REVIEW ARTICLE

Reactivity to dietary gluten: new insights into differential diagnosis among gluten-related gastrointestinal disorders

Antonio Picarelli, Raffaele Borghini, Claudia Isonne, Marco Di Tola

Center for Research and Study of Celiac Disease – Department of Internal Medicine and Medical Specialties, Sapienza University, Rome, Italy

KEY WORDS

celiac disease, nonceliac gluten sensitivity, organ culture, wheat allergy

ABSTRACT

The ingestion of dietary gluten sometimes may trigger allergic, autoimmune or nonallergic and nonautoimmune response. The typical gluten-related allergic disorder is the wheat allergy (WA). Celiac disease (CD) is a well-known gluten-related autoimmune condition. The clinical expression of a gluten-related nonallergic and nonautoimmune response is nonceliac gluten sensitivity (NCGS), an emerging condition whose framework is yet unclear and whose diagnosis is suggested only by demonstration of gluten-dependency in patient' symptoms after exclusion of WA and CD. This review discusses the current tools to identify patients suffering from WA, CD, and NCGS, as well as the most recent insights in the differential diagnosis among these gluten-related gastrointestinal disorders.

Introduction Wheat allergy (WA) and celiac disease (CD) are 2 distinct immunologically-mediated diseases associated with the ingestion of proteins from wheat and some related cereals. Both conditions usually recede after a gluten-free diet (GFD). Currently, the spectrum of gluten-related disorders includes also nonceliac gluten sensitivity (NCGS).[1] This review discusses the current tools to identify patients suffering from WA, CD, and NCGS, as well as the most recent insights in differential diagnosis among these gluten-related gastrointestinal disorders.

Wheat allergy In WA children, wheat ingestion elicits typical immunglobulin E (IgE)-mediated reactions of immediate onset, including urticaria, angioedema, bronchial obstruction, nausea, and abdominal pain, or systemic anaphylaxis in severe cases. Late manifestations appear about 24 h after wheat ingestion and include gastrointestinal symptoms and exacerbation of atopic dermatitis. In adults, allergy to ingested wheat seems to be infrequent, with a prevalence of about 0.1%, and may lead to exacerbation of atopic dermatitis or gastrointestinal symptoms. As the diagnostic performances of wheat-specific skin prick tests and in vitro IgE assays have been shown unsatisfactory, often the diagnosis of WA is almost exclusively based on the results of oral wheat challenges.[2] On the other hand, to define the involvement of circulating basophils in allergic reactions, it has been recently proposed a flow cytometric test able to investigate the allergen-induced activations of basophilic granulocytes. The basophil activation test (BAT) evaluates the percentage of basophils expressing 1 or more activation markers (e.g., CD63 and CD203c) after in vitro whole blood stimulation, in order to address a hypersensitivity reaction to a specific allergen.[3-5] However, BAT has still not been currently applied in studies including allergenic extracts from wheat or gluten.[6,7]

Celiac disease CD is a gluten-related immunological disorder different from WA. It is a chronic inflammatory, autoimmune disorder, and one of the most common gastrointestinal and systemic diseases worldwide, with a prevalence of about 1%.[8,9] This condition is triggered by the ingestion of gluten-containing foods in genetically susceptible individuals carrying HLA-DQ2 and/or -DQ8 alleles (90%–95% of CD patients).[10] The gold standard for its diagnosis is still based on the finding of villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis on histological examination of duodenal biopsies. On the other hand,

Correspondence to:
Antonio Picarelli, MD, Department of Internal Medicine and Medical Specialties, Sapienza University – Policlinico Umberto I, Viale del Policlinico, 155, 00161, Rome, Italy, phone: +39-06-499-783-70, fax: +39-06-499-783-33, e-mail: antonio.picarelli@uniroma1.it
Received: August 26, 2013.
Revision accepted: September 25, 2013.
Published online: September 26, 2013.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2013; 123 (12): 708-712

the presence of only intraepithelial lymphocytosis is often used, perhaps erroneously, to discriminate whether or not patients really present CD.[11,12]

Recent literature emphasizes that an adequate number of duodenal biopsies should always be taken in order to improve the accuracy of CD diagnosis,[13] since the CD-specific histological lesions often may have a discontinuous distribution along the small bowel, showing a pattern called "patchy atrophy". In newly diagnosed CD, some variability of histological lesions can even be found within the same duodenal biopsy, in which areas of apparently normal mucosa with increased intraepithelial lymphocyte (IEL) number often coexist with sites of villous atrophy.[14-16]

Nowadays, it is general opinion that serum antibodies play a supportive role in CD diagnosis. In fact, the presence of circulating autoantibodies against tissue transglutaminase (anti-tTG) and endomysium (EMA) is also necessary to make a proper diagnosis of CD.[17] Present guidelines are generally in agreement as to which serum test(s) is best. Immunoglobulin A anti-tTG antibodies are recommended as the most reliable and cost-effective serum test for CD, even if an increase of their levels can also occur in other pathological conditions involving tissue damage, such as arthritic diseases, inflammatory bowel disease (IBD), and cardiovascular disorders.[18-20] Recent studies even suggest that duodenal biopsies may not be necessary when anti-tTG serum levels are extremely high. In fact, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recommends this option for individuals with typical symptoms of CD and serum anti-tTG >10 times the upper limit of normal (ULN) together with a positive serum EMA and presence of a HLA-DQ2 or -DQ8 allele.[21] Although anti-tTG serum test has a specificity ranging between 90% and 95%, serum EMA are often required for diagnostic confirmation, because of their high specificity approaching 100%.[22,23] However, the interpretation of EMA is operator-dependent and this can seriously affect the CD diagnosis if data are not contextualized. Anti-gliadin antibodies (AGA) are considered unreliable and no longer recommended for routine screening purposes even if a new enzyme immunoassay using deamidated gliadin peptides (DGP) as antigen has proved to be very sensitive and specific for CD diagnosis.[24,25]

Current guidelines recommend concomitant measurement of total IgA serum levels to identify selective IgA deficiency (SIgAD).[26,27] In SIgAD patients, IgG-based tests (EMA, anti-tTG, and/or anti-DGP) have been suggested.[28-30]

However, in some cases, the diagnosis is not straightforward and represents a challenge for clinicians. Potential dilemmas include patients with positive serology but normal histology, negative serology but abnormal histology, failure to respond to a GFD or response to a GFD without evidence of CD. In recent years, development of new assays and modifications of diagnostic algorithms for CD have even called into question the crucial role traditionally played by duodenal histology.[31]

Nonceliac gluten sensitivity Recently, NCGS has been described as a distinct gluten-related clinical entity, with an estimated prevalence of 6%. It is characterized by gastrointestinal symptoms such as abdominal pain, bloating, bowel habit abnormalities (either diarrhea or constipation), and extraintestinal manifestations such as "foggy mind", headache, fatigue, joint and muscle pain, leg or arm numbness, dermatitis (eczema or skin rash), depression, and anemia. All these manifestations usually occur soon after gluten ingestion, disappear with gluten withdrawal and relapse in short time following a gluten challenge, within hours or few days.

In clinical practice, it has become relevant to differentiate CD from NCGS, in light of the increasing prevalence of both these gluten-related disorders and their relevant dietary, medical, social, and economic implications.[1] NCGS is lacking of sensitive and specific diagnostic tools, and its possible pathogenetic mechanisms are yet to be known. The absence of CD-specific serum antibodies and villous atrophy (with or without HLA-DQ2 and/or -DQ8 alleles) currently identifies NCGS, although first-generation AGA test frequently presents positive results.[32] Anyway, the use of double-blinded placebo-controlled gluten challenge should be recommended in patients suspected to be affected by NCGS.

Though there is a clear cause-effect relationship between gluten ingestion and symptoms reported by NCGS patients, pathogenetic mechanisms are not yet known.

The hypothesis that, in gluten-sensitive patients, a favorable response to a GFD as well as the exacerbation of symptoms after a gluten-containing diet are due actually to gluten, could be a trap. Importance could be given to other wheat-related food constituents able to cause gastrointestinal symptoms. The reluctance to acknowledge other components of wheat, such as nongluten proteins, fructans, galacto-oligosaccharides, and other short-chain carbohydrates (fermentable oligo-, di-, monosaccharides and polyols; FODMAPs), as other potential pathogenetic factors often hamper the correct interpretation of clinical observations.[33] Therefore, is it questionable whether these patients are recognizable as irritable bowel syndrome (IBS)-like patients?[34]

For many years, IBS and CD have been considered 2 completely separate entities: CD as a gluten-related condition and IBS without relation with gluten intake. The IBS and CD symptoms may be, however, indistinguishable, especially when diarrhea, bloating, or abdominal pain predominate. In the last decade, several studies have further shown that the boundary between CD and IBS is not always so clear. Consistently, some patients who have been identified as IBS, suffer actually from CD. In addition, it seems that there is another group of patients who, without having CD,

suffer from gluten intolerance causing them digestive symptoms similar to those of IBS. Since gluten sensitivity is defined as the spectrum of clinical and functional abnormalities that respond to a GFD, it is mandatory to establish in which patients this diet will be beneficial as well as when this is not justified.[35]

In light of all these findings, it is evident the needs to make a correct diagnosis among gluten-related disorders to avoid unnecessary and repeated over time diagnostic tests. It is, therefore, necessary to use the most sensitive and specific diagnostic tests and strategies.

Organ culture system In 1996, it has been demonstrated that EMA can be detected in culture media of duodenal biopsies from untreated CD patients, as well as from treated CD patients after in vitro exposure to peptic-tryptic digest of gliadin (PT-gliadin).[36] Three years later, a first improvement in EMA determination has been achieved by using a synthetic peptide corresponding to 31–43 a.a. position of the α-gliadin (activator peptide), shown to be active at concentrations 20-fold lower than those necessary for the PT-gliadin.[37] In 2001, the extension of the time of culture from 24 to 48 h, in concert with the replacement of the "on dish" standard method with a more easy and quick "in batch" new method, has led to a further improvement in EMA determination, as well as a substantial simplification of the entire organ culture system.[38] One year later, Carroccio et al.[39] have started a series of clinical validation studies, highlighting the usefulness of the organ culture system in identifying CD also in seronegative patients. The slight differences in sensitivity among data achieved in the latter study and those obtained in previous investigations are attributable to indirect immunofluorescence analysis (IFA) used for EMA detection. In fact, this is a qualitative method leading to subjective interpretations. A multicenter study dated 2006 has shown a good correlation between the organ culture system and duodenal histology and, furthermore, has demonstrated that this new method can be useful to identify CD also in patients presenting a normal villous morphology. To further improve the performance of the organ culture system, this study has also pointed out that in vitro stimulation must be always performed, and that particular attention must be always paid to the biopsy sample size.[40] In the same year, it has been demonstrated that measurement of anti-tTG in culture media increases the ability of the organ culture system to identify CD in seronegative patients.[41] Since anti-tTG are measured by enzyme-linked immunosorbent assay, a quantitative and objective method, the use of these antibodies appears clearly helpful to standardize the organ culture system for diagnostic purposes. In 2008, Santaolalla et al.[42] have demonstrated that measurement of anti-tTG in culture media improves the ability of the organ culture system in identifying CD also in patients with an increased density of γ/δ+ IEL but normal villous morphology.[42] Afterwards activator peptide's performance improvement,[43] the organ culture system could be proposed as an ancillary method to perform the correct CD diagnosis.[44-46]

The use of the organ culture system has also allowed to demonstrate that the immune response to gluten involves not only the small bowel mucosa, but also that of other areas of the gastrointestinal tract. Specifically, EMA and anti-tTG antibodies can also be detected in culture supernatants of oral and colonic mucosa biopsy specimens, suggesting that these mucosal areas could be used as alternative and/or opportunistic sites in which adverse effects to gluten are reproducible.[47,48]

Concluding remarks and future perspectives Summarizing, WA is an IgE-mediated basophil degranulation that may be triggered by gluten fractions ingestion and other wheat proteins. Its diagnosis is suggested by wheat-specific skin prick tests and by in vitro IgE assays, while food challenge and BAT can be used as confirmatory test.[2] CD is an autoimmune enteropathy triggered by wheat gluten ingestion and related prolamines in rye and barley. Its diagnosis is based on the presence of serum EMA, anti-tTG and anti-DGP antibodies, intestinal villous atrophy with increased IEL number.[21] NCGS is a non-allergic and non-autoimmune disorder associated with gluten intake. Its diagnosis is suggested only by demonstration of gluten-dependency in patients' symptoms after exclusion of WA and CD.[49] Therefore, the need to make a correct diagnosis among these gluten-related disorders by using the most sensitive and specific diagnostic strategies and tests is evident. The organ culture system, has been recently proposed as an ancillary method to perform a correct CD diagnosis, mainly in cases without villous atrophy or in seronegative patients.[46] The proofs that organ culture system sensitivity is higher than that of duodenal histology alone, confirm its inclusion among diagnostic procedures in differential diagnosis of gluten-related gastrointestinal disorders. Future studies aimed to confirm and extend this observations will be welcome.

REFERENCES

1 Sapone A, Bai JC, Ciacci C, et al. Spectrum of gluten-related disorders: consensus on new nomenclature and classification. BMC Med. 2012; 10: 13.

2 Inomata N. Wheat allergy. Curr Opin Allergy Clin Immunol. 2009; 9: 238-243.

3 Sturm EM, Kranzelbinder B, Heinemann A, et al. CD203c-based basophil activation test in allergy diagnosis: characteristics and differences to CD63 upregulation. Cytometry B Clin Cytom. 2010; 78: 308-318.

4 Chirumbolo S. Monitoring of CD63% in basophil activation test and suggested new parameters for allergy diagnosis. Inflamm Res. 2012; 61: 171-176.

5 McGowan EC, Saini S. Update on the performance and application of basophil activation tests. Curr Allergy Asthma Rep. 2013; 13: 101-109.

6 Chinuki Y, Kaneko S, Dekio I, et al. CD203c expression-based basophil activation test for diagnosis of wheat-dependent exercise-induced anaphylaxis. J Allergy Clin Immunol. 2012; 129: 1404-1406.

7 Tammaro A, Narcisi A, Amodeo R, et al. CD63 cell expression detected by flow-cytometric determination of basophil activation in allergic patients. Int J Immunopathol Pharmacol. 2012; 25: 1143-1147.

8 Mustalahti K, Catassi C, Reunanen A, et al; Celiac EU Cluster, Project Epidemiology. The prevalence of celiac disease in Europe: results of a centralized, international mass screening project. Ann Med. 2010; 42: 587-595.

9 Katz KD, Rashtak S, Lahr BD, et al. Screening for celiac disease in a North American population: sequential serology and gastrointestinal symptoms. Am J Gastroenterol. 2011; 106: 1333-1339.

10 Megiorni F, Pizzuti A. HLA-DQA1 and HLA-DQB1 in celiac disease predisposition: practical implications of the HLA molecular typing. J Biomed Sci. 2012; 19: 88.

11 Shmidt E, Smyrk TC, Faubion WA, Oxentenko AS. Duodenal intraepithelial lymphocytosis with normal villous architecture in pediatric patients: Mayo Clinic experience, 2000-2009. J Pediatr Gastroenterol Nutr. 2013; 56: 51-55.

12 Hammer ST, Greenson JK. The clinical significance of duodenal lymphocytosis with normal villus architecture. Arch Pathol Lab Med. 2013; 137: 1216-1219.

13 Rostami-Nejad M, Villanacci V, Hogg-Kollars S, et al. Endoscopic and histological pitfalls in the diagnosis of celiac disease: a multicentre study assessing the current practice. Rev Esp Enferm Dig. 2013; 105: 326-333.

14 Picarelli A, Maiuri L, Mazzilli MC, et al. Gluten-sensitive disease with mild enteropathy. Gastroenterology. 1996; 111: 608-616.

15 Ravelli A, Villanacci V, Monfredini C, et al. How patchy is patchy villous atrophy?: distribution pattern of histological lesions in the duodenum of children with celiac disease. Am J Gastroenterol. 2010; 105 (9): 2103-2110.

16 Valitutti F, Di Nardo G, Barbato M, et al. Mapping histologic patchiness of celiac disease by push enteroscopy. Gastrointest Endosc. 2013 Jul 22 [Epub ahead of print].

17 Sandström O, Rosén A, Lagerqvist C, et al. Transglutaminase IgA antibodies in a celiac disease mass screening and the role of HLA-DQ genotyping and endomysial antibodies in sequential testing. J Pediatr Gastroenterol Nutr. 2013; 57: 472-476.

18 Picarelli A, Di Tola M, Sabbatella L, et al. Anti-tissue transglutaminase antibodies in arthritic patients: a disease-specific finding? Clin Chem. 2003; 49: 2091-2094.

19 Di Tola M, Sabbatella L, Anania MC, et al. Anti-tissue transglutaminase antibodies in inflammatory bowel disease: new evidence. Clin Chem Lab Med. 2004; 42: 1092-1097.

20 Di Tola M, Barillà F, Trappolini M, et al. Antitissue transglutaminase antibodies in acute coronary syndrome: an alert signal of myocardial tissue lesion? J Intern Med. 2008; 263: 43-51.

21 Husby S, Koletzko S, Korponay-Szabo IR, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr. 2012; 54:136-160.

22 Leffler DA, Schuppan D. Update on serologic testing in celiac disease. Am J Gastroenterol. 2010; 105: 2520-2524.

23 Giersiepen K, Lelgemann M, Stuhldreher N, et al. Accuracy of diagnostic antibody tests for coeliac disease in children: summary of an evidence report. J Pediatr Gastroenterol Nutr. 2012; 54: 229-241. ESPGHAN Working Group on Coeliac Disease Diagnosis.

24 Tonutti E, Visentini D, Picierno A, et al. Diagnostic efficacy of the ELISA test for the detection of deamidated anti-gliadin peptide antibodies in the diagnosis and monitoring of celiac disease. J Clin Lab Anal. 2009; 23: 165-171.

25 Brusca I, Carroccio A, Tonutti E, et al. The old and new tests for celiac disease: which is the best test combination to diagnose celiac disease in pediatric patients? Clin Chem Lab Med. 2011; 50: 111-117.

26 Cataldo F, Marino V, Ventura A, et al. Prevalence and clinical features of selective immunoglobulin A deficiency in coeliac disease: an Italian multicentre study. Italian Society of Paediatric Gastroenterology and Hepatology (SIGEP) and "Club del Tenue" Working Groups on Coeliac Disease. Gut 1998; 42: 362-365.

27 McGowan KE, Lyon ME, Butzner JD. Celiac disease and IgA deficiency: complications of serological testing approaches encountered in the clinic. Clin Chem. 2008; 54: 1203-1209.

28 Cataldo F, Lio D, Marino V, et al. IgG(1) antiendomysium and IgG antitissue transglutaminase (anti-tTG) antibodies in coeliac patients with selective IgA deficiency. Working Groups on Celiac Disease of SIGEP and Club del Tenue. Gut. 2000; 47: 366-369.

29 Picarelli A, di Tola M, Sabbatella L, et al. Identification of a new coeliac disease subgroup: antiendomysial and anti-transglutaminase antibodies of IgG class in the absence of selective IgA deficiency. J Intern Med. 2001; 249: 181-188.

30 Volta U, Granito A, Parisi C, et al. Deamidated gliadin peptide antibodies as a routine test for celiac disease: a prospective analysis. J Clin Gastroenterol. 2010; 44: 186-190.

31 Ma MX, John M, Forbes GM. Diagnostic dilemmas in celiac disease. Expert Rev Gastroenterol Hepatol. 2013; 7: 643-655.

32 Aziz I, Sanders DS. Emerging concepts: from coeliac disease to non-coeliac gluten sensitivity. Proc Nutr Soc. 2012; 71: 576-580.

33 Gibson PR, Barrett JS, Muir JG. Functional bowel symptoms and diet. Intern Med J. 2013; 43: 1067-1074.

34 Biesiekierski JR, Muir JG, Gibson PR. Is Gluten a cause of gastrointestinal symptoms in people without celiac disease? Curr Allergy Asthma Rep. 2013 Sep 12. [Epub ahead of print].

35 Mearin F, Montoro M. Irritable bowel syndrome, celiac disease and gluten. Med Clin (Barc). 2013 Sep 9. [Epub ahead of print]

36 Picarelli A, Maiuri L, Frate A, et al. Production of antiendomysial antibodies after in-vitro gliadin challenge of small intestine biopsy samples from patients with coeliac disease. Lancet. 1996; 348: 1065-1067.

37 Picarelli A, Di Tola M, Sabbatella L, et al. 31-43 amino acid sequence of the alpha-gliadin induces anti-endomysial antibody production during in vitro challenge. Scand J Gastroenterol. 1999; 34: 1099-1102.

38 Picarelli A, Sabbatella L, Di Tola M, et al. Forty-eight hours of biopsy culture improve the sensitivity of the in vitro gliadin challenge in the diagnosis of celiac disease. Clin Chem. 2001; 47: 1841-1843.

39 Carroccio A, Iacono G, D'Amico D, et al. Production of anti-endomysial antibodies in cultured duodenal mucosa: usefulness in coeliac disease diagnosis. Scand J Gastroenterol. 2002; 37: 32-38.

40 Picarelli A, Di Tola M, Sabbatella L, et al.; Multicentre Organ Culture System Study Group. Usefulness of the organ culture system in the in vitro diagnosis of coeliac disease: a multicentre study. Scand J Gastroenterol. 2006; 41: 186-190.

41 Carroccio A, Di Prima L, Pirrone G, et al. Anti-transglutaminase antibody assay of the culture medium of intestinal biopsy specimens can improve the accuracy of celiac disease diagnosis. Clin Chem. 2006; 52: 1175-1180.

42 Santaolalla R, Fernández-Bañares F, Rodríguez R, et al. Diagnostic value of duodenal antitissue transglutaminase antibodies in gluten-sensitive enteropathy. Aliment Pharmacol Ther. 2008; 27: 820-829.

43 Picarelli A, Libanori V, De Nitto D, et al. Organ culture system as a means to detect celiac disease. Ann Clin Lab Sci, 2010; 40: 85-87.

44 Carroccio A, Iacono G, Di Prima L, et al. Antiendomysium antibodies assay in the culture medium of intestinal mucosa: an accurate method for celiac disease diagnosis. Eur J Gastroenterol Hepatol. 2011; 23: 1018-1023.

45 Tosco A, Aitoro R, Auricchio R, et al. Intestinal anti-tissue transglutaminase antibodies in potential celiac disease. Clin Exp Immunol. 2013; 171: 69-75.

46 Picarelli A, Di Tola M, Marino M, et al. Usefulness of the organ culture system when villous height/crypt depth ratio, intraepithelial lymphocyte count, or serum antibody tests are not diagnostic for celiac disease. Transl Res. 2013; 161: 172-180.

47 Vetrano S, Zampaletta U, Anania MC, et al. Detection of anti-endomysial and anti-tissue transglutaminase autoantibodies in media following culture of oral biopsies from patients with untreated coeliac disease. Dig Liver Dis. 2007; 39: 911-916.

48 Picarelli A, Di Tola M, Borghini R, et al. Colonic involvement in celiac disease and possible implications of the sigmoid mucosa organ culture in its diagnosis. J Clin Immunol. 2013; 33(7): 1250-1256.

49 Carroccio A, Mansueto P, Iacono G, et al. Non-celiac wheat sensitivity diagnosed by double-blind placebo-controlled challenge: exploring a new clinical entity. Am J Gastroenterol. 2012; 107: 1898-1906.

ARTYKUŁ POGLĄDOWY

Nadwrażliwość na gluten pokarmowy: nowe poglądy na diagnostykę różnicową glutenozależnych zaburzeń przewodu pokarmowego

Antonio Picarelli, Raffaele Borghini, Claudia Isonne, Marco Di Tola

Center for Research and Study of Celiac Disease – Department of Internal Medicine and Medical Specialties, Sapienza University, Rzym, Włochy

SŁOWA KLUCZOWE

alergia na pszenicę, celiakia, hodowla narządów, nieceliakalna nadwrażliwość na gluten

STRESZCZENIE

Spożycie pokarmów zawierających gluten może wywołać reakcje alergiczne, autoimmunologiczne lub niealergiczne i nieautoimmunologiczne. Typową alergiczną chorobą glutenozależną jest alergia na pszenicę (*wheat allergy* – WA). Dobrze znaną autoimmunologiczną chorobą glutenozależną jest celiakia (*celiac disease* – CD). Manifestacją kliniczną niealergicznej i nieautoimmunologicznej reakcji na gluten jest nieceliakalna nadwrażliwość na gluten (*nonceliac gluten sensitivity* – NCGS) – nowo wyodrębniony stan, którego patogeneza jest wciąż niejasna, a rozpoznanie sugeruje tylko wykazanie związku objawów z glutenem, po wykluczeniu WA i CD. W niniejszym przeglądzie omówiono dostępne metody rozpoznawania WA, CD i NCGS, a także najnowsze poglądy na temat diagnostyki różnicowej tych zaburzeń przewodu pokarmowego związanych z glutenem.

Adres do korespondencji: Antonio Picarelli, MD, Department of Internal Medicine and Medical Specialties, Sapienza University – Policlinico Umberto I, Viale del Policlinico, 155, 00161, Rzym, Włochy, tel.: +39-06-499-783-70, fax: +39-06-499-783-33, e-mail: antonio.picarelli@uniroma1.it

Praca wpłynęła: 26.08.2013.
Przyjęta do druku: 25.09.2013.
Publlikacja online: 26.09.2013.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2013; 123 (12): 708-712
Tłumaczył lek. Łukasz Strzeszyński