LETTERS

Coeliac genetic testing: prone to misuse
Neil J Porter, Huy A Tran and Glenn EM Reeves

TO THE EDITOR: Optimism about our growing ability to recognise coeliac disease (CD) is tempered by a worrying trend towards misuse of genetic testing for CD risk, as illustrated by this salutary case.

A 42-year-old woman with nausea and lethargy attended her doctor, concerned that she may have CD, because her niece had the condition, and she knew it was “genetic”. A laboratory representative had told her doctor that a test for the HLA-DQ gene was the best test for CD; this test was performed, and detected genotype susceptibility for CD (HLA-DQ2 and HLA-DQ8 alleles). The patient was told she had CD and was referred to a dietitian to commence a gluten-free diet. She contacted the Coeliac Society of Australia and learned that this was an unusual way of diagnosing CD. This led to her being referred to a gastroenterologist.

Further testing showed normal IgA and IgG transglutaminase antibody (TGA) levels (8 enzyme-linked immunosorbent assay [ELISA] units [reference range, 0–20 ELISA units]), and normal iron, folate and IgA levels. Mild nausea and diagnostic ambiguity prompted gastroscopy and duodenal biopsy. Findings of these tests were normal, showing no intraepithelial lymphocytosis.

CD is common, affecting up to 1% of Australians,1 and causing a spectrum of complaints from classic malabsorption to more subtle problems (eg, osteoporosis and iron deficiency). It is clarified by sensitive serological detection methods (TGA levels).2 This gluten-triggered autoimmune disease represents one of the best characterised models of gene–environment interaction, in that an “at-risk” genome is needed to provide disease predisposition.3 However, CD genotyping (looking for HLA-DQ2 and HLA-DQ8 alleles) is increasingly requested under the misconception that a “genetic” test must be a more reliable detector of disease than other tools.

The HLA risk genotype is necessary but not sufficient for development of CD: 20% of Australians share this risk factor, but only 5% of these express CD. Serological testing (TGA) provides approximately 90% sensitivity and specificity for CD in the appropriate clinical setting, but the diagnostic “gold standard” still involves biopsy confirmation of gluten-responsive tissue changes to justify the life-long social and financial costs of gluten avoidance.

CD genotyping should be considered when: gluten challenge is not possible or acceptable; serological–histological discrepancies exist; or endoscopic biopsy is difficult or potentially non-diagnostic (eg, certain paediatric cases, or patients being treated with anticoagulants or immunotherapies [eg, prednisolone] that may normalise biopsy appearances).

Our group is seeing more misuse of CD genotyping, with some practitioners using a positive result to confirm CD. As a centre of expertise in CD, we recommend that CD genotyping be confined to its negative predictive role: negative CD genotyping indicates a substantially reduced likelihood of CD (< 1%).4

Competing interests: Hunter Area Pathology Service performs diagnostic tests for coeliac disease, including serology and genetic testing.

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