

# Coeliac disease and pernicious anaemia

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**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' gastritis<sup>1</sup> 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 increased<sup>2</sup> which could result in binding of gluten to intestinal epithelial cells with subsequent tissue damage.<sup>3</sup>

Coeliac patients have an increased frequency of serum histocompatibility antigen HLA-B8,<sup>3</sup> the latter may be linked to immune response genes.<sup>4</sup> Pernicious anaemia is associated with various endocrine diseases which are strongly linked with HLA-B8 antigen<sup>1</sup> 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.<sup>5</sup> 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.<sup>8</sup> This may be due to failure to recognize multiple causes of vitamin B<sub>12</sub> deficiency in the same patient.

## Case report

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

mouth, abdominal pain, steatorrhoea, night sweats and weight loss. Physical examination revealed an anaemic emaciated looking patient with small axillary and inguinal lymphadenopathy but no hepatosplenomegaly. Fundoscopy showed marked retinal vein engorgement.

Investigations showed a macrocytic anaemia with haemoglobin concentration 85 g/l and mean cell volume 119 fl; white cell and platelet counts were normal. ESR was 126 mm in the first hour. Haematinic assays were as follows: serum vitamin B<sub>12</sub> 89 ng/l (normal range 270–900), red cell folate 149 ng/ml (normal range 170–700), serum iron 26 µmol/l (normal range 14–29), total iron binding capacity 36 µmol/l (normal range 45–72) and iron saturation 72% (normal range 15–35). Schilling test showed malabsorption of vitamin B<sub>12</sub> which was corrected by addition of intrinsic factor. A diagnosis of pernicious anaemia was made. Bone marrow examination showed megaloblastic erythropoiesis but also a diffuse infiltration by lymphoplasmacytoid cells. Serum immunoglobulin assays and protein electrophoresis showed normal levels of IgG and IgA but an IgM paraprotein of 34 g/l. A second diagnosis of Waldenstrom's macroglobulinaemia was made. The results of xylose excretion test and faecal fat measurement indicated intestinal malabsorption. A small bowel biopsy was performed and the histology showed villous atrophy, crypt hyperplasia and plasma cell infiltrate with no evidence of giardiasis or lymphoma. A third diagnosis of coeliac disease was made.

Her abdominal pain and steatorrhoea soon settled following a gluten-free diet. However, it took 2 years of the gluten-free diet before the mucosal villi of the small intestine returned to normal. She received regular intramuscular injections of vitamin B<sub>12</sub> for her pernicious anaemia. For her Waldenstrom's macroglobulinaemia she was started on oral

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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<sub>12</sub> 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<sub>12</sub> absorption. Vitamin B<sub>12</sub> absorption is impaired in 40% to 50% of patients with untreated adult coeliac disease<sup>1</sup> and subnormal serum vitamin B<sub>12</sub> levels will occur in one third of cases.<sup>1</sup> However, while the vitamin B<sub>12</sub> 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.<sup>2</sup> A very low serum vitamin B<sub>12</sub> accompanied by megaloblastic erythropoiesis in a patient with coeliac disease should therefore prompt further investigations to exclude other possible causes of vitamin B<sub>12</sub> deficiency, including pernicious anaemia. One should also be aware of the definite association between pernicious anaemia and hypogammaglobulinaemia<sup>1</sup> which may present as the malabsorption syndrome.

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