Diseases of the Esophagus (2011) **24**, 470–475
DOI: 10.1111/j.1442-2050.2011.01190.x

DISEASES OF THE ESOPHAGUS

Review article

Esophageal manifestations of celiac disease

A. J. Lucendo

Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Ciudad Real, Spain

SUMMARY. **Celiac disease (CD) may often be associated with various motor disorders affecting the different segments of the digestive tract, including the esophagus. Although it has not been universally reported, some available evidences indicate that pediatric and adult celiac patients could manifest a higher frequency of esophagitis and gastroesophageal reflux disease-related symptoms compared to nonceliac patients. In addition, several published studies have consistently shown the efficacy of a gluten-free diet in rapidly controlling esophageal symptoms and in preventing their recurrence. Since the participation of gluten in the esophageal symptoms of CD seems clear, its intimate mechanisms have yet to be elucidated, and several hypothesis have been proposed, including the specific immune alterations characterizing CD, the reduction in nutrient absorption determining the arrival of intact gluten to distal gastrointestinal segments, and various dysregulations in the function of gastrointestinal hormones and peptides. Recent studies have suggested the existence of a possible relationship between CD and eosinophilic esophagitis, which should be more deeply investigated.**

KEY WORDS: **celiac disease, eosinophilic esophagitis, gastroesophageal reflux, nonerosive reflux disease, peptic esophagitis.**

ABBREVIATIONS: CD, celiac disease; EE, erosive esophagitis; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter, NERD, nonerosive reflux disease

INTRODUCTION

Celiac disease (CD) is frequently associated with motility disorders affecting the digestive tract. Up to 60% of untreated celiac patients may report symptoms consistent with motility disorders of the upper gastrointestinal tract,[1] specially affecting the stomach and small bowel, and the association of CD with gallbladder and colonic dysmotility has also been described. In the last few years, several studies have described CD patients presenting with esophageal symptoms,[2] whose association is increasingly recognized, despite the fact that it has not been widely studied. Recent evidences show that untreated celiac patients can develop clinical symptoms consistent with gastroesophageal reflux disease (GERD), and it has been postulated that there is an association between CD and eosinophilic esophagitis (EoE), a chronic allergic inflammatory condition characterized by predominant esophageal symptoms.

Institution of a gluten-free diet (GFD) has been associated with improvement and/or resolution of esophageal symptoms in celiac patients, who usually have limited responses to antisecretory treatment. This leads us to the consideration of whether the presence of CD should be actively excluded in patients with atypical esophageal symptoms or who are nonresponsive to conventional treatments.

These questions are discussed on the following pages through a review of the literature. A search was performed using the Medline and Cochrane libraries combining the following key words: celiac disease, gluten-sensitive enteropathy, gastroesophageal reflux disease, reflux symptoms, esophagitis, and eosinophilic esophagitis. Articles concerning both pediatric and adult populations were considered. References to the articles obtained were also searched in order to identify other potential sources of information.

Address correspondence to: Dr Alfredo J. Lucendo, MD, PhD, Department of Gastroenterology, Hospital General de Tomelloso, Vereda de Socuéllamos, s/n, 13700 Tomelloso, Ciudad Real, Spain. Email: alucendo@vodafone.es
Conflict of interests: Nothing to declare.

GERD AND CD

GERD is a clinical condition defined by chronic symptoms with a tendency to relapse, and characterized by high response rates to proton pump inhibitors (PPI). The presence of endoscopic lesions determines the subclassification between erosive esophagitis (EE) and nonerosive reflux disease (NERD). A few articles in recent years have prospectively explored the association between both diseases and CD through case series studies. Available studies have evaluated different aspects of this association by using endoscopy, clinical questionnaires, and, in some cases, by esophageal manometry and pH-metry, which are presented below.

Presence of reflux esophagitis in celiac patients

The association between CD and the presence of GERD-related endoscopic lesions was described some time ago, but available evidence shows inconsistent results. In both pediatric[2] and adult celiac patients,[3] a high prevalence of reflux esophagitis has been reported (defined by the presence of at least one erosion in the distal mucosa of the esophagus observed during endoscopy). Cuomo *et al.* found that up to 19% of 205 celiac adults studied in their series had at diagnosis some erosions in the distal mucosa of the esophagus (compared to only 8% of nonceliac dyspeptic controls, $P < 0.0001$), with no differences in the frequency of hiatal hernia between both groups. A recent study of Lamanda *et al.* documented esophageal lesions in 23% of 65 adult patients diagnosed with CD over a year,[4] a proportion far above that was established for the general population.

In contrast, two studies have shown conflicting results. Oderda *et al.* found that celiac children had a lower prevalence of esophagitis than nonceliac children.[5] In turn, Collin *et al.* studied the prevalence of esophagitis and CD in a large series of predominantly adult patients referred from general practitioners for endoscopic examination. They found that patients with esophagitis, with or without symptoms of GERD, did not show an increased risk of CD.[6]

Prevalence of GERD-related symptoms in celiac patients

Several papers have estimated the prevalence of GERD-related symptoms in celiac patients, and available data suggest that, at diagnosis, celiac patients exhibit GERD-related symptoms at a higher frequency than in control population. In a recently published study, Nachman *et al.* observed that up to 30.1% out of the 133 adult celiac patients showed mild to severe symptoms of GERD (defined as score >3 in the Gastrointestinal Symptoms Rating Scale[7]), compared to only 5.7% in controls ($P < 0.001$).[8] Usai *et al.* found in another study that 27.6% out of 105 celiac patients enrolled reported GERD-related symptoms of heartburn or acid regurgitation after a standard interview. All cases were NERD patients because no visible mucosal damage was found.[9] Lamanda *et al.* documented, in a series of 65 adult celiacs, 11 cases of NERD (with a prevalence of 17%), the symptoms being moderate in seven patients and severe in four patients.[4] Iovino *et al.* reported a relationship between severity of CD and prevalence of esophageal symptoms on documenting a significantly higher frequency of esophageal symptoms in celiac patients with steatorrhea compared to those without steatorrhea and to control subjects.[2]

In contrast, a study by Collin *et al.* was unable to report a greater prevalence of esophageal disorders in CD,[6] concluding that GERD would not be a major symptom of CD.

pH-metric alterations in patients with CD

Twenty-four-hour esophageal pH monitoring is an objective method to document the presence of pathological gastroesophageal reflux. However, this information has not been systematically assessed in published articles on the relationship between GERD and CD, since only two studies have analyzed some patients using this technique.

Cuomo *et al.* determined esophageal pH monitoring in only 15 out of the 39 celiac patients included in their case series; 14 out of 15 showed a pathologic pH recording. Furthermore, lower esophageal sphincter (LES) pressure values were lower than those observed in healthy controls, although not reaching statistical significance.[3] Only eight patients gave their consent for pH-metry in the study carried out by Usai *et al.* Only one out of them showed pathological reflux. These data greatly prevent us from obtaining valid conclusions.

Effect of GFD on control of GERD symptoms

A few studies have analyzed the effect of a GFD on GERD-related symptoms associated to CD, showing concordant results in this case. The GFD effectively relieves reflux symptoms, as it alone significantly reduced severity of both heartburn and regurgitation in adults with CD.[2,6] In addition, in celiac patients treated with PPI, the GFD also reduced the risk of recurrence of GERD-related symptom after discontinuation of antisecretory treatment. Nachman *et al.* found that after 3 months from the start of the GFD, GERD-related symptom scores had significantly decreased in his series of adult celiac patients, reaching values similar to those of healthy controls.[8] Lamanda *et al.* showed that GERD symptoms had remitted in 91% of adult CD patients after 4 weeks of treatment with PPI at standard doses, with no relapse

in any case after 12 months of follow-up on GFD.[4] These data contrast with the more limited efficacy of PPI in patients with EE, and particularly those with NERD, in whom response rates after 4-week PPI therapy were 56% and 37%, respectively, in a review study.[10]

Effect of GFD in preventing the relapse of GERD symptoms

The GFD prevents recurrence of GERD-related symptoms in celiac patients with both erosive and nonerosive forms of esophagitis. Lamanda *et al.* observed that no patient of those whose symptoms had remitted after 4 weeks of PPI therapy showed recurrence of symptoms after 12 months of follow-up.[4] Cuomo *et al.* documented that celiac patients with endoscopic esophagitis showed 12 months after the start of GFD and 10 months after discontinuation of PPI therapy a relapse of GERD symptoms in only 25.6% of cases (which were related to the presence of a hiatal hernia) versus 71% in nonceliac patients with endoscopic esophagitis.[3] Usai *et al.* studied reflux symptom recurrence rates in 29 adult celiac patients after starting GFD in comparison to nonceliac patients with NERD. After 8 weeks of treatment with omeprazole 40 mg daily and GFD, 86.2% of adult celiac patients with NERD had resolved their symptoms, compared to 66.7% of the NERD controls. At 24 months of starting the study, GERD symptoms had recurred in 85% of the NERD controls and in only 20% of CD patients, occurring in the latter for the first 6 months after discontinuing PPI.[9] Again, GERD-related symptom remission achieved following GFD in celiac patients seems to be longer lasting than that achieved with PPI therapy in GERD patients because only 10–25% of the patients with previous EE and 25–45% of patients with NERD remained in remission after 6 months of withdrawal of PPI therapy.[10]

Treatment compliance and refractoriness to the GFD

Of note is the observation that the long-term benefit of GFD on GERD symptoms still persists in the event of partial compliance. Two studies[8,9] have shown that from 2 to 4 years after the start of treatment, patients with partial dietary compliance did not have a greater frequency or severity of GERD-related symptoms than compliant patients. It has been reported that GFD, even when partially met, may have a protective effect in celiac patients against progression from nonerosive to erosive GERD.[9] Patients with NERD have a risk of endoscopic lesions of up to 24.9% after 2 years of follow-up,[11] compared to only 10% in celiac patients.[9]

Finally, celiac patients in whom villous atrophy persisted, despite treatment with GFD, were associated with the presence of 'atypical' symptoms of CD. An Italian research studied 42 adult celiac patients in whom several symptoms persisted despite following GFD adequately; of these, 12 patients showed GERD-like symptoms (28.6%),[12] a proportion exceeding that expected for the general population.

POSSIBLE PHYSIOPATHOLOGICAL INTERACTIONS BETWEEN CD AND GERD

Different studies have shown that CD patients may show different gastrointestinal motor disorders[13] that could explain many of their symptoms. Celiac patients show delayed gastric emptying[13,14] that may resolve after withdrawal of gluten from the diet,[14] or persist as a sign of incomplete dietary compliance.[15] An abnormally long colonic transit time[16] and an anomalous long orocecal transit time[17] have also been reported.

A study that was conducted years ago analyzed, using manometry, the presence of specific esophageal motor disorders in a series of adult celiac patients, reporting motor abnormalities in 67% of examinations, consisting of nutcracker esophagus, low pressure in LES associated with simultaneous contractions, and frequent repetitive contractions.[18] Interestingly, these abnormalities were similar in patients newly diagnosed with CD and in those treated with GFD. The prevalence of symptoms has been positively associated with severity of CD. Celiac patients with steatorrhea showed a LES pressure within normal ranges but significantly lower than those found in patients without steatorrhea and in control subjects.[2]

Few studies have attempted to clarify the genesis of esophageal motor disorders associated with CD, which would mainly involve three mechanisms (Table 1).

Reduction of nutrient absorption

It has been hypothesized that the retardation in gastric emptying and in orocecal transit time could be due to nutrient malabsorption itself, caused by the decreased absorptive surface of the jejunum in CD, which causes other more distal segments to come into contact with digestion products.[1] The presence in the distal small bowel of unabsorbed fats[19] and starch[20] is capable of inducing delayed gastric emptying and orocecal transit time and decreased tone of the gastric wall and LES.

Gastrointestinal hormonal disorders

Various hormones and gastrointestinal peptides regulating function and coordination of the different gastrointestinal segments have been reported to

Table 1 Hypothetical physiopathological interactions between CD and GERD

Physiopathological mechanism	Immediate consequences	Final effects
Reduction of nutrient absorption	Distal intestinal segments come into contact with digestion products.	Retardation in gastric emptying.
	Presence in the distal small bowel of unabsorbed fats and starch.	Retardation in orocecal transit time. Decreased tone of the gastric wall and LES
Gastrointestinal hormonal disorders	Increased plasma levels of endogenous glucagon and neurotensin.	LES pressure decreases, and somatostatin levels increases. Reduction in both gastric emptying and secretion.
	Increased levels of plasma peptide YY.	Reduction in the LES pressure.
Inflammatory reaction against gluten, because of the presence of gliadin and its inflammatory fragments in the intestinal lumen	Zonulin releasing and opening of tight junctions between intestinal cells.	Passage of gliadin toward the intestinal lamina propria, which activates the mucosal immune system.
	Lymphocytes sensitized to gluten trigger a Th1/Th0-type inflammatory response in the esophagus.	Increased permeability of the esophageal epithelial barrier. Increased passage of water, electrolytes, and acid. Abnormal normal tissue resistance and increased risk of reflux.

CD, celiac disease; GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter.

show several abnormalities in celiac patients.[1] These include increased plasma levels of endogenous glucagon[21] and neurotensin,[22] which can decrease LES, and increased levels of somatostatin[23] or plasma peptide YY,[24] which can reduce both gastric emptying and secretion and also the LES pressure.

Inflammatory reaction against gluten

It has been shown that gliadin and its inflammatory fragments present in the intestinal lumen induce zonulin release that causes opening of tight junctions between intestinal cells.[25] This phenomenon facilitates the passage of gliadin itself toward the intestinal lamina propria, which activates the mucosal immune system.[9] CD is characterized by a Th1/Th0-type inflammatory response triggered by CD4+ T-lymphocytes sensitized to gluten,[26] similar to that observed in the inflammatory response of reflux esophagitis.[27] Thus, it has been hypothesized that increased permeability of the epithelial barrier at the level of the esophagus could also increase the passage of water, electrolytes, and acid,[9] reducing abnormal tissue resistance and increasing the risk of reflux.[25]

DIAGNOSIS OF CD BASED ON ESOPHAGEAL SYMPTOMS

CD-related symptoms can be indistinguishable from those of dyspepsia or irritable bowel syndrome, and there is no question that this disease must be ruled out in these clinical scenarios. We have seen that CD is associated with several esophageal motor disorders[2,28] that may cause symptoms of GERD. Because GERD is a very common disease in the general population, the question remains as to whether CD should be routinely excluded in all patients with heartburn or regurgitation.

Young patients with esophageal symptoms, such as heartburn, regurgitation, intermittent chest or epigastric pain or eructation, which typically do not respond satisfactorily to PPI therapy, are frequently seen in clinical practice, eventually requiring an endoscopic exam. Endoscopic findings tend to be normal at the level of the esophagus or cardia, but could allow the diagnosis of CD based on duodenal biopsies. It is also frequent that these patients have some other associated clinical manifestations, such as iron deficiency with or without anemia, rhinitis or nasal congestion with no evidence of allergies, or hormonal disorders. Tursi illustrated this clinical scenario in a publication in which he presented three patients with symptoms attributable to refractory to antisecretory treatment reflux, who were diagnosed with CD after duodenal biopsies and who had rapid and long-lasting remission of symptoms after starting GFD.[29]

The only prospective study which extensively evaluated the usefulness of performing a careful screening for CD in patients with reflux esophagitis advised against this strategy after concluding that the association between the two conditions is weak and the frequency of CD among patients with GERD symptoms is similar to that of the general population.[6] However, the lack of response to PPI therapy to improve GERD symptoms, even after increasing the doses, could be the key for suspecting and actively excluding CD. Regardless of what is the etiology of GERD symptoms in celiac patients, the question arises whether GFD should be added to antisecretory treatment, while it appears that symptom improvement is more related in these patients to gluten suppression than with the PPI themselves. Tursi pro-

posed using antacids such as sodium alginate to temporarily treat GERD symptoms in celiac patients with no significant endoscopic lesions at the esophagus and cardia, while gluten elimination reverses clinical symptoms.[29]

EOE AND CD

The existence of a possible relationship between EoE and CD has recently been proposed based on certain clinical observations. Kagawalla *et al.* presented in 2007 the case of a 7-year-old black male sharing both diseases, resolved after a six-food exclusion diet.[30] Esophageal symptoms and histological lesions reappeared after reintroduction of milk. In a case series of 10 patients with EoE correlatively diagnosed in Australia, it was reported that eight out of them expressed HLA-DQ2 haplotype (with a frequency affecting approximately 45% of the local population), and one more showed DQ8.[31] In an Italian pediatric case series of 16 EoE patients, six children were simultaneously diagnosed with CD based on serological criteria and duodenal villous atrophy.[32] Another Italian case report presented three children with both EoE and CD who showed favorable clinical and histological esophageal evolution after they followed GFD.[33] Lastly, a recently published study attempted to demonstrate the relationship between the two diseases by estimating the prevalence of EoE among children diagnosed with CD in an Australian institution over an 8-year period. The authors retrospectively analyzed the esophageal biopsies taken in the patients by endoscopy for suspected CD, and found that at least 4% of children with CD also suffered from EoE. They also suggested that this percentage could have been higher if esophageal biopsies had been systematically sampled in each patient undergoing an endoscopy for suspected CD.[34]

In contrast to these results, a recent study examined the frequency of HLA-DQ2 and DQ8 alleles predisposing to CD in a series of EoE adult patients from two Spanish hospitals, which showed to be genetically homogeneous with respect to these alleles.[35] The frequencies of CD predisposing haplotypes were not increased in patients as compared to controls (taken from databases of healthy organ donors of the same hospitals representative of the general population), so it could not establish a true association between both diseases.

However, the latter results do not allow to totally ruling out the possibility that gluten plays an etiological role in some small groups of EoE patients exhibiting HLA-DQ2 and/or DQ8. Although the proportion of these alleles is not increased in adult EoE as compared to healthy subjects, this study does not provide any detail into the reverse issue, that is, if patients with CD are more likely to have EoE, as suggested by previous studies in children.[34] EoE can be reversed by a food elimination diet, but no published studies have evaluated until now the efficacy of GFD in resolving eosinophilic inflammation in EoE pediatric or adult patients, although it has been suggested that the disease does not typically respond to gliadin avoidance.[35]

Therefore, and until definitive studies are available, we need to keep in mind that eosinophilic infiltration could be a manifestation associated with exposure to gluten at least in a small number of children with CD and could be caused by CD itself.[36]

CONCLUSIONS

The studies conducted to date provide different evidence that CD may be associated with esophageal symptoms which require future systematic investigations. Although these esophageal symptoms may not be major manifestations of CD, it seems clear that gluten plays a key role in their origin, while withdrawal from the diet is the effective treatment for these symptoms. Therefore, the possible presence of CD should be considered and investigated in patients with recurrent esophageal symptoms unresponsive to conventional treatments, particularly if they are associated with other signs suggestive of CD.

References

1 Tursi A. Gastrointestinal motility disturbances in celiac disease. J Clin Gastroenterol 2004; 38: 642–5.
2 Iovino P, Ciacci C, Sabbatini F *et al*. Esophageal impairment in adult celiac disease with steatorrhea. Am J Gastroenterol 1998; 93: 1243–9.
3 Cuomo A, Romano M, Rocco A *et al*. Reflux oesophagitis in adult coeliac disease: beneficial effect of a gluten free diet. Gut 2003; 52: 514–7.
4 Lamanda R, Panarese A, De Stefano S. Coeliac disease and gastroesophageal non-erosive reflux: prevalence and effect of gluten free-diet. Dig Liver Dis 2009; 41 (Suppl 1): S90.
5 Oderda G, Forni M, Morra I *et al*. Endoscopic and histologic findings in the upper gastrointestinal tract of children with coeliac disease. J Pediatr Gastroenterol Nutr 1993; 16: 172–7.
6 Collin P, Mustalahti K, Kyrönpalo S *et al*. Should we screen reflux oesophagitis patients for coeliac disease? Eur J Gastroenterol Hepatol 2004; 16: 917–20.
7 Revicki D A, Wood M, Wiklund I *et al*. Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease. Qual Life Res 1998; 7: 75–83.
8 Nachman F, Vázquez H, González A *et al*. Gastroesophageal reflux symptoms in patients with celiac disease and the effects of a gluten-free diet. Clin Gastroenterol Hepatol 2011; 9: 214–9.
9 Usai P, Manca R, Cuomo R *et al*. Effect of gluten-free diet on preventing recurrence of gastroesophageal reflux disease-related symptoms in adult celiac patients with nonerosive reflux disease. J Gastroenterol Hepatol 2008; 23: 1368–72.
10 Dean B B, Gano A D Jr, Knight K *et al*. Effectiveness of proton pump inhibitors in nonerosive reflux disease. Clin Gastroenterol Hepatol 2004; 2: 656–64.
11 Labenz J, Nocon M, Lind T *et al*. Prospective follow-up data from the ProGERD study suggest that GERD is not a categorial disease. Am J Gastroenterol 2006; 101: 2457–62.

12 Carroccio A, Ambrosiano G, Di Prima L *et al*. Clinical symptoms in celiac patients on a gluten-free diet. Scand J Gastroenterol 2008; 43: 1315–21.
13 Bassotti G, Castellucci G, Betti C *et al*. Abnormal gastrointestinal motility in patients with celiac sprue. Dig Dis Sci 1994; 39: 1947–54.
14 Perri F, Pastore M, Zicolella A *et al*. Gastric emptying of solids is delayed in celiac disease and normalizes after gluten withdrawal. Acta Paediatr 2000; 89: 921–5.
15 Bassotti G, Villanacci V, Mazzocchi A *et al*. Antroduodenojejunal motor activity in untreated and treated celiac disease patients. J Gastroenterol Hepatol 2008; 23: e23–8.
16 Bai J C, Mauriño E, Martínez C *et al*. Abnormal colonic transit time in untreated celiac sprue. Acta Gastroenterol Latinoam 1995; 25: 277–84.
17 Chiarioni G, Bassotti G, Germani U *et al*. Gluten-free diet normalizes mouth-to-cecum transit of a caloric meal in adult patients with celiac disease. Dig Dis Sci 1997; 42: 2100–5.
18 Usai P, Bassotti G, Usai Satta P *et al*. Oesophageal motility in adult coeliac patients. Neurogastroenterol Motil 1995; 7: 239–44.
19 Lin H C, Doty J E, Reedy T J *et al*. Inhibition of gastric emptying by sodium oleate depends on length of intestine exposed to nutrient. Am J Physiol 1990; 259: G1031–6.
20 Jainin N K, Boivin M, Zinsmeister A R *et al*. Effect of ileal perfusion of carbohydrates and amylase inhibitor on gastrointestinal hormones and emptying. Gastroenterology 1989; 96: 377–87.
21 Kilander A F, Dotevall G, Lindstedt G *et al*. Plasma enteroglucagon related to malabsorption in coeliac disease. Gut 1984; 25: 629–35.
22 Bardella M T, Fraquelli M, Peracchi M *et al*. Gastric emptying and plasma neurotensin levels in untreated celiac patients. Scand J Gastroenterol 2000; 35: 269–73.
23 Fraquelli M, Bardella M T, Peracchi M *et al*. Gallbladder emptying and somatostatin and cholecystokinin plasma levels in celiac disease. Am J Gastroenterol 1999; 94: 1866–70.
24 Wahab P J, Hopman W P, Jansen J B. Basal and fat-stimulated plasma peptide YY levels in celiac disease. Dig Dis Sci 2001; 46: 2504–9.
25 Drago S, El Asmar R, Di Pierro M *et al*. Gliadin, zonulin and gut permeability: effects on celiac and non-celiac intestinal mucosa and intestinal cell lines. Scand J Gastroenterol 2006; 41: 408–19.
26 Nilsen E M, Lundin K E, Krajci P *et al*. Gluten specific, HLA-DQ restricted T cells from coeliac mucosa produce cytokines with Th1 or Th0 profile dominated by interferon gamma. Gut 1995; 37: 766–76.
27 Fitzgerald R C, Onwuegbusi B A, Bajaj-Elliott M *et al*. Diversity in the oesophageal phenotypic response to gastro-oesophageal reflux: immunological determinants. Gut 2002; 50: 451–9.
28 Usai P, Usai Satta P, Lai M *et al*. Autonomic dysfunction and upper digestive functional disorders in untreated adult coeliac disease. Eur J Clin Invest 1997; 27: 1009–15.
29 Tursi A. The treatment of gastro-esophageal reflux disease in adult celiac disease. J Clin Gastroenterol 2004; 38: 724–6.
30 Kagalwalla A F, Shah A, Ritz S *et al*. Cow's milk protein-induced eosinophilic esophagitis in a child with gluten-sensitive enteropathy. J Pediatr Gastroenterol Nutr 2007; 44: 386–8.
31 Lipschitz B. Eosinophilic oesophagitis: association with HLA-DQ2 and HLA-DQ8. Gastroenterology 2008; 134 (Suppl 1): A-289.
32 Quaglietta L, Coccorullo P, Miele E *et al*. Eosinophilic oesophagitis and coeliac disease: is there an association? Aliment Pharmacol Ther 2007; 26: 487–93.
33 Verzegnassi F, Bua J, De Angelis P *et al*. Eosinophilic oesophagitis and coeliac disease: is it just a casual association? Gut 2007; 56: 1029–30.
34 Leslie C, Mews C, Charles A *et al*. Celiac disease and eosinophilic esophagitis: a true association. J Pediatr Gastroenterol Nutr 2010; 50: 397–9.
35 Rothenberg M E. Biology and treatment of eosinophilic esophagitis. Gastroenterology 2009; 137: 1238–49.
36 Lucendo A J, Arias A, Pérez-Martínez I *et al*. Adult patients with eosinophilic esophagitis do not show an increased frequency of the HLA-DQ2/DQ8 genotypes predisposing to celiac disease. Dig Dis Sci 2011: DOI: 10.1007/s10620-010-1383-2.