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Pseudopolycythaemia and coeliac disease

J R CRAMPTON, M V TOBIN, AND R B McCONNELL

From the Gastroenterology Unit, Royal Liverpool Hospital, Liverpool

SUMMARY We report two patients in whom introduction of a gluten free diet for coeliac disease was associated with the development of pseudopolycythaemia.

Haematological abnormalities are common in coeliac disease.[1] Anaemia may be secondary to deficiency of iron, or folate and red cell morphology may vary from microcytic to macrocytic. Leucopenia and thrombocytopenia are uncommon but can occur if severe folate or B_{12} deficiency is present. Thrombocytosis may be present and reflects splenic atrophy which may also be indicated by the presence of red cell inclusions, Howell-Jolly bodies. Abnormalities caused by malabsorption usually revert to normal after treatment with a gluten free diet but blood film evidence of hyposplenism may remain. Pseudopolycythaemia is a benign condition of uncertain aetiology which has not been previously associated with treatment of coeliac disease.

CASE 1

A 48 year old woman presented in 1975 with a history of chronic diarrhoea for at least 15 years. In 1961 a diagnosis of ulcerative colitis had been made on uncertain grounds as when she had continuously taken sulphasalazine 1 g twice daily. She was a non-smoker with no family history of bowel disease. Barium enema and sigmoidoscopy were normal on this presentation but she was mildly anaemic (haemoglobin 11·8 g/dl), normochromic normocytic film. The sulphasalazine was stopped and she was treated empirically. Apart from occasional loose bowels she remained in good health but in 1979 a jejunal biopsy was carried out because of the appearance of a macrocytosis on a routine blood count. This showed total villous atrophy. After the commencement of a gluten free diet she remained asymptomatic although it was noted that her haemoglobin rose progressively reaching a peak of 21·4 g/dl in 1983 (Figure). The macrocytosis persisted and further investigations at this stage showed a normal serum iron, folate, vitamin B_{12} and leucocyte alkaline phosphatase. The red cell mass measured with chromium labelled (^{51}Cr) red cells was at the upper limit of normal (31·5 ml/kg, normal range 20–30 ml/kg) with a low plasma volume (34·6 ml/kg, normal range 40–50 ml/kg) consistent with pseudopolycythaemia. Her haemoglobin has since fluctuated from 15–20 g/dl but she remains asymptomatic.

CASE 2

A 51 year old dentist presented in 1977 with a 10 year history of reccurent diarrhoea and recent weight loss. Apart from an uncomplicated myocardial infarction in 1962 there was no other significant medical history. Clinical examination was normal although he had a macrocytic anaemia (haemoglobin 9·8 g/dl, MCV 124) with a normal white cell and platelet count. Both the serum vitamin B_{12} and folate were low at 60 pg/ml (normal 150–970 pg/ml) and 1·0 ng/ml (normal 4–12 ng/ml) respectively with a mild prolongation of prothrombin time to 14 seconds (control 12 secs). A jejunal biopsy confirmed total villous atrophy. Treatment with a gluten free diet and folic acid 5 mg daily was started in February 1977, resulting in marked symptomatic improvement and a normal haemoglobin and red cell indices within two months. All haematinics were stopped but his haemoglobin continued to rise reaching a peak of 19·2 g/dl in 1982 (Figure). His white cell and platelet counts were normal as was a Schilling test, bone marrow aspirate and leucocyte alkaline phosphatase. His red cell mass was also normal (28·5 ml/kg) with a plasma volume just below normal at 39·7 ml/kg (normal range 40–50

Address for correspondence: Dr J R Crampton, Gastroenterology Unit, Hope Hospital, Eccles Old Road, Salford M6 8HD.

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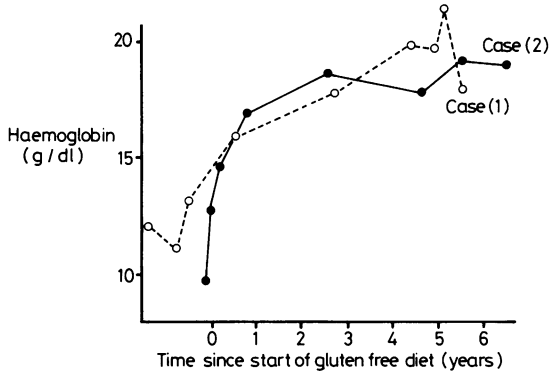

Figure *Haemoglobin in both patients after start of gluten free diet.*

ml/kg) indicating pseudopolycythaemia. Despite a haemoglobin of 18·3 g/dl at present he remains well on no treatment apart from a gluten free diet.

Discussion

Relative polycythaemia can occur acutely after loss of extracellular fluid as in severe burns or dehydration but it may also be chronic. Gaisbock in 1922 described a group of patients who had a high haemoglobin, plethora and hypertension, without the splenomegaly or leucocytosis frequently seen in polycythaemia rubra vera.[2] He termed the condition 'polycythaemia hypertonica' but red cell mass was not determined in these patients. Nonetheless, the term Gaisbock's syndrome is frequently used to describe patients with a high haematocrit the cause of which is unclear. Lawrence and Berlin reported 18 cases in whom low plasma volume appeared to explain the relative polycythaemia.[3] Many of the patients had hypertension and psychosomatic complaints and consequently the term 'stress polycythaemia' was coined. With the advent of techniques to measure red cell mass directly it has become clear that this group of patients have a normal red cell mass,[4,5] differentiating them from the true polycythaemias. Furthermore, the condition is not a precursor of a neoplastic process[6] and follow up does not yield true polycythaemia. The cause of the high haemoglobin is relative haemoconcentration because of reduced plasma volume, often of uncertain cause, and now frequently called pseudopolycythaemia. It appears to be more common in men than women, in middle age and in smokers, and probably also in alcoholics.[7] Symptoms are non-specific or absent but hypertension is found in approximately 50% and facial plethora is often present. The prognosis is generally good although vascular complications may occur.[8,9] Treatment is rarely necessary and radioactive phosphorus should not be used because the marrow is not hyperplastic.[6]

It is of interest that two of our patients should develop pseudopolycythaemia after institution of a gluten free diet for coeliac disease. Both were non-smokers and normotensive. Whatever the cause of the condition it is possible that the predisposition was present in both before diagnosis of the enteropathy and that the haematinic deficiency caused by malabsorption was protecting against the development of a high haemoglobin. Alternatively, a rebound phenomenon may have occurred after removal of an erythropoiesis suppressing toxin analogous to the thrombocytosis which may follow alcohol induced thrombocytopenia.

Neither coeliac disease nor pseudopolycythaemia is particularly rare so that occasionally the two conditions may be expected to concur by chance. The close temporal relationship of the development of pseudopolycythaemia to the commencement of a gluten free diet in these patients is intriguing, however, and suggests a true association which may ultimately shed some light on the mechanism of pseudopolycythaemia and the haematological consequences of coeliac disease.

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