Gastric Atrophy in Childhood

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Chronic gastritis and gastric atrophy are common in later adult life. Hebbel (1943) investigated the incidence of chronic gastritis at necropsy in patients dying from a variety of causes but whose history revealed no evidence of gastric symptoms. He found that gastric changes of any degree were rare below the age of 30 years and severe changes uncommon below the age of 50 years. Atrophic gastritis was found in 30% of his cases over 50 years old, but was uncommon below this age. He concluded that it bore no demonstrable relation to any process other than age. Subsequent investigations have shown that as age advances, gastritis appears with increasing frequency in patients suffering from a variety of conditions (Coghill, 1960) as well as in normal subjects. The occurrence of chronic gastritis and gastric atrophy in childhood is not well recognized and has been rarely recorded. 2 cases are presented here, the first associated with iron-deficiency anaemia and the Paterson-Kelly syndrome, and the second associated with auto-immune hypothyroidism.

Case Reports

Case 1. First seen at a school clinic at the age of 10 years, she was pale, breathless on exertion, and easily tired. There was no history of abdominal discomfort or pain, bowel disturbance, or obvious blood loss from the gastro-intestinal tract. Her mother said that for as long as she could remember the child had never been a 'good eater' and had complained of a choking sensation in her throat when swallowing food. In the previous 2-3 years she had complained of definite post-cricoid dysphagia resulting in almost complete avoidance of solid foods. Her diet during this time consisted mainly of fluids and she had acquired the habit of eating soap. She was admitted to Bridgend General Hospital under the care of Dr. R. Isaacs.

Physical examination showed a pale girl 109 cm. in height and weighing 17.7 kg. (both below the 3rd centile). There was marked koilonychia and brittleness of the nails, angular stomatitis, and her tongue was smooth and devoid of papillae. A soft systolic murmur was heard over the praecordium, maximal at the apex. No other clinical abnormality was detected.

Investigations. Hb 4.8 g./100 ml., MCHC 24%, reticulocytes 0.5%, leucocyte count 3400/cu.mm., with a normal differential count. Platelet count 225,000/cu.mm. Serum iron 30 µg./100 ml., total iron-binding capacity 570 µg./100 ml., serum vitamin B12 600 pg./ml., serum folate 4.2 ng./ml. Sternal marrow aspirate showed a highly cellular marrow with normoblastic erythropoiesis, no stainable iron present. Serum bilirubin 0.5 mg./100 ml., serum cholesterol 157 mg./100 ml., blood urea 15 mg./100 ml. Repeated testing for faecal occult blood was negative and the total 5-day fat output was 5.6 g. The xylose tolerance test, tryptic activity of the stools, and the sweat sodium were all normal. Barium swallow examination showed the presence of a marked post-cricoid web, and after a transfusion of 1.0 l. blood had been given oesophagoscopy was carried out by Mr. Mervyn Landeg. He found a tight post-cricoid stricture extending for 2 cm. down the oesophagus. A thick anterior web at the upper end of the stricture was divided with punch forceps and a biopsy was taken. The stricture was dilated. Histologically, the web tissue showed non-specific subepithelial chronic inflammation but no other significant features.

The patient was treated with oral iron and transferred to Cardiff where further studies were carried out. When she was first seen at the Cardiff Royal Infirmary her haemoglobin concentration was 11.5 g./100 ml. and her physical condition was much improved. Swallowing presented no difficulty and she was eating well. Histamine infusion (Lawrie, Smith, and Forrest, 1964) resulted in a maximal acid output of 1.4 mEq/hr. Inorganic iron absorption after a week without treatment was 17%. Schilling test showed 11.7% vitamin B12 excretion in 24 hours. Gastric biopsy was carried out by Mr. J. Kirkpatrick, and all specimens showed an atrophic mucosa with infiltration by lymphocytes, plasma cells and a few eosinophils. No peptic or parietal cells could be identified and there was no evidence of intestinal metaplasia. The only epithelial cells present were those of the surface mucus-producing area (Fig. 1). Serum from this patient was strongly positive for parietal cell antibody when tested by the immunofluorescent sandwich technique, but gave no reaction with thyroid tissue. Intrinsic factor antibody was not present. Subsequent clinical improvement has been maintained and the patient is now a lively, non-anaemic girl aged 13.

There was no family history of anaemia, thyroid disease, or gastric disease. The parents, four sibs,

FIG. 1.—Gastric biopsy of Case 1 showing gastric atrophy.

and one surviving maternal grandparent were examined. None was anaemic and in none were gastric or thyroid antibodies detected. A histamine infusion test was carried out on both parents. The father's gastric function was normal, but the mother, aged 48, had a complete achlorhydria, and biopsy showed chronic gastritis but not complete atrophy. Her serum iron was 55 $\mu\text{g.}/100\text{ ml.}$, iron-binding capacity 480 $\mu\text{g.}/100\text{ ml.}$

Case 2. Her general practitioner first saw her when she was 10 years old; he found her to be anaemic and prescribed oral iron. Eight months later she had not shown a satisfactory response and was referred to the Cardiff Royal Infirmary. The child had no complaints even on direct questioning, but her parents had noted that for several years she had been less active than other children, shunning games and preferring to stay at home close to the radiator. Her features had become more 'podgy'. Nevertheless, her academic performance was average and adequate to pass the 11-plus examination.

On examination her height and weight were within normal limits. Her hair was rather coarse and she had a puffy face. There was seborrhoeic eczema on the vertex of the scalp and retro-auricular eczema. She was pale and clinically anaemic though without koilonychia, angular stomatitis, or glossitis. The thyroid was not enlarged. There were no abnormal signs in the cardiorespiratory systems, in the abdomen, or on neurological examination.

Investigations. Hb 10.8 g./100 ml., MCHC 34%, MCV 60 $\mu\text{m.}$, reticulocyte count 1.2%, WBC 7,800/cu.mm., normal differential. Platelets 200,000/cu.mm., ESR 17 mm. in 1 hour, serum iron 60 $\mu\text{g.}/100\text{ ml.}$, total iron-binding capacity 390 $\mu\text{g.}/100\text{ ml.}$,

serum B12 506 pg./ml., serum folate 6.2 ng./ml., serum protein-bound iodine 1.6 $\mu\text{g.}/100\text{ ml.}$ Blood urea 30 mg./100 ml. Serum contained parietal cell antibody and thyroid cytoplasmic antibody when tested by an immunofluorescent technique. The tanned red cell agglutination technique gave a titre of 1/25. No intrinsic factor antibody detected. Vitamin B12 absorption, measured by whole body counting was 37%. Histamine infusion test—maximal acid output 0.8 mEq/hr. Gastric biopsy (Mr. J. Kirkpatrick) showed complete gastric atrophy. No peptic or parietal cells could be seen and there was some chronic inflammatory infiltration with plasma cells and lymphocytes. No intestinal metaplasia was found (Fig. 2).

A diagnosis of hypothyroidism was made and treatment with thyroxine, 0.1 mg. daily, resulted in a return of the blood picture to normal without the administration of any further haematinics. The change to a euthyroid state resulted in the patient becoming a lively and active schoolgirl. Subsequent barium swallow examination showed no abnormality in the pharynx or oesophagus. There was no family history of pernicious anaemia, gastric carcinoma, or thyroid disease. The patient's mother had become anaemic 2 years previously, but this had responded completely to oral iron therapy. Both parents, the patient's 2 sisters, aged 6 and 16 years, and both grandmothers were examined. None was anaemic. Parietal cell antibodies were present in both grandmothers, aged 69 and 78 years, and in the 16-year-old sister. No thyroid antibodies were detected. Gastric secretion was normal in both parents but one grandmother had a complete histamine fast achlorhydria and the other a maximal acid output of 1.17 mEq/hr. No assessment of the elder sisters' acid excretion was made, but a gastric biopsy showed unmistakable chronic gastritis

FIG. 2.—Gastric biopsy of Case 2 showing gastric atrophy.

with the presence of lymphoid follicles in the mucosa (Fig. 3).

Discussion

Chronic gastritis is common in late adult life. Its incidence increases with age and it is more

common in women (Doig and Wood, 1952). Chronic gastritis with gastric atrophy is not well documented in childhood, though individual cases have been described in young patients of about 20 years of age (Gasparov *et al.*, 1960). More recently Sedláčková and Bednář (1967) described

FIG. 3.—Gastric biopsy of sister of Case 2 showing infiltration with chronic inflammatory cells, and a lymphoid focus.

histological evidence of chronic gastritis in 13 out of a group of 54 children without any gastrointestinal complaints, and suggested that the origin of chronic gastritis lay in childhood and the disease pursued an asymptomatic course. However, none of their cases presented with atrophic changes of comparable severity to the two cases described here, and they do not state whether gastric auto-antibodies were present or whether gastric function was impaired.

Gastric atrophy of the degree found in the present cases has not been previously described at this early age. Gastric secretion was minimal in both cases, even after a histamine infusion. No glandular tissue was found in the gastric biopsies. The correlation between gastric secretion and histology is well established (Rohrer and Welsh, 1967). Progressive gastric mucosal damage leads to decreased secretion of acid, pepsin, and intrinsic factor. Significant amounts of intrinsic factor may, however, remain long after acid production has failed and enable vitamin B12 to be absorbed in normal amounts (Ardeman and Chanarin, 1966). This was the case in both girls, for despite severe mucosal atrophy and hypochlorhydria, their vitamin B12 absorption patterns were within the normal range. Subnormal absorption of vitamin B12 may occur in adults with atrophic gastritis and no history of pernicious anaemia (Whiteside *et al.*, 1964), and in older patients actual vitamin B12 deficiency may result (Wood *et al.*, 1964). It is, therefore, possible that with the passage of time and probable progression of their gastric lesions both children may develop pernicious anaemia. The first girl had suffered from iron-deficiency anaemia, and the severe oropharyngeal and nail changes suggest that this had been present for a long time. Badenoch, Evans, and Richards (1957) have shown that atrophic gastritis may result from chronic iron deficiency anaemia and it is possible that this was the course of events leading to the present clinical condition.

Te Velde *et al.* (1964) found parietal cell antibodies in 20% of a large group of relatives of patients with pernicious anaemia compared with 6% in control subjects. Patients with iron deficiency anaemia and latent pernicious anaemia have relatives with a significantly higher incidence of parietal cell antibody than those without latent pernicious anaemia (Dagg *et al.*, 1966). McFadyen *et al.* (1966) proposed that, in those with latent pernicious anaemia, the atrophic gastritis was initiated by a genetically determined immunological process. In those without latent pernicious anaemia, iron deficiency was thought to be re-

sponsible for gastric mucosal damage leading to atrophic gastritis and the subsequent formation of gastric auto-antibodies in the absence of a genetic predisposition. It seems likely that if a genetic background existed, then the addition of iron deficiency resulting in gastric mucosal damage would lead to the development of gastritis earlier in life than otherwise. Because of the early age of presentation of atrophic gastritis in these 2 young girls, their families were examined for the presence of auto-antibodies in an attempt to demonstrate an underlying genetic disorder. Living relatives of Case 1 on both the maternal and paternal side were screened for anaemia and the presence of gastric and thyroid antibodies: none were found, and serum B12 levels were all normal. The mother had complete achlorhydria and gastritis without evidence of atrophy, but the significance of these findings in relation to the daughter is not obvious. In Case 2 in addition to the immediate family, all 16 living relatives were similarly screened, but no abnormality was detected in any, except the two surviving grandmothers in whom parietal cell antibody and impaired gastric secretion were found. At this age, these findings are not uncommon. Both parents were normal but the elder sister of Case 2 was found to have parietal cell antibody in her serum. This led to a gastric biopsy which confirmed the presence of atrophic gastritis. Both sisters therefore have an auto-immune gastritis. Case 1 also had circulating thyroid antibodies and hypothyroidism, a known association with pernicious anaemia, and atrophic gastritis (Doniach, Roitt, and Taylor, 1963; Fisher and Taylor, 1965). It appears that this family has a genetic predisposition to auto-immune gastritis and thyroiditis, which has manifested itself most severely in Case 1 and has partial expression in her elder sister.

Summary

Two young girls with gastric atrophy are described. The first girl had iron-deficiency anaemia and a post-cricoid web; the second girl had primary hypothyroidism. A 15-year-old sister of the second patient was also found to have an auto-immune gastritis.

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