CASE REPORT

'For a quart of ale is a dish for a king': not always

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SUMMARY

We report the case of a man with a clear diagnosis of coeliac disease who nevertheless drank gluten-containing beer. We found that a 4-week period of drinking gluten-containing beer did not provoke significant changes in the intestinal mucosa of this patient with coeliac disease nor did it elicit any relevant symptoms. Serum antibody levels rose but did not reach a pathological threshold. However, a more prolonged gluten challenge may have led to clinically relevant changes in IgA antitransglutaminase titres. This case demonstrates how important individual sensitivity to gluten in a patient with coeliac disease is in determining symptoms, immunological response and intestinal mucosa damage.

BACKGROUND

Patients with coeliac disease often claim symptoms related to occasional gluten intake due to contamination of food that they thought to be gluten-free. However, it is hard to demonstrate that inadvertent gluten intake is always the cause of the gastrointestinal symptoms in a patient with coeliac disease.

On the other hand, many patients with coeliac disease request permission for some lapses in their gluten-free diet (GFD), claiming that inadvertent or intentional gluten intake provokes no symptoms. We present this case to show how patients' tolerance to gluten is unpredictable in determining symptoms, intestinal damage and the rise in gluten-related serum antibodies. Clinical or research purposes may require a gluten challenge, so as to verify a coeliac disease diagnosis or when planning clinical trials. Individual sensitivity is relevant in designing a gluten challenge but the need for standardisation often overlooks the variable individual response.

CASE PRESENTATION

We report a case of a 40-year-old man, a 'slow-food' blogger and sommelier. He loved beer and had once been a connoisseur of beer, but no longer, because he discovered he had coeliac disease. The unequivocal coeliac disease diagnosis was made based on gastrointestinal symptoms, the presence of serum antitransglutaminase IgA (a-TTG IgA) antibodies and antiendomysial antibodies, and an intestinal biopsy showing intestinal damage. The patient had started a GFD 3 years before this visit. Occasionally, he would drink beer containing variable amounts of gluten. Aside from consuming these small amounts of beer, he was very well compliant with the GFD.

Several beers contain gluten, specifically those derived from malt barley.¹ However, after the coeliac disease diagnosis, this patient's interest in beer did not change, but only shifted to gluten-free

beer, and he currently studies fermentation processes that can reduce the gluten content in beer. The notion that the fermentation process may reduce the gluten content of beer is popular, and patients with coeliac disease, as did our patient, often request permission to drink beer.

Our patient asked us to test his tolerance to beer gluten content with a complete work up for coeliac disease before and after a 4-week period with addition of a gluten-containing beer to his diet. During the 'beer challenge', our patient with coeliac disease liberally drank beer (on some days up to 4000 mL) with a gluten content ranging from 150 to >800 mg/L (average beer gluten content 623 mg/L).

INVESTIGATIONS

We performed a complete work up for coeliac disease before and after the 4-week beer challenge, including recording of symptoms, anthropometry, upper endoscopy and intestinal biopsy. Serology for coeliac disease was investigated before and weekly during the beer challenge, up to 2 weeks after the end of the challenge. The challenge took place during a beer festival the patient was keen to attend. The participant tasted or drank any beer he wanted to, keeping an accurate record of the type and quantity of the beer. In the month before, during the challenge and up to 2 weeks after the beer challenge, the patient observed a strict GFD. Therefore, he underwent endoscopy with duodenal biopsies before and after the beer challenge, and investigation for a-TTG IgA and a-TTG IgG antibodies every week up to 2 weeks after the end of the challenge.

DIFFERENTIAL DIAGNOSIS

After the beer challenge, we found endoscopic and histology signs of acute gastritis. Acute gastritis could be related to alcohol consumption and/or gluten-related damage. However, the fact that this patient's duodenal mucosa after the challenge did not show any histological change nor signs of inflammation suggests the possibility that his acute gastritis may have been mainly due to the (excessive) alcohol intake.

The patient reported modest abdominal bloating. Again, bloating can be due to both beer consumption (source of fermentable sugars), and/or beer's gluten content and subsequent malabsorption. Also, in this case, the absence of histological signs of intestinal damage suggests that beer intake may have been responsible for the abdominal bloating.

TREATMENT

Strict GFD and moderate alcohol consumption.

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OUTCOME AND FOLLOW-UP

Before introduction of the gluten-containing beer, a normal gastric and duodenal mucosa was described at endoscopy. Gastric biopsies showed superficial inflammation confined mainly to mucosa occupying gastric pits, with no *Helicobacter pylori* infection. The duodenal mucosa was also undamaged; intraepithelial lymphocytes count was <25/100 enterocytes (Corazza–Villanacci 0).

During the beer challenge, the patient was on a strict GFD and registered no clinically relevant symptoms besides some modest bloating that he related to the quantity of beer intake (the greater the intake, the greater the feeling of bloating). The endoscopy performed after the challenge showed the presence of acute gastritis, which was confirmed by histology (figure 1). Unexpectedly, the histology of the duodenal mucosa was comparable with that of the prechallenge. In particular, we were not able to detect any modification in the intraepithelial lymphocyte count nor to find significant TTG 2 deposits in the mucosa. Figure 2 shows that, 2 weeks after the beer challenge, the serum a-TTG IgA antibody level, although always within the normal range, was increased $\times 10$ compared with baseline; the greatest value detected was 1.6 U/mL, well below the limit of 7 that is the cut-off value for positivity.

DISCUSSION

Studies have demonstrated that a 2-week period of a gluten challenge with 3 g gluten/day was sufficient time to provoke intestinal lesions in 20 patients with coeliac disease.² In this case, a gluten challenge with a quantity of gluten below the standardised 3 g/day but for twice the time (4 weeks), provoked no symptoms; an increase in a-TTG levels; but no relevant mucosal damage. However, we hypothesise that a more prolonged gluten challenge may have led to clinically relevant changes in a-TTG IgA titres.

Considering gluten tolerance is important, as patients and physicians always attribute gastrointestinal symptoms during GFD to gluten contamination. Gluten quantity and time of exposure are relevant, but individual tolerance may play a significant role.

Our case confirms that the design of a gluten challenge—when needed—is, in itself, a challenge.

Therefore, larger trials are needed to standardise the gluten challenge methodology.

Firstly we discouraged the patient from introducing gluten-containing beer to his diet, even if for a short period. However, since he was determined to take this challenge regardless of our

Figure 2 Time course of antitransglutaminase IgA and IgG antibodies levels. a-TTG, antitransglutaminase.

advice, we decided to follow the case. The case gives a valuable opportunity to demonstrate how patients' tolerance to gluten is unpredictable in determining symptoms, intestinal damage and the rise in gluten-related serum antibodies. The beer challenge is not the model for a clinical trial for several reasons. First, the beer challenge was a request from a patient who was going to voluntarily expose himself to gluten. Second, we could not standardise the daily amount of gluten intake due to the variability of gluten content in beers from artisanal brewing and the variable volume drunk per day. Third, a gluten challenge involving the usage of alcohol as a gluten-containing medium must be discouraged. This procedure might expose the patient to various risks of a psychophysiological nature and impede good observation of clinical signs.

Despite the fact that we could demonstrate only a clinically insignificant rise in TTG levels, at the end of our experiment, our advice to this patient with coeliac disease was to stay on the safe side and to limit his exposure to safe gluten-free beers.

Shakespeare was not aware, back in his time, that ale is not a dish for a king with coeliac disease.

Patient's perspective

I now have clear in my mind that gluten-containing beers are not the right choice for me, nor for other patients with coeliac disease, and that symptoms are not a guide to testing gluten tolerance. I wrote an article describing my experience and hope that my experience might be of help to other people.

Learning points

- ▶ There are few studies about how to design a gluten challenge; one indication is that 3 g of gluten/day is a sufficient amount and a 2-week period ample time.
- ▶ Individual sensitivity/tolerance plays a significant role in determining gluten-induced damage, and this fact is indeed overlooked in planning a gluten challenge.
- ▶ A gluten concentration lower than 3 g/day but for a longer period (4 weeks) it is not enough to determine symptoms nor can it assess clinically significant immunological damage.
- ▶ This case demonstrates that the variable gluten sensitivity of those with coeliac disease may require caution when attributing the disease to gluten, if any gastrointestinal symptoms appear while following a gluten-free diet.

Figure 1 Endoscopy: gastric mucosa appearance at follow-up.

Contributors CC designed the study and performed the procedure. FZ assisted the patient during the challenge. IR and AM performed the laboratory work up. All the authors wrote the manuscript and approved the manuscript.

Competing interests None declared.

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