SUBACUTE COMBINED DEGENERATION OF THE CORD AFTER PARTIAL GASTRECTOMY

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The occurrence of anaemia after partial gastrectomy is common and has attracted considerable interest in recent years (*Brit. med. J.*, 1959). It is usually the consequence of deficiency of iron (Baird *et al.*, 1959), but may occasionally be associated with megaloblastic erythropoiesis. Since this latter condition is usually due to vitamin-B₁₂ deficiency and responds to treatment with cyanocobalamin given by injection, it might be expected that subacute combined degeneration of the cord (S.C.D.) would occasionally result. In fact, however, reports of such a development are remarkably few, the two cases described by Rowlands and Simpson (1932) being the only ones of which we are aware. In both of their patients the operation had been carried out because of the presence of a large gastric ulcer, but in one the diagnosis of S.C.D. was in doubt, in view of the fact that the patient had a positive Wassermann reaction. The ulcer in this case was thought to be syphilitic in origin. In the second patient the ulcer was proved histologically to be carcinomatous.

Because of the extreme rarity of S.C.D. after partial gastrectomy for peptic ulceration and because we were able to apply current investigative techniques, we report the following case.

Case Report

A high-grade mentally defective patient aged 32, an unemployed labourer, was admitted to hospital on October 17, 1959, with a three-months history of progressive weakness and unsteadiness of his legs. In March, 1949, he had been admitted to hospital for the third time within a period of a year because of gastro-intestinal haemorrhage. A barium-meal examination revealed a large gastric ulcer on the posterior aspect of the lesser curvature just above the incisura, associated with coarsening of the mucosal pattern, and an all-night gastric analysis showed hypersecretion of hydrochloric acid. On April 8, 1949, a Polya gastrectomy removing three-quarters of the stomach, and careful examination of the ulcer, failed to reveal any evidence of malignancy.

After the operation the patient had no complaints referable to the stomach, but he remained unemployed on account of his mental incapacity. On July 15, 1959 (ten years after the operation), he was readmitted to a surgical ward with symptoms of subacute intestinal obstruction. At that time the haemoglobin level was 12.1 g./100 ml., the red-cell count 3,500,000/c.mm., and colour index 1.2. The blood film showed anisocytosis and macrocytosis of the red blood cells, together with some hypochromia. At operation two days later intestinal obstruction was found due to a fibrous band running across the distal ileum. This band was divided and the obstruction relieved. The previous partial gastrectomy was examined and no abnormality was noted.

He was discharged on July 24, and he then developed paraesthesiae in the palms of both hands and later in both thighs. This was associated with progressive numbness and

stiffness in all four limbs, and he noticed that he was prone to drop things. His disability progressed, and when he was readmitted on October 17 he was almost bedridden. He made no complaint of sore tongue or diarrhoea. There was no obvious dietary deficiency. Before this admission to hospital he had been given no haematinic therapy.

Examination showed him to be a thin, ill-looking man, of low intelligence. The mucous membranes were pale, and the tongue was clean and markedly atrophic. Koilonychia was not present, and there was no enlargement of the liver or spleen. Cranial-nerve function was intact, but there was generalized hypotonia and loss of muscle power. Tendon reflexes were elicited with difficulty, and both ankle-jerks were absent. The abdominal reflexes were absent, and the left plantar response was extensor. Vibration sense was absent in both legs up to and including the anterior superior iliac spine, but was present in the arms. Position sense was severely impaired in both legs and to a less extent in the arms, but tactile and thermal sensations were intact. There was muscle tenderness in both calves; no sphincter disturbance was present.

Investigations.—The haemoglobin level was 9 g./100 ml., red-cell count 3,630,000/c.mm.; colour index 0.8; packed cell volume 34%, mean corpuscular volume 94 cubic microns, mean corpuscular haemoglobin concentration 26%, white-cell count 5,600/c.mm., erythrocyte sedimentation rate 15 mm. in the first hour (Westergren). A blood film showed anisocytosis and macrocytosis of the red cells, but the picture was dimorphic, many of the cells being hypochromic. The bone-marrow was megaloblastic. The Wassermann reaction and Kahn test were negative; x-ray examination of the chest, skull, and cervical spine showed no significant abnormality. A lumbar puncture produced clear, colourless cerebrospinal fluid under normal pressure, and contained 1 cell per c.mm. The protein content was 69 mg./100 ml. and the sugar 67 mg./100 ml.

Studies of Vitamin-B₁₂ Metabolism.—The pretreatment serum vitamin-B₁₂ level was 90 µg./ml., as estimated by microbiological assay using *Lactobacillus leichmannii* as the test organism (Girdwood, 1960) (normal values, 110–810 µg./ml.). Malabsorption of cyanocobalamin was demonstrated by the faecal test of Heinle *et al.* (1952) (81% faecal recovery of radioactivity after 0.5 µg. oral dose of ⁵⁷Co-labelled cyanocobalamin). Absorption was not corrected when the test was preceded by a five-day course of oral tetracycline in a dose of 1 g./day (82% faecal recovery of radioactivity), but complete correction was obtained when the test dose was administered along with 50 mg. of a preparation of hog intrinsic factor (29% faecal recovery of radioactivity).

The folic acid excretion test (Girdwood, 1960) was normal: the 24-hour urinary excretion after a subcutaneous dose of 5 mg. of pteroylglutamic acid was 3.5 mg. and after a 5-mg. oral dose of the same substance the 24-hour urinary excretion was 4.4 mg. (excretion index 126%). The oral glucose-tolerance test gave a result characteristic of partial gastrectomy with a rapid rise and fall in the blood-sugar levels. The serum-calcium level was 10.2 mg./100 ml., and the excretion of faecal fat estimated from a three-day stool collection with the patient on an ordinary ward diet was 28 g./day. An augmented histamine secretion test (Kay, 1953) revealed achlorhydria. Gastric and jejunal biopsies were performed by means of the Crosby small-intestinal biopsy capsule (Crosby and Kugler, 1957), and were reported as follows (Dr. A. Wynn Williams): "The gastric mucosa presents the features of chronic atrophic gastritis. Parietal cells are still present in places, but most of the glands are pyloric in type. There is marked elongation of the necks of the glands, and the surface epithelium shows hyperplastic 'tufting.' Intestinal metaplasia is also present. Inflammatory cells are not abundant in the stroma. The jejunal mucosa is normal, except for a mild degree of villous blunting in a few areas."

Barium-meal and follow-through examination, using a fine emulsion of barium, showed a normally functioning

Polya gastrectomy with normal transit of barium through the small intestine and a normal mucosal pattern.

Treatment and Progress

Cyanocobalamin therapy was begun on October 21 in an initial dose of 1,000 μ g. daily for six days by injection. After six days the patient looked and felt much better, and the dose of cyanocobalamin was reduced to 1,000 μ g. twice weekly. On October 29 treatment was begun with ferrous gluconate in a dose of 600 mg., together with 150 mg. of ascorbic acid. There was no reticulocyte response, presumably because of the relatively high level of haemoglobin at the beginning of treatment, but a repeat examination of the bone-marrow on November 23 showed normoblastic erythropoiesis, and on November 26 the haemoglobin level was 13.9 g./100 ml., the red blood count 4,810,000/c.mm., colour index 0.96, packed cell volume 48%, mean corpuscular volume 99 cubic microns, mean corpuscular haemoglobin concentration 28.9%. With the aid of physiotherapy the patient's disability slowly subsided, and on November 23 he remarked that he could again feel the ground under his feet. By December 4 the papillae on the tongue had reappeared. When the patient was examined as an out-patient on January 19, 1960, his cerebation was much improved, and, although the left plantar response was still extensor, there was no residual sensory impairment. There was marked improvement in his balance, although he still walked with rather a stamping gait and on a slightly wider base than normal. Romberg's test was negative. Faecal-fat excretion at this time still remained elevated at 28 g./day.

Discussion

The occurrence of S.C.D. in a known Addisonian megaloblastic anaemia has been reviewed by Richmond and Davidson (1958). Any disorder which gives rise to vitamin-B₁₂ deficiency may produce this condition, but such disorders are usually confined to the stomach or small intestine, or both. It is therefore essential to exclude impaired absorption of vitamin B₁₂ due to small-intestinal disease before accepting the gastric lesion as the sole cause of vitamin-B₁₂ deficiency in this patient. It has been suggested that after partial gastrectomy of the Polya type the duodenal stump might act as a large diverticulum (Ogg, 1959) or stagnant loop harbouring coliform organisms and give rise to megaloblastic anaemia, but this theory has not been well substantiated, and in this case the absorption of cyanocobalamin did not return to normal after a five-day course of tetracycline. We cannot, of course, be certain that a stagnant loop was not present prior to the division of the adhesions which were responsible for producing the small-intestinal obstruction. The patient had increased faecal excretion of fat, but there was no other evidence of malabsorption.

In a group of nine patients described by Doig and Girdwood (1960) after partial gastrectomy three had an average daily faecal excretion of fat exceeding 20 g., but one had pancreatitis and one had diabetes. In four of the remaining six patients the daily excretion of fat exceeded 7 g. Badenoch *et al.* (1955) described six cases of megaloblastic anaemia which followed gastric operations, and three had mild steatorrhoea, with no other absorption defects. Shiner (1959) and Joske and Blackwell (1959) consider that partial gastrectomy may occasionally trigger off symptoms in a patient with "latent" idiopathic steatorrhoea, and these latter workers have demonstrated atrophic jejunitis in three out of four cases of steatorrhoea after partial gastrectomy. Shiner (1959), however, in a group of 15 such cases, found that only one had partial villous

atrophy, the remaining 14 patients having a normal mucosa, but in a group of 23 patients suffering from idiopathic steatorrhoea the same author found mucosal abnormalities in every instance.

In our patient the jejunal mucosa was normal, and this suggests that the steatorrhoea was due to some mechanical or secretory malfunction produced by surgery, rather than to the presence of a "latent" idiopathic steatorrhoea. Moreover, if the impaired absorption of cyanocobalamin had been due to small-intestinal disease, little or no improvement would have been expected with the simultaneous administration of 50 mg. of hog intrinsic factor (Callender and Evans, 1955). Radiological examination showed no evidence of disease of the small bowel, including the lower ileum, which is thought to be the site of vitamin-B₁₂ absorption.

There is considerable evidence, on the other hand, to suggest that the gastric lesion was responsible for impaired secretion of intrinsic factor which, in turn, had resulted in malabsorption of vitamin B₁₂. The patient was achlorhydric, and the impaired absorption of cyanocobalamin was fully corrected by intrinsic factor. Loewenstein (1958) showed that in a group of 33 patients 30 had normal absorption of ⁶⁰Co-labelled cyanocobalamin after partial gastrectomy: the time interval between the operation and the measurement of vitamin-B₁₂ absorption ranged from one month to eleven years. The remaining three patients, who showed malabsorption, had undergone the operation at least six years previously.

Lous and Schwartz (1959) found that in a series of 51 patients in whom partial gastrectomy had been performed for duodenal ulceration, seven showed reduced absorption of vitamin B₁₂, whereas in a group of 45 patients who had been operated on for gastric ulceration 15 showed reduced absorption of vitamin B₁₂. The extent of the resection did not appear to be decisive. From these findings it would appear that severe vitamin-B₁₂ deficiency is more likely to arise in the patient whose partial gastrectomy has been performed for gastric ulceration. The demonstration of atrophic gastritis in our patient suggests that this is the true cause of the condition. This is in keeping with the views of Doig and Girdwood (1960). Joske *et al.* (1955) showed that in 68% of patients who had undergone previous gastric surgery some degree of gastritis was present on histological examination of the biopsy specimens, and the interval of time between surgery and biopsy did not influence the incidence of gastritis. Moreover, in 65 biopsies from cases of proved gastric ulcer and 98 cases of proved duodenal ulcer severe atrophic gastritis was present in 29.2% of patients with gastric ulcer as against 5.1% of those with duodenal ulcer.

There was evidence of iron deficiency in our patient, and it is probable that the body stores were severely depleted. Iron deficiency has been claimed by some workers (Badenoch *et al.*, 1957; Cox *et al.*, 1959) to give rise to impaired secretion of intrinsic factor with reduced absorption of vitamin B₁₂, and this may have been an added factor in the production of vitamin-B₁₂ depletion in this instance.

The biological half-life of vitamin B₁₂ in the liver is considered to be approximately one year (Schlosser *et al.*, 1958), and it is therefore not surprising that Paulson and Harvey (1954) have shown that, after total

gastrectomy, as long as seven years may elapse before development of megaloblastic anaemia. It took 10 years before evidence of frank vitamin-B₁₂ deficiency occurred in our patient, in whom some secretion of intrinsic factor was almost certainly present immediately after the operation. The time interval is of the same order as in the two cases described by Rowlands and Simpson (1932), the symptoms in these cases developing 6 and 15 years after the operation.

Summary

A case is described of subacute combined degeneration of the cord after partial gastrectomy for gastric ulceration in a man aged 32. Evidence is presented to show that the vitamin-B₁₂ deficiency was consequent upon impaired secretion of intrinsic factor owing to the presence of chronic atrophic gastritis. Attention is drawn to the higher incidence of atrophic gastritis and malabsorption of vitamin B₁₂ after partial gastrectomy for gastric ulceration as compared with that following this operation for duodenal ulceration.

We thank Dr. R. M. Murray-Lyon for permission to publish this case. We are grateful to Dr. A. Wynn Williams for his report on the biopsy material, and to Dr. R. H. Girdwood for his interest and advice.

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"A further example of prolonged research which in this year has progressed substantially towards a successful solution is provided by the Audible Playing Ball. All such balls so far developed have been based upon the concept of a hollow ball containing small objects, such as dried peas, which rattled as the ball was bounced. All suffered from the disadvantage that, when at rest, the ball ceased to sound. The new ball, at present undergoing intensive tests, consists of a small electronic sounding unit housed in sponge rubber within an outer casing. Powered by a miniature accumulator, rechargeable from a dry battery, this emits a bleeping sound continuously for up to ten hours on one charge. The built-in on/off switch is so designed as not to interfere with true bounce. Simple though such an object may appear to those with sight, it will fill a long-felt want in the lives of blind children and, it is hoped, enable them to add both cricket and football—those twin national pastimes—to the growing list of sports in which they now take part." (*Report of the Executive Council for the year ended March 31, 1959*, Royal National Institute for the Blind.)

PROLAPSED CORD

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The last 10 years have seen little change in stillbirth and neonatal death rates. Prolapse of the umbilical cord accounts for some of these deaths, and, as it is believed that prompt and adequate treatment would save many more of these potentially normal babies, it seemed worth while to report the results of treatment of 100 consecutive cases seen at Queen Charlotte's Hospital during the period 1951–9. The mode of death in such cases has been investigated by post-mortem examination and by experimental investigations into the role of arterial hypotension.

TABLE I.—Incidence and Results

	Total Cases	Prolapsed Cord	Incidence
Deliveries ..	25,885	100	0.4%
Stillbirths ..	589	19	3.2%
Neonatal deaths ..	461	9	2%

The overall results in this series are given in Table I, there being an uncorrected perinatal mortality of 28% with no maternal deaths.

Aetiology

Clinical

Numerous factors have been invoked as being of importance in the production of cord prolapse, including disproportion, hydramnios, surgical and medical induction of labour, low placental implantation, tumours, anaesthesia, and obstetrical manipulations. No correlation could be demonstrated with any of these conditions in the present series. The ratio of primigravidae to multigravidae was 45 to 55, this being a reversal of the ratio of total admissions over the same period. Only five patients had had more than four children. The factors which appeared to be of importance were as follows:

TABLE II.—Mortality Associated with Presentation

Presentation	Total No. ^a	Stillbirths	Neonatal Deaths
Vertex ..	56	6	4
Breech ..	26	7	3
Oblique or transverse ..	10	4	1
Compound ..	6	2	1
Brow ..	2	0	0

Malpresentation.—The presentation in these cases is shown in Table II. Of the cases in which the vertex presented, the head was not engaged in nine; thus the head was presenting and engaged in only 47% of cases. It is also of interest that of the 26 cases in which the breech presented the legs were flexed in all except two.

Birth Weight.—The baby weighed 5½ lb. (2,495 g.) or less in 32 cases. Fifteen deaths occurred in this group, including all 10 babies weighing 3½ lb. (1,590 g.) or less. In three cases the baby weighed 10 lb. (4,535 g.) or more, and all three died. Of the 65 remaining babies, between 5½ and 10 lb. (2,496 and 4,535 g.), 10 died in the perinatal period.

Multiple Pregnancy.—There were 14 cases of twin pregnancy in the series. During the period under consideration there were 400 twin pregnancies altogether,