Coeliac disease and pernicious anaemia

Jean-Pierre Ng, S.T. Green, D. Cham Lam1 and S. Shahriari1

Departments of Haematology and Medicine, Stobhill General Hospital, Glasgow and 1Department of Haematology, Hairmyres Hospital, Lanarkshire, UK.

Summary: Despite the often reported autoimmune basis for coeliac disease and pernicious anaemia, there have been only occasional reports of the two conditions occurring together. We wish to report of such an association occurring in a 61 year old patient and comment on the diagnostic and prognostic implications.

Introduction

Pernicious anaemia appears to arise on the basis of a local 'autoimmune' gastritis1 with the appearance of intrinsic factor antibodies in the gastric juice which inhibit any remaining intrinsic factor. In coeliac disease (gluten-sensitive enteropathy), local synthesis of anti-gluten antibodies is increased2 which could result in binding of gluten to intestinal epithelial cells with subsequent tissue damage.3 Coeliac patients have an increased frequency of serum histocompatibility antigen HLA-B8,3 the latter may be linked to immune response genes.4 Pernicious anaemia is associated with various endocrine diseases which are strongly linked with HLA-B8 antigen1 in addition to the HLA-B12 and HLA-BW15. Moreover anti-parietal cell antibodies, which are present in the sera of nearly 90% of patients with pernicious anaemia, have also been found to occur more frequently in association with the dermatitis herpetiformis variant of coeliac disease.5 As pernicious anaemia and coeliac disease are also both relatively common conditions, it is therefore not unexpected to see the two diseases co-exist in some patients. However the combination of coeliac disease and pernicious anaemia occurring in a single patient has been rarely documented.8 This may be due to failure to recognize multiple causes of vitamin B12 deficiency in the same patient.

Case report

A 61 year old woman presented to Hairmyres Hospital with a 6-month history of lethargy, sore

Correspondence: Jean-Pierre Ng, M.R.C.P., Department of Haematology, Coventry and Warwickshire Hospital, Stoney Stanton Road, Coventry, UK. Accepted: 26 May 1988

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cyclophosphamide. However, as she was also troubled with episodic symptoms of hyperviscosity, namely lethargy, headache, dizziness and blurring of vision, she was subjected to intermittent plasma exchange. Five years after presentation, the patient is doing well and as yet there is no clinical, biochemical or immunological evidence of other possible co-existing endocrine or autoimmune disorders.

Discussion

The mechanism of vitamin B\textsubscript{12} deficiency in pernicious anaemia is due to lack of intrinsic factor which is required for effective absorption of the vitamin at the intact terminal ileum. In coeliac disease, there is destruction and atrophy of the small bowel mucosa which leads to impairment of the vitamin B\textsubscript{12} absorption. Vitamin B\textsubscript{12} absorption is impaired in 40\% to 50\% of patients with untreated adult coeliac disease\textsuperscript{1} and subnormal serum vitamin B\textsubscript{12} levels will occur in one third of cases.\textsuperscript{1} However, while the vitamin B\textsubscript{12} deficiency in pernicious anaemia eventually produces a megaloblastic anaemia, that in coeliac disease is usually not severe and probably never leads to a megaloblastic anaemia.\textsuperscript{2} A very low serum vitamin B\textsubscript{12} accompanied by megaloblastic erythropoiesis in a patient with coeliac disease should therefore prompt further investigations to exclude other possible causes of vitamin B\textsubscript{12} deficiency, including pernicious anaemia. One should also be aware of the definite association between pernicious anaemia and hypogammaglobulinaemia\textsuperscript{3} which may present as the malabsorption syndrome.

Coeliac disease is associated with an increased risk of gastrointestinal malignancy, namely intestinal lymphoma but also carcinoma of colon and oesophagus.\textsuperscript{4} Similarly, gastric carcinoma is three times commoner in patients with pernicious anaemia.\textsuperscript{1} Patients with both coeliac disease and pernicious anaemia should therefore be closely followed up with regard to the greater risk of developing gastrointestinal malignancy. Very often iron deficiency, especially in middle-aged or elderly patients, is the first and only clue to gastrointestinal malignancy. However coeliac patients may develop iron deficiency because of intestinal malabsorption and pernicious anaemia may also give rise to iron deficiency because of achlorhydria.\textsuperscript{7} Although it is important to recognize the benign causes of iron deficiency in these two conditions, it is equally important to appreciate the potential danger of not suspecting gastrointestinal malignancy early in those patients who are already on iron supplements for reasons stated above. They should also be screened for a wide group of other autoimmune disorders which may co-exist.\textsuperscript{8}

Finally, the co-existence of Waldenstrom's macroglobulinaemia (a B-cell lymphoproliferative disorder) in this case raises an interesting hypothesis that a common primary immunological disturbance might underline the development of pernicious anaemia, coeliac disease and Waldenstrom's macroglobulinaemia in this patient.

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References

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