Coeliac disease in an Indian patient: an important diagnosis to consider

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Clinical record

A 47-year-old woman — an Australian resident of North Indian origin — was referred to our outpatient clinic. She had a 4-year history of lethargy on a background of primary hypothyroidism that was diagnosed 2 years earlier. She reported weakness, myalgia, poor concentration and chronic diarrhoea, which had been attributed to irritable bowel syndrome after a colonoscopy found no abnormalities. Given her racial origin, coeliac disease had not previously been considered. Rather, a chronic pain syndrome was diagnosed as the cause of the myalgia, and was managed with narcotic analgesia. The patient's medications also included thyroxine (50 μg daily). Her body mass index was 29.5 kg/m^2; normal findings were obtained on physical examination, and she was clinically euthyroid on thyroxine replacement.

Hashimoto's hypothyroidism with under-replacement of thyroxine, secondary hyperparathyroidism with vitamin D deficiency, and impaired fasting glycaemia were biochemically confirmed (Table). A high vitamin B_{12} level was also noted, and this was attributed to recent intramuscular injection of vitamin B_{12}. Bone density was measured using the Lunar Prodigy DXA system (GE Healthcare, Madison, Wis, USA), which revealed osteopenia with lumbar bone mineral density (BMD) of 1.02 g/cm^2 (T-score, –1.9 SD) and total femoral BMD of 1.02 g/cm^2 (T-score, –1.6 SD).

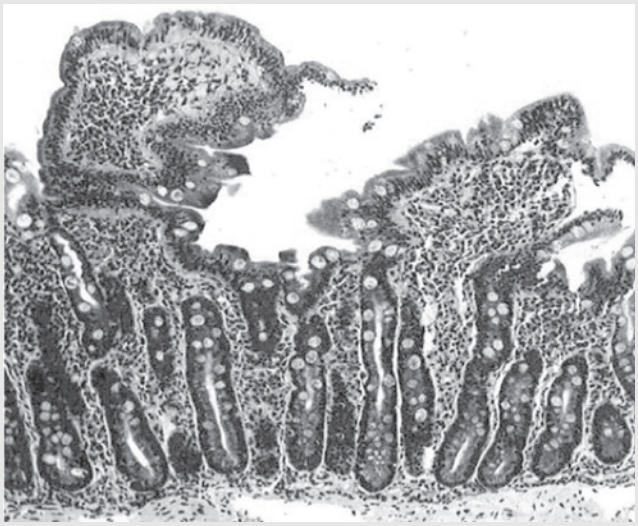
Titration of thyroxine to a weekly dose of 1400 μg and vitamin D_3 replacement dosage of 6000 IU daily, over a 6-month period with confirmed compliance, failed to ameliorate hypothyroidism and vitamin D deficiency. In view of her history, previous investigations and progress, serological testing for coeliac disease was carried out. Results were positive for endomysial IgA antibodies, with normal total IgA antibody titre. Also, histological analysis of a small bowel biopsy specimen was consistent with coeliac disease (Figure).

A 6-month gluten-free diet resulted in complete resolution of lethargy, diarrhoea and myalgia. Hypothyroidism was corrected with a weekly dose of 750 μg thyroxine, and both secondary hyperparathyroidism and impaired fasting glycaemia resolved (Table).

Results of laboratory investigations

	At presentation	After 6 months of gluten-free diet	Reference range
Thyroid-stimulating hormone (mIU/L)	13.4	8.3	0.3–4.0
Thyroxine, free (pmol/L)	12	15	10–25
Thyroid antimicrosomal antibody titre	25 600	—	< 100
Calculated ionised calcium (mmol/L)	1.08	—	1.00–1.25
25-hydroxyvitamin D (nmol/L)	< 15	34	40–150
Parathyroid hormone (pmol/L)	6.0	4.5	1.0–5.2
Fasting glucose (mmol/L)	6.3	5.4	< 5.6
Glycated haemoglobin (%)	6.2	5.5	< 6.0
Vitamin B_{12} (pmol/L)	> 1470	—	145–637
Ferritin (μg/L)	124	—	15–200

Histological examination of small bowel mucosa



Histological examination showed focal, partial villous atrophy and crypt hyperplasia, with evidence of chronic inflammation in the lamina propria (original magnification, x 400) — consistent with coeliac disease. ◆

While the prevalence of coeliac disease in the European population has been estimated to range from 1 in 150 to 1.5 in 1000,[1] the prevalence in the Indian population is unknown due to lack of population-based data,[2] leading to the common misconception that coeliac disease is rare. However, recent studies using new serological screening methods have demonstrated gross underdiagnosis of coeliac disease in the past,[1-3] and an unexpectedly frequent prevalence in countries populated by non-Europeans. The highest reported population prevalence is in the Saharawi people of Arab–Berber origin, who live in the Sahara desert, with a prevalence of 5.6% — almost tenfold higher than that reported from most European countries.[4] Similarly, recent studies in India found a prevalence of 9%–26% in patients who presented with chronic diarrhoea or malabsorption.[5,6]

The pathogenesis of coeliac disease is related to intolerance of gluten that results in a T-lymphocyte-mediated, small intestinal enteropathy in genetically predisposed individuals, who commonly express the HLA-DQ2 or HLA-DQ8 haplotypes.[7] Such genetic predisposition is common in Europeans, but also occurs in Indian patients, as evident from detection of the HLA-DQ2 heterodimer in 14 out of 15 North Indian patients with coeliac disease.[8] The HLA-DQ2 haplotype is also found in almost 25% of

Lessons from practice

- Coeliac disease is not limited to Europeans; it has been increasingly reported in patients from non-European backgrounds.
- Not all patients with coeliac disease are underweight, and a significant minority are overweight or obese.
- Serological testing is non-invasive and should be considered in patients with suggestive symptoms or associated autoimmune conditions, regardless of racial background.
- Presentation of coeliac disease can be non-specific, and is not limited to gastrointestinal manifestations. A high index of suspicion is required to screen for the condition in patients with predominant extraintestinal presentation. ◆

the healthy North Indian population, similar to the Western population,[9] which has led to speculation that some Indians share ancestral origin with "ancient Caucasians" from the Fertile Crescent.[9,10]

Environmental challenge from the increasingly popular Western diet, which is gluten-rich, may also contribute to observed changes in the epidemiology of coeliac disease. For example, "summer diarrhoea" has been described in communities of Punjabis and Gujaratis from India. Traditionally, wheat replaces maize during summer in India, and Punjabis and Gujaratis residing in England and Canada have been reported to develop coeliac disease when exposed to a gluten-rich diet.[11,12]

Another misconception about coeliac disease patients is that they are all underweight. In one study, the mean body mass index of 371 patients with coeliac disease was 24.6 kg/m^2, with only 5% being underweight, while 39% and 13% were in the overweight and obese ranges, respectively.[13] Our patient's body mass index was in the overweight range, which may have contributed to the delay in diagnosis until she was referred to our clinic.

Coeliac disease is also associated with a wide range of autoimmune conditions. The presence of Hashimoto's hypothyroidism was a clue to an autoimmune cluster in our patient, and persistent hypothyroidism despite large replacement doses of thyroxine is highly suggestive of a malabsorption disorder, such as coeliac disease.

The complex symptomatology of our patient illustrates the non-specific, extraintestinal manifestations of coeliac disease, including lethargy, neuropsychiatric complaints, and myalgia from vitamin D deficiency; the latter may also lead to impaired insulin secretion and result in impaired fasting glycaemia.[14] A high index of suspicion is required to screen for the disease, which is associated with significant morbidity.

In conclusion, screening for coeliac disease with serological testing is non-invasive and should be considered in Indian patients with suggestive symptoms or associated autoimmune conditions. It is important for clinicians to overcome historical bias and consider coeliac disease as a diagnosis in non-European patients. Early diagnosis may help to avoid unnecessary investigation and reduce the long-term risk of small bowel malignancies associated with coeliac disease. Compliance with a gluten-free diet not only reduces symptoms, but also rectifies malabsorption of micronutrients and medications, which impact on comorbidity such as, in this case, abnormalities of thyroid replacement and metabolism of bone and glucose.

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References

1 Fasano A, Berti I, Gerarduzzi T, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. *Arch Intern Med* 2003; 163: 286-292.
2 Bhatnagar S, Tandon N. Diagnosis of celiac disease. *Indian J Pediatr* 2006; 73: 703-709.
3 Sood A, Midha V, Sood N, et al. Increasing incidence of celiac disease in India. *Am J Gastroenterol* 2001; 96: 2804-2805.
4 Catassi C, Doloretta Macis M, Rätsch IM, et al. The distribution of DQ genes in the Saharawi population provides only a partial explanation for the high celiac disease prevalence. *Tissue Antigens* 2001; 58: 402-405.
5 Ranjan P, Ghoshal UC, Aggarwal R, et al. Etiological spectrum of sporadic malabsorption syndrome in northern Indian adults at a tertiary hospital. *Indian J Gastroenterol* 2004; 23: 94-98.
6 Sachdev A, Srinivasan V, Maheswary S, et al. Adult onset celiac disease in north India. *Trop Gastroenterol* 2002; 23: 117-119.
7 Schuppan D. Current concepts of celiac disease pathogenesis. *Gastroenterology* 2000; 119: 234-242.
8 Agrawal S, Gupta A, Yachha SK, et al. Association of human leucocyte-DR and DQ antigens in coeliac disease: a family study. *J Gastroenterol Hepatol* 2000; 15: 771-774.
9 Kaur G, Sarkar N, Bhatnagar S, et al. Pediatric celiac disease in India is associated with multiple DR3-DQ2 haplotypes. *Hum Immunol* 2002; 63: 677-682.
10 Catassi C. Where is celiac disease coming from and why? *J Pediatr Gastroenterol Nutr* 2005; 40: 279-282.
11 Sher KS, Fraser RC, Wicks AC, Mayberry JF. High risk of coeliac disease in Punjabis. Epidemiological study in the south Asian and European populations of Leicestershire. *Digestion* 1993; 54: 178-182.
12 Freeman HJ. Biopsy-defined adult celiac disease in Asian-Canadians. *Can J Gastroenterol* 2003; 17: 433-436.
13 Dickey W, Kearney N. Overweight in celiac disease: prevalence, clinical characteristics, and effect of a gluten-free diet. *Am J Gastroenterol* 2006; 101: 2356-2359.
14 Pittas AG, Lau J, Hu F, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab* 2007; 92: 2017-2029.

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