg. of iron intravenously. In May her haemoglobin had risen to 82% and the red-cell count was 4,550,000. In July she complained of a gradual recurrence of malaise, breathlessness, and precordial distress on exertion and her haemoglobin had fallen to 56%. From then until June, 1949, her haemoglobin ranged from 60% to 76% in spite of continuous oral iron therapy.

When next seen in February, 1952, her haemoglobin was 37% and red-cell count 2,900,000. She had palpitations, dyspnoea, and precordial distress on exertion. It was estimated that she had lost about 14 lb. (6.4 kg.) in weight during the preceding six months. Abdominal examination revealed a mass the size of a foetal head to the left of the umbilicus. The tumour was smooth and not fixed to skin. At laparotomy on March 10 a large tumour involving the proximal 2 ft. (60 cm.) of jejunum was found. At one point it had invaded the peritoneum, but there was no gross evidence of metastases. The tumour was resected and an end-to-end anastomosis performed. Microscopically the tumour consisted of clumps of polyhedral, epithelial cells with a peripheral zone of columnar cells. No true acinus formation was seen, though foci of degeneration had given rise to pseudo-acini. Mitotic figures were frequent. The appearances were much more suggestive of a carcinoid tumour than of a carcinoma, though they were not altogether characteristic of the former.

On the third post-operative day it was discovered that the patient was leaking bile-stained fluid from her wound. Within a few hours a further operation was performed and a small leak from the anastomotic site was found and repaired. Despite repeated transfusions, she gradually became weaker, and died six days later. At necropsy localized peritonitis following leakage at the anastomotic site was found. Macroscopically there was no evidence of secondary growths, but microscopical examination revealed deposits in the liver.

Case 3

A man aged 43 was well until December, 1949, when he first noticed swelling of both ankles. This subsided spontaneously during the next few weeks. In October, 1950, he first complained of diarrhoea, characterized by four or five frothy, yellowish, watery stools a day. This continued intermittently for eleven months and he was admitted to the Royal Infirmary, Edinburgh, on September 14, 1951, for investigation. During the preceding months he had lost 42 lb. (19 kg.) in weight in spite of a reasonably good appetite. There was no history of abdominal pain. The family, social, occupational, and past histories revealed no information of diagnostic value.

On examination he was seen to be a thin, pale, middle-aged man. The tongue was atrophic. The respiratory, nervous, and cardiovascular systems were normal except for the presence of hypotension; his blood pressure was 90/60. The liver and spleen were not palpable and no abdominal masses were felt. He had gross clubbing of the fingers. There was minimal sacral oedema, but a moderate degree of bilateral ankle swelling. X-ray examination of the chest, urine analysis, and the stool benzidine test were negative. The initial blood count was haemoglobin, 69%; red cells, 4,600,000; colour index, 0.75; mean corpuscular volume, 86.9 μ^3 . The serum calcium was 7.7 mg. per 100 ml., and Trousseau's sign was positive. The serum sodium equalled 136 mEq./l. (312 mg. per 100 ml.); serum potassium, 4.1 mEq./l. (16 mg. per 100 ml.); plasma albumin, 2.37 g.%; and plasma globulin 2.21 g.%. Liver-function tests were negative. The Robinson-Kepler-Power water test gave a positive result. The glucose-tolerance curve was flat. 17-ketosteroid excretion was 8.4 mg. per 24 hours. A three-day fat-balance study showed that there was only 66% fat absorption and a barium meal gave evidence of a "deficiency" pattern.

About a month after admission the patient developed frank tetany with carpal spasm. This was relieved with antitetanic therapy, including calcium gluconate, "parathormone," and vitamin D. The Sulkowitch test consistently revealed the absence of calcium from the urine. A diagnosis of idiopathic steatorrhoea was made and he was given folic acid, 20 mg. daily, ferrous sulphate, 4 gr. (0.26 g.) thrice daily, multivitamin therapy, added salt (10 g. daily), and added protein ("casinal"), 100 g. daily. A total of 100 mg. of intravenous iron was given during his last week in hospital. At the time of his discharge (December 11) he was subjectively much improved. Moreover he had gained 28 lb. (12.7 kg.) in weight, the blood pressure had risen to 100/74 and the serum calcium to 11.3 mg. per 100 ml. The haemoglobin level was 77%. He was having only one or two stools a day and was completely free of oedema.

He returned to work during January and February, 1952, but had to stop because of weakness. In May he developed colicky abdominal pain which gradually increased in severity. Laparotomy was carried out in another centre, and a tumour of the ileum was found completely obstructing the intestinal lumen. Microscopically this was a reticulo-sarcoma which had invaded the adjacent mesenteric glands. The tumour was resected. Although relieved of his obstructive symptoms the patient continued to feel tired and was readmitted to the Royal Infirmary, Edinburgh, in September. The liver was now palpable three fingerbreadths below the right mid-costal margin and a chest x-ray film showed consolidation in the left lower lobe with a large hilar shadow on the left side, suggesting metastatic tumour formation. The patient has continued to become progressively weaker.

Summary and Conclusions

Two cases of tumour of the small intestine are presented in order to emphasize that an obscure anaemia may exist for months or years before obstructive symptoms occur, an abdominal mass is felt, or positive radiological evidence is obtained. The difficulty in arriving at an early correct diagnosis is evident. It is suggested

that the presence of a hypochromic anaemia, with a persistently positive stool benzidine test, the origin of which cannot be explained by clinical, instrumental, or radiological investigations, is an indication for laparotomy. If such an anaemia is refractory to oral iron therapy, this is an additional reason for operation, as it suggests that the loss of blood is of a degree that cannot be counteracted by iron therapy or that malabsorption of iron from the small intestine is occurring.

The third case is described because of the rarity with which the clinical and biochemical features of idiopathic steatorrhoea are associated with a neoplasm of the small intestine (Fairley and Mackie, 1937).

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THE SYNDROME OF HIGH-TITRE COLD HAEMAGGLUTINATION

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Occasional normal sera contain an antibody which agglutinates red cells in the cold, but it is usually present only in low titre. The physiological significance of this agglutinin is unknown and its presence is of practical importance only in blood transfusion work. A considerably raised titre of such a cold agglutinin is commonly found in cases of virus pneumonia, and rarely in a variety of unrelated conditions, including haemolytic anaemia, hepatic cirrhosis, and trypanosomiasis. In cases in which the titre is exceptionally high, exposure to cold may result in marked agglutination of red cells in the vessels of the extremities, with symptoms of vascular insufficiency. This is usually a transient phenomenon occurring at the height of the illness or during convalescence.

Cold agglutinins are, however, sometimes found in the blood of persons who have not suffered from any recent illness. They appear suddenly in very high titre and are persistent rather than transient. They give rise to a prolonged illness characterized by Raynaud's phenomenon, peripheral gangrene, intravascular haemolysis, haemoglobinuria, and anaemia.

We have recently had the opportunity of studying two further cases of this syndrome.

Case 1

A 47-year-old cycle-repairer noticed in the winter of 1950 that at times his hands became numb and blue up to the wrists and the fingers dead-white. After each attack he experienced abdominal discomfort and passed black urine. At no time was there numbness or cyanosis of the feet, but the tip of the nose often became blue, and this he recognized as a sign of an impending attack. He was careful to avoid exposure to cold, as he soon realized that