Paterson–Kelly Syndrome in Adolescence: A Report of Five Cases

M. D'A. CRAWFURD,* M.B., B.S., D.PATH.; A. JACOBS,† M.D., M.C.PATH.; B. MURPHY,‡ M.B., B.S., D.OBST.R.C.O.G.; D. K. PETERS,§ M.B., B.CH., M.R.C.P.

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Dysphagia in the post-cricoid region is usually found in middle-aged women and may be associated with anaemia (Jacobs and Kilpatrick, 1964). Patients with this condition sometimes have a post-cricoid web which can be seen radiologically. Although cases may occasionally be seen in women below the age of 30, no cases occurring during adolescence have been reported before in the literature. The present report describes the cases of three boys and two girls aged 14 to 19 years in whom post-cricoid webs were found. All these patients suffered from iron-deficiency anaemia.

Case 1

A boy aged 14 was referred to the Cardiff Royal Infirmary in November 1963 from his school clinic, where he was noticed to be pale. He made no complaints, but on direct questioning admitted to breathlessness on exertion and getting tired easily. Later, again after direct questioning, he admitted that food occasionally stuck in the post-cricoid region. His diet seemed normal and there was no history of abdominal pain or diarrhoea. His elder sister had been treated for iron-deficiency anaemia.

Examination showed a pale boy, height 5 ft. 2 in. (157 cm.), weight 50 kg. His tongue was smooth at the edges. Angular stomatitis was present. Nails were brittle but there was no koilonychia. There were no other abnormal signs.

Investigations.—Hb 7.1 g./100 ml.; P.C.V. 27%; M.C.H.C. 26%; W.B.C. 3,400/c.mm.; blood urea 19 mg./100 ml.; serum iron 3 μg./100 ml.; total iron-binding capacity (T.I.B.C.) 650 μg./100 ml.; serum vitamin B_{12} 282 $\mu\mu$g./ml. Continuous histamine infusion (Lawrie, Smith, and Forrest, 1964), maximal gastric acid output 4.1 mEq/hour. Faecal occult blood negative (x 6). Faecal fat (five-day collection), 2 g./day. Schilling test, 12% excretion in 24 hours. Iron absorption, using ^{59}Fe in a standard test meal, 4% absorbed (normal 0–20%). Barium swallow showed a small web on the anterior wall of the hypopharynx. The stomach, duodenum, and small intestine were normal.

The patient was given an intravenous infusion of Imferon equivalent to 1,800 mg. of iron, and when he was seen again four months later his haemoglobin had risen to 15.7 g./100 ml. and he no longer complained of dysphagia. When the barium swallow was repeated the web could not be demonstrated. The histamine test was not repeated.

Case 2

A girl aged 17 was seen at the Cardiff Royal Infirmary in February 1964. She had been pale for three to four years, and when aged 14 she was given 100 iron tablets by her family doctor. She said she had always had a small swallow. In the past year food had stuck in the post-cricoid region and friends had remarked on her slowness in eating, which was the result of careful chewing of all food to enable her to swallow it. She had had cracks at the corners of her mouth for as long as she could remember. There had recently been increasing tiredness and shortness of breath on exertion. Menstruation was said to have been normal since its onset at the age of 11 years. There was no diarrhoea and no family history of anaemia. Her diet seemed normal.

Examination showed a pale, normally developed girl, height 5 ft. (152 cm.), weight 50 kg. Her nails were brittle but there was no koilonychia. Her tongue was normal. Slight angular stomatitis was present. There were no other abnormal signs.

Investigations.—Hb 7.7 g./100 ml.; P.C.V. 27%; M.C.H.C. 28%; M.C.V. 69 cubic microns; W.B.C. 5,000/c.mm. (normal differential count); E.S.R. 8 mm./hr. (Westergren); serum iron 3 μg./100 ml.; T.I.B.C. 508 μg./100 ml.; serum vitamin B_{12} 467 $\mu\mu$g./ml. Faecal occult blood negative (x 7). Faecal fat 3.7 g./day (seven-day collection). Iron absorption, using ^{59}Fe in a standard test meal, 51% absorbed. Schilling test, 11% ^{58}Co-labelled vitamin B_{12} excreted in 24 hours. Continuous histamine infusion (Lawrie, Smith, and Forrest 1963)—maximum gastric acid output—13 mEq/hour. Barium swallow showed two upper oesophageal webs.

She was treated with an intravenous infusion of Imferon equivalent to 1,800 mg. of iron. When seen in the follow-up clinic three months later, her haemoglobin was 13.1 g./100 ml., M.C.H.C. 33%. Her dysphagia had greatly improved but there was still slight difficulty in swallowing. A histamine test at this time showed that the gastric acid output was 20 mEq/hour.

Case 3

A girl aged 19 was admitted to Paddington General Hospital in March 1959. She complained of feeling tired and unwell for two months. She had always been rather pale and had had shortness of breath and palpitations on exertion for two months. She had noticed a tendency for food to stick in her throat during the past three or four weeks. Her appetite was good, she had no gastro-intestinal disturbances, and her diet was apparently normal. Menstruation started at the age of 12 years and had been somewhat irregular. No family history of anaemia.

Examination showed a pale girl with angular stomatitis. Her tongue and finger-nails were normal. There were no other abnormal physical signs.

Investigations.—Hb 3.7 g./100 ml.; W.B.C. 8,200/c.mm.; M.C.H.C. 24%; serum iron 12 μg./100 ml.; T.I.B.C. 432 μg./100 ml.; serum protein 6.3 g./100 ml. A histamine test meal showed normal acid secretion. Occult blood tests, negative. Sternal marrow, hyperplastic normoblastic haemopoiesis. Barium swallow showed an anterior web in the upper part of the oesophagus. The stomach and duodenum were normal. Chest *x*-ray picture was normal.

Treatment with intramuscular iron (Astrafer) was started. The patient was discharged with a haemoglobin level of 8.9 g./100 ml., serum iron 142 μg./100 ml., T.I.B.C. 392 μg./100 ml. She returned to her native Ireland and was not seen again.

Case 4

A schoolboy aged 14 was admitted to Fulham Hospital in June 1962 with a five-day history of central abdominal discomfort. A routine blood count revealed: Hb 7.1 g./100 ml., P.C.V. 32%, M.C.H.C. 22%, R.B.C. 4,400,000/c.mm. The film showed marked hypochromia and anisocytosis of the red cells. He had been tired for some nine months and had moderate breathlessness on exertion, for which reason he had stopped taking part in any athletic activities. These symptoms were attributed by his mother to the fact that he had grown considerably in the preceding 18 months. His appetite

* Late Lecturer in Pathology, Charing Cross Hospital Medical School. Present address: Department of Clinical Genetics, University College Hospital.
† Senior Lecturer in Haematology, Welsh National School of Medicine, Cardiff Royal Infirmary.
‡ Lecturer in Pathology, Charing Cross Hospital Medical School.
§ Research Fellow, Medical Unit, Welsh National School of Medicine, Cardiff Royal Infirmary.

was fairly good but the diet unbalanced, consisting mainly of carbohydrate. Assessment of the total dietary iron intake indicated that this was of the order of 9–12 mg. daily. He stated that food occasionally stuck in his throat (in the post-cricoid region) and that to avoid this occurring he had always chewed his food for a long time. Bowel and stool appearances were normal and had remained unaltered for some years. He had not had any serious illness. Other members of his family were well, and none had at any time suffered from anaemia.

On examination he was of normal build for his age (height 5 ft. 6 in. (168 cm.), weight 63 kg.). There was a marked angular stomatitis, which was said to have been present for six months. Nails and tongue appeared normal. There were no other abnormal physical signs.

Investigations.—Augmented histamine test meal showed moderate amounts of free acid present. Haemoglobin electrophoresis, normal. Serum vitamin B_{12} 240 $\mu\mu$g./ml. Serum haptoglobin level, normal. Bone marrow: active erythropoiesis with appearances suggesting severe iron deficiency. Normal xylose-tolerance test. No excess Figlu excretion after histidine-loading. Faecal fat excretion (five-day collection), 5 g. daily. Stool examination: occult blood negative on five occasions; no parasites found. Barium studies of the gastro-intestinal tract revealed an upper anterior oesophageal web (Fig. 1). No abnormality was seen in the stomach, duodenum, or small bowel.

He was treated with oral iron, and, although attempts to get him to eat a more balanced diet were not very successful, his haemoglobin level rose to 14.4 g./100 ml. in two months and was still normal when he was seen 15 months later.

Case 5

A youth of 19 was referred to Fulham Hospital in 1960 after a visit to his dentist, who drew attention to his marked pallor. The patient considered himself to be in good health and did not think his complexion had changed in recent years. His weight had remained steady and his appetite was good. His diet was adequate and well balanced. He did not complain of dysphagia. His bowel habits and stool appearances were normal and had not altered for some years. The father and two younger siblings were in good health. He himself had had no previous illnesses. His mother had had recent hospital treatment for a severe iron-deficiency anaemia on two occasions, but no other members of the family had ever suffered from anaemia.

On examination he was wiry and well proportioned despite his small stature (height 5 ft. 1 in. (155 cm.), weight 51 kg.). The finger-nails, tongue, and mouth were normal. Secondary sex characteristics had developed normally. The spleen was palpable two fingerbreadths below the costal margin and felt quite soft. There were no other abnormalities.

Investigations.—Hb 5.6 g./100 ml.; P.C.V. 26%; M.C.H.C. 25%; R.B.C. 3,600,000/c.mm. Red cells showed marked hypochromia and marked anisocytosis. Serum iron 36 μg./100ml. Free acid present in resting gastric juice. Bone marrow: erythropoiesis was normoblastic. Folic-acid-absorption test normal. Faecal fat excretion (three-day collection) 1.5 g./day. Occult blood negative on four occasions. ^{59}Fe 5 μc. was given with a standard meal, 32% of the dose being absorbed.

Administration of oral iron resulted in a satisfactory response, the haemoglobin level rising to 12.9 g./100 ml. after four weeks, treatment. Oral iron was given for 15 months and examination in December 1963 showed a haemoglobin of 15.3 g./100 ml. Barium swallow showed an anterior post-cricoid web (Fig. 2). Questioning at the time of this *x*-ray examination failed to reveal any difficulty in swallowing.

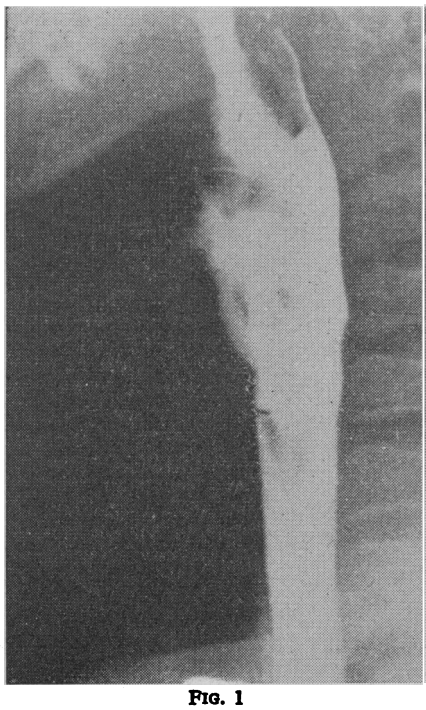

FIG. 1

FIG. 1.—Case 4. Radiograph showing upper anterior oesophageal web.

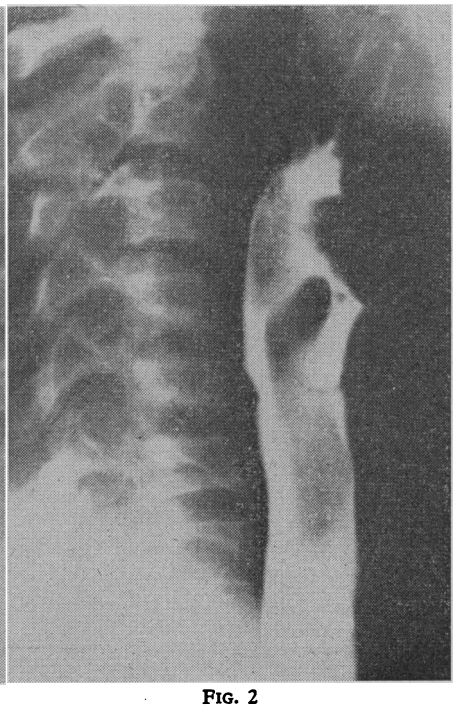

FIG. 2

FIG. 2.—Case 5. Radiograph showing anterior post-cricoid web.

Discussion

Dysphagia localized to the post-cricoid region in association with iron-deficiency anaemia was first fully described by Paterson (1919) and Kelly (1919). These and later authors emphasized that the syndrome occurred in middle-aged women. It is only rarely found in men: Wynder and Fryer (1958) found 17 males in 150 cases, and McNab Jones (1961) 4 men in 94 cases. Moersch and Conner (1926) described 65 cases, all in women aged 23–63 years. Witts (1931) reported 13 cases (all female) aged 35–50. Smiley, McDowell, and Costello (1963) described 27 cases (25 women, 2 men) all of whom were more than 30 years old. The 55 patients of Jacobs and Kilpatrick (1964) were aged 31–84 years and included two men. There have previously been no published reports of post-cricoid webs in adolescents, although two of Jacobs and Kilpatrick's patients said they had had symptoms since girlhood.

Iron deficiency in adolescents is well documented. Thus Kilpatrick (1961), sampling a normal population, found no less than 28% of women in the age-group 15–24 years had iron-deficiency anaemia (Hb<12 g./100 ml.). Iron deficiency in young adult males, though less common, is also well recognized. Nolan (1925) described two cases in youths aged 16 and 18 and drew attention to features of infantilism in these patients. Witts (1930) reported five cases in which no cause for the anaemia was found. His eldest patient was 28. Thomson (1943) described nine cases in patients aged 17–20, and Shorthouse and King (1951) 20 cases in patients under 23. Leonard (1954) found 50 cases of iron-deficiency anaemia among 4,221 R.A.F. recruits and in 47 no primary organic cause was discovered; Brumfitt (1960) examined 2,000 recruits to the R.A.M.C. and found 30 with unexplained iron-deficiency anaemia. Dysphagia was not mentioned in any of these papers. The development of anaemia in this age-group is usually thought to be due to increased iron demands resulting from adolescent growth; in the female it is related to the onset of menstruation.

All the cases reported here came to hospital with marked iron-deficiency anaemia. In no case was dysphagia the primary symptom and in one case this symptom was never elicited even after a web had been demonstrated radiologically. Although the Paterson-Kelly type of dysphagia is commonly associated with anaemia in hospital patients, the present group being no exception, it is not clear what part iron deficiency plays in the causation of the post-cricoid lesion. An epidemiological survey of a South

Wales population has shown that in the community as a whole iron deficiency is no more common in those with dysphagia or webs than in those without (Elwood, Jacobs, Pitman, and Entwistle, 1964). Patients sent to hospital, as the present cases were, tend to be selected from the general population by reason of their anaemia, while those with webs who are not anaemic might tend not to be seen. The criteria for the radiological diagnosis of post-cricoid webs have been clarified by Pitman and Fraser (1965). They have shown that this lesion must be distinguished from the appearance due to varicosity of the post-cricoid venous plexus. The *x*-ray pictures in the present cases were reviewed by Dr. Pitman, and the diagnosis of post-cricoid web was confirmed in all but Case 1, where the appearance was felt to be equivocal. It is of interest that the web in Case 1 could not be seen radiologically after full treatment with iron. In Case 5, however, the web was discovered only after the iron-deficiency anaemia had been cured.

Previous reports have emphasized that achlorhydria is common in patients with the Paterson-Kelly syndrome (Moersch and Conner, 1926 ; Jacobs and Kilpatrick, 1964). Badenoch, Evans, and Richards (1957) found dysphagia only in those patients who had both iron deficiency and gastric atrophy. Gastric-function tests in the present cases were carried out by different techniques, so that no quantitative comparison can be made. Cases 2–4 undoubtedly had acid secretion within the normal range. Cases 1 and 2 were subjected to a continuous histamine infusion by the technique of Lawrie *et al.* (1964), and the maximum secretory rate of 4 mEq/hour in Case 1 is unequivocally subnormal. The Schilling test in Cases 1 and 2 was within normal limits. Gastric biopsy was not performed in any of the cases. Gastric atrophy is rare in adolescence and becomes more common with increasing age. The significance of its presence in one of the five cases is difficult to assess.

There was no evidence of steatorrhoea in any of the patients. Iron absorption from a test meal was measured in three patients before the anaemia was treated. In two, with normal gastric secretion of acid, increased absorption of iron was found, as would be expected with a severe iron-deficiency anaemia. In the third patient, a boy aged 14 (Case 1), only 4% of the oral dose of iron was absorbed despite his severe anaemia. This patient had a low acid output in response to histamine, and the failure to increase his iron absorption is in keeping with the findings in other such patients with hypochlorhydria or achlorhydria (Goldberg, Lochhead, and Dagg, 1963 ; Peters, Lawrie, and Jacobs, unpublished).

Severe atrophic changes in the tongue were not seen in any of the present cases ; nor was koilonychia present. The clinical picture was otherwise similar to that seen in older hospital patients in that iron deficiency was present in all cases and there was marked angular stomatitis in three of them. The accidental discovery of five patients below the age of 20 with post-cricoid webs indicates that this condition may occur at an earlier age than has been previously recognized.

Summary

The cases of five patients in whom post-cricoid webs were discovered during adolescence are described. All had iron-deficiency anaemia when first seen, and in one case there was evidence of gastric atrophy and impaired iron absorption.

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Jaundice During Treatment with an Oral Contraceptive, Lyndiol

GÖRAN CULLBERG,* M.B. ; ROLF LUNDSTRÖM,† M.D. ; UNNE STENRAM,‡ M.D.

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The possibility of liver damage during treatment with oral contraceptives has recently been considered in the *British Medical Journal*. As only a few cases of jaundice have been reported (see Table), and as attention should be paid to all possible adverse effects of drugs, we present the following case of icterus which we suspect of being caused by Lyndiol.

Case Report

The patient, a 2-para born in 1925, had been treated for pulmonary tuberculosis from 1945 to 1948. During her last pregnancy, in 1958, she developed pyelitis. She has also had cystitis several times, the last occasion being in May 1964, when sulphonamides were given and blood samples were taken. She had occasionally taken Medapan sleeping-tablets, containing heptabarbitone. She has not received any injections during the last year, and has had no contacts with other cases of jaundice.

From the beginning of July 1964 she took one tablet of Lyndiol a day. After three to four days she experienced nausea and vomited a few times, but continued to take the tablets for 10 more days. She gradually lost her appetite, got tired, and developed pruritus. At the end of July the urine became dark, and she was slightly jaundiced. She was admitted to hospital on 31 July. Her jaundice reached its maximum in the middle and end of August, then gradually subsided. She left hospital on 18 September. When seen on 7 October she felt quite well and was in full working capacity.

Investigations.—Among the laboratory data the following may be mentioned. As a rule tests were repeated, but only the most important pathological findings are given:

Serum bilirubin (25 August, 8.42 mg./100 ml., 7.52 mg. direct-acting ; serum alkaline phosphatase (8 September), 75.8

* Research Assistant of Pathology, University of Uppsala, Sweden.
† Assistant Professor, Department of Epidemiology, Centrallasarettet, Eskilstuna, Sweden.
‡ Associate Professor of Pathology, University of Uppsala, Sweden.