

CASE STUDY OF Ms BM – COELIAC DISEASE

Jim Bartley, MBChB, FRACS, FFPMANZCA

PRESENTING HISTORY

Ms BM was a 29-year-old European lady who presented with a 4-year history of left cheek pain. The pain was continual, rated 6/10 in severity and could be associated with nausea and vomiting. The pain was said to have started following an episode of infective sinusitis. She mentioned that she might have been iron deficient at the time. She had had extensive dental work done looking for a dental cause of the pain. Three dentists and three otolaryngologists had been unable to find a cause for the pain. She had no neck pain, shoulder pain or low back pain. There were no irritable bowel symptoms or period problems. There was no past history of anxiety or depression. The pain was poorly controlled with conventional anti-inflammatory drugs and Amitriptyline. She had had normal ultrasound and MRI scans of the area. Previous blood tests had shown an iron deficiency, but no anaemia. She was married with two children. She had tertiary and post-graduate qualifications.

EXAMINATION

Height 165 cm, weight 42kg, BMI 16. Tender left masseter muscle; palpation of muscle replicates pain. No other significant physical findings. Trigger point in left masseter muscle.

INITIAL MANAGEMENT

1. Injection of the left masseter muscle with local anaesthetic. This completely relieved the pain for 6 days.
2. She was advised regarding heat and self massage techniques to the masseter muscle.
3. Investigations were initially performed firstly to exclude metabolic causes for the trigger point and secondly looking for causes of the repeated iron deficiency.

RESULTS OF INITIAL INVESTIGATIONS

Iron 12µg/L, ferritin 42µg/L, vitamin B12 528pmol/L, zinc 11 µmol/L and random urinary iodide 50µmol/L, tissue transglutaminase (IgG) 2 and tissue transglutaminase (IgA) 2, Vitamin D 69 nmol/L, MCV 86fl and MCH 27pg.

INITIAL MANAGEMENT UPON RECEIPT OF INVESTIGATIONS

She was advised to take vitamin D, zinc and iodine. A gluten-free, dairy-free diet was also discussed but the patient was extremely reluctant to trial this.

A blood test 3 months later showed an iron level of 3µmol/L. Because of the long history of intermittent iron deficiency and her low BMI, she was sent to a gastroenterologist to exclude Coeliac Disease (CD) as a cause of her persisting iron deficiency. The duodenal biopsies (six) were positive for CD:

“Villi are of a variable height, some quite short. The lamina propria contains increased chronic inflammatory cells. The surface epithelium is heavily infiltrated by lymphocytes. No parasites are identified. Appearances are consistent with coeliac disease.”

SUBSEQUENT MANAGEMENT

When placed on a gluten-free diet her pain resolved almost completely and she was able to stop all pain medication. She put on 2kg in weight. Despite my advice to also go dairy free she was reluctant to and did not do this.

DISCUSSION

This case illustrates the difficulties in diagnosing CD. Classic textbook symptoms include abdominal bloating, vomiting, diarrhoea, weight loss, and in children, stunted growth. However abnormal bowel symptoms, particularly in adults and also in this case, may be limited or even absent. With this patient, the clue was the repeated low iron levels. There was very little on blood testing alone that caused one's suspicions to be raised. There were minimal other clues to suggest other nutritional deficiencies. MCV and MCH were in the lower half of the normal range. While she was zinc deficient, zinc deficiency is common in the New Zealand population. New Zealand soils are frequently deficient in both zinc and selenium. Blood testing for zinc status is also notoriously unreliable. While this lady had a low BMI in keeping with CD, this is not necessarily a reliable clinical sign¹.

INVESTIGATIONS

Antibody testing for transglutaminase IgA antibodies has a reported sensitivity (diagnosis of disease) of greater than 90% and a specificity (exclusion of disease) of greater than 95%. HLA testing is more useful in excluding CD. Duodenal biopsy remains the gold standard due to the false-negative rate associated with serology alone. This was the situation with this patient. Multiple samples (ideally 6) need to be taken from the second part of the duodenum and beyond on endoscopy. Not all areas may be equally affected; if biopsies are taken from healthy bowel tissue, the result will be a false negative².



PATHOPHYSIOLOGY

CD is a complex multifactorial condition in that while genetic factors are important, other factors are necessary for the disease to manifest itself. The vast majority of coeliac patients express the HLA-DQ2 or HLA-DQ8 genes, which are part of the MHC class II antigen presenting receptor system distinguishing cells between self and non-self in the immune system. However in the West, 25-30% of the population express HLA DQ2 and are exposed to gluten, but only a minority develop CD. Around 5% of patients with CD do not have the HLA-DQ2 gene³. The HLA-DQ molecules bind to and present gluten derived peptides to T lymphocytes, initiating the autoimmune process. Most coeliac patients have a two-gene HLA-DQ2 haplotype referred to as DQ2.5 haplotype. While most coeliac patients inherit only one copy of this DQ2.5 haplotype, some inherit it from both parents. This latter group is especially at risk for CD, as well as being more susceptible to severe complications⁴. The frequency of the HLA-DQ genes varies geographically. DQ2.5 has a high frequency in peoples of North and Western Europe; Ireland particularly has a high frequency⁵. While genetic predisposition is a factor, the amount of gluten in the diet may also predispose people to CD. In the Swedish CD epidemic an increase in gluten content in the food resulted in a tripling of CD incidence⁶. However a diet high in gluten is also recognised to cause intestinal damage, regardless of whether a person has CD or not⁷.

Gliadin in wheat belongs to a group of storage proteins called prolamins, rich in proline (*prol*-) and glutamine (*-amin*). Hordein in barley and secalin in rye are also prolamins. One particular region in α -gliadin stimulates enterocytes in the gut allowing the leakage of larger molecules between the cells. These gliadin peptides then stimulate both the innate and the adaptive (T-helper cell mediated) immune

response. The innate immune response to gliadin results in inflammation.

The enzyme tissue transglutaminase (τ TG) generates gluten peptides that bind with high affinity to HLA-DQ2 or HLA DQ8. Antibodies to the enzyme τ TG are present in most coeliac patients. Gluten peptides are modified by τ TG in two ways, deamination or transamination. In deamination, a glutamate residue is formed. In transamination, cross-linking of a glutamine residue from the gliadin peptide to a lysine residue of τ TG occurs. Cross-linking may occur either within or outside the active site of the enzyme. This results in the formation of new epitopes, which are believed to then trigger the primary immune response by which the autoantibodies against τ TG develop^{8,9}. The inflammatory process, mediated by T cells, leads to disruption of the structure and function of the small bowel's mucosal lining causing malabsorption.

MUSCLES AND COELIAC DISEASE

Myopathy in the context of gluten sensitivity exists, but has not been well characterized. The myopathy normally presents as a proximal muscle weakness. Endomysium-specific antibodies (antibodies that bind with high affinity to cell-surface τ TG) are thought to be involved, but these are also the most sensitive markers for the presence of enteropathy, which were not present in this patient. A spectrum of abnormalities has been described on muscle histology in gluten sensitivity-associated myopathy. Muscle inflammation is a common feature. IgA deposits against τ TG have been demonstrated in extra intestinal target sites such as muscle in a patient with coeliac disease and myopathy and cerebellar tissue in a patient with gluten ataxia. Myopathy may be a manifestation of gluten sensitivity and may have an immune mediated pathogenesis¹⁰.

CONCLUSION

This case report documents an unusual presentation of CD, where a high index of clinical suspicion was necessary to make the diagnosis. The reasons for the isolated masseter muscle pain are difficult to explain, but a potential etiological mechanism is described.

References:

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