VIA MEDICA

ORIGINAL PAPER / GYNECOLOGY

Ginekologia Polska
2022, vol. 93, no. 10, 793–798

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/GP.a2022.0102

The analysis of coexistence of celiac disease and vulvar lichen sclerosus in girls

Kacper Nizinski[1], Dominika Orszulak[1], Marta Janik[2], Kaja Skowronek[1], Rafal Stojko[1], Agnieszka Drosdzol-Cop[1]

[1]Chair and Department of Gynecology, Obstetrics and Oncological Gynecology, Medical University of Silesia in Katowice, Poland
[2]Euroimmun Polska Sp. z o.o., Wroclaw, Poland

ABSTRACT

Objectives: Vulvar lichen sclerosus (VLS) is a chronic inflammatory disease of unclear etiology. Recent studies show that 15–34% of cases in adult women and 14% in girls coexist with allergies or autoimmune diseases, among others — celiac disease (CD). Most of the research on the coexistence of VLS and autoimmune diseases has been carried out on a group of adult women. Literature data on this issue are very scarce.

Material and methods: The presented work is a pioneering project in which we tried to elucidate a possible relationship between celiac disease and lichen sclerosus in girls. The aim of the research was to study the antibodies characteristic of celiac disease in girls with VLS. The control group consisted of 35 heathy adolescent girls and the study group consisted of 20 girls aged 2–18 years old diagnosed with vulvar lichen sclerosus recruited at the Gynecological Clinic for Girls at the Women's Health Center in Katowice.

Results: There were no significant differences in the concentrations of antibodies characteristic for CD in the blood serum between the studied groups.

Conclusions: The main limitation of our study was the small size of the study group. It is therefore legitimate to conduct further research on a larger study group to find the mutual correlations between the analyzed antibodies and the onset and the course of VLS in girls. The finding of a positive correlation between the coexistence of VLS and CD may prevent potentially serious, long-term complications.

Key words: vulvar lichen sclerosus; celiac disease; adolescent

Ginekologia Polska 2022; 93, 10: 793–798

INTRODUCTION

Vulvar lichen sclerosus (VLS) is a chronic inflammatory disease of unclear etiology. The most popular theories relate to its autoimmune and genetic conditioning, although theories concerning hormonal and infectious etiology have also been raised [1]. VLS is a relatively common chronic inflammatory skin disease that predominantly affects the anogenital region. Vulvar lichen sclerosus has a clear female preponderance, with female:male ratios of 6–10:1 reported in the literature [2]. The exact prevalence of VLS is unknown, but estimates range from 1 in 300 to 1 in 1000 among patients referred to a dermatology department [3]. It has two peaks of onset: prepuberty and postmenopause. Common symptoms of the condition include anogenital pruritus and soreness. In young children, constipation and dysuria may also be presenting features. Ivory-white atrophic patches, erosions, fissures and ecchymoses in the anogenital region are typical clinical findings [4]. Recent studies show that 15–34% of cases in adult women and 14% in girls coexist with allergies or autoimmune diseases, such as the following: vitiligo, thyroiditis, type 1 diabetes mellitus, alopecia areata, or celiac disease [1]. Celiac disease (CD) is an autoimmune disease associated with the genetic predisposition to human leukocyte antigen (HLA) and tissue transglutaminase (tTG) autoantigen [5]. CD is one of the most common diseases, resulting from both environmental (gluten) and genetic factors (HLA and non-HLA genes). The prevalence of CD has been estimated to approximate 0.5–1% in different parts of the world [6]. The latest ESPGHAN 2020 guidelines recommend the indication of IgA antibodies against human tissue transglutaminase (tTG-IgA) along with the assessment of total IgA concentration as the basic test in the diagnosis of celiac disease (performed regardless of the child's age). In children with tTG-IgA antibody level 10-times

Corresponding author:
Kacper Nizinski
Chair and Department of Gynecology, Obstetrics and Oncological Gynecology, Medical University of Silesia in Katowice, Poland
e-mail: kacpern@op.pl

Received: 30.03.2022 Accepted: 30.03.2022 Early publication date: 10.10.2022

above the upper limit of normal concentration, CD can be diagnosed without biopsy, provided that the anti-endomysial antibodies (EMA-IgA) (assessed in the blood sample from the second collection) are detected. If the above conditions are met, it is not necessary to perform genetic testing of the HLA-DQ2/DQ8 haplotype to diagnose CD without intestinal biopsy.

Objectives

According to the literature data, lichen sclerosus may be accompanied by autoimmune diseases with an increased frequency. Most of the existing scientific studies on the etiopathogenesis of VLS were conducted on a group of adult women. The aim of the present research was to study the antibodies characteristic of celiac disease in girls with VLS, in order to provide the patient with multidisciplinary medical care. Understanding the pathogenesis of both diseases in the future may allow the detection of markers of VLS and CD comorbidity in the blood serum and the creation of new standards of these patient's treatment.

MATERIAL AND METHODS

The study group consisted of 20 girls aged 2–18 years old diagnosed with vulvar lichen sclerosus. They were diagnosed by a vulval specialist based on a thorough medical history interview with the patient/guardian, and a physical examination according to the guidelines of the British Dermatological Society. The control group consisted of 35 girls (presenting, among others, infections of the genital tract/glued labia or a family history burden towards VLS) recruited at the Gynecological Clinic for Girls at the Women's Health Center in Katowice. Case notes were reviewed and all data on clinical presentation, comorbidities, predisposing factors, family history, therapy and outcome were collected. A predesigned data-collection form was used. The presence of IgA and IgG antibodies against tissue transglutaminase was assessed using the ELISA method and a new, highly specific test for the presence of anti-gliadin antibodies: Anti-Gliadin (GAF-3X) ELISA. Thanks to the intensive development of the state of knowledge, there was an antigen "designed", whose immunologically reactive surface provides the anti-Gliadin (GAF-3X) ELISA and the Anti-Gliadin (GAF-3X) IIFT EUROPLUS tests a specificity equal to almost 100% [7].

Both groups met the criteria for inclusion and exclusion from the study.

Inclusion criteria

1. Age 2–18 years old,
2. Lack of systemic diseases (*e.g.,* cardiovascular diseases, peptic ulcer disease, epilepsy),
3. Consent of the girl and/or her legal guardian to participate in the study.

Exclusion criteria:

1. Pharmacotherapy used in the last 6 months (including hormonal drugs, contraceptives, NSAIDs),
2. Systemic diseases (e.g., cardiovascular diseases, peptic ulcer disease, epilepsy, liver and kidney diseases),
3. Lack of consent of the girl and/or her legal guardian to participate in the study,
4. Addictions,
5. Pregnancy.

All study participants and their parents/legal guardians were informed about its purpose and conducting method. A written consent (in case of adolescents at the age 16–18 years — of both the girl and her parent/legal guardian) from all respondents to carry out the procedures included in the study protocol was obtained.

The study was approved by the Bioethical Committee of the Medical University of Silesia in Katowice — KNW/0022/KB1/5/19.

Statistical analysis

For statistical data analysis, the STATISTICA 12 PL software (StatSoft Inc., USA) and MS Excel spreadsheet were used. In all calculations, the statistical significance for the level of $p < 0.05$ was adopted. The Student's t-test (with a normal distribution) was used as a test of the significance of differences for two independent samples. The CHI^2 test (and its modification in the form of the Fisher test for 2×2 contingency tables) was used to analyze the differences between the groups in terms of qualitative variables.

RESULTS

Patient characteristics

The study group consisted of 20 girls diagnosed with vulvar lichen sclerosus. The average age of the study group was 10.45 years. The control group consisted of 35 healthy adolescent girls. The average age of the control group was 10.37 years.

The average age of initial symptoms in the study group was 7.08 years. The average age of the diagnosis of VLS was 8.23 years. All patients in the study group developed symptoms in premenarcheal age. The mean time between the initial symptoms and the vulval diagnosis was 13.4 months.

Signs and symptoms

In the study group, patients presented several signs and symptoms (Fig. 1 and 2). The most common symptoms were itching (14/20; 70%) and soreness/skin burning (10/20; 50%). Many patients had excoriations (11/20; 55%), erythema/skin irritations (8/20; 40%), pallor (8/20; 40%) and vulvar bleeding (8/20; 40%). Anal involvement was observed in five out of 20 cases (25%). Constipation was present in three cases

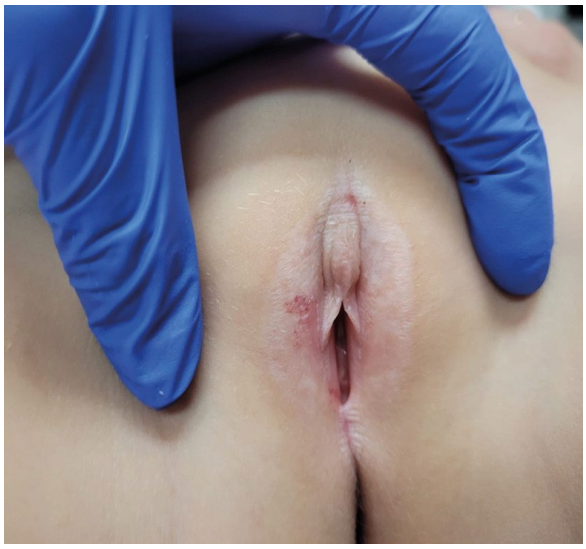

Figure 1. Clinical features of vulvar lichen sclerosus (own material)

Figure 2. Clinical features of vulvar lichen sclerosus: classic "Figure 8" (own material)

(15%). Four patients (20%) showed signs o the urinary tract symptoms. None of the patients developed extragenital VLS (Tab. 1).

Family history

In the study group four patients (20%) had a personal history of asthma, allergy or both. Nine patients (45%) had a positive family history towards autoimmune diseases in a first-degree relative. The most frequent diseases were Hashimoto's thyroiditis (4/20) and rheumatoid arthritis (3/20). In the control group, none of the patients (0/35) had a personal history of allergy or asthma. 22 patients (63%) had a positive family history towards autoimmune diseases in a first-degree relative. The most frequent diseases were Hashimoto's thyroiditis (9/35); rheumatoid arthritis (7/35) and psoriasis (6/35).

Table 1. Symptoms and signs of vulval lichen sclerosus in study group

Presenting symptoms/signs	Frequency (n)
Clinical symptoms	
Itching	14
Soreness/skin burning	10
Vulvar bleeding	8
Urinary tract symptoms	4
Constipation	3
Clinical signs	
Excoriations	11
Erythema	8
Pallor	8
Classic "Figure 8"	5

Treatment

All 20 patients were initially treated with a 3-month induction regimen (super-potent topical steroid once a day in the first month, once a day every second day in the second month and twice a week together with the emollient in the third month). In two patients (10%) no control over the disease was obtained and its progression was noticed which led to a maintenance therapy with potent steroid containing methylprednislone or clobetasole and retinol. The remaining 18 patients were treated with a maintenance therapy of a potent/super-potent steroid at least twice a week with the emollient included.

Antibodies of CD in the studied population

Using the chi-squared test there were no significant differences in the concentrations of IgA tTG ($p = 0.247$), IgG tTG ($p = 0.247$), IgA GAF-3X ($p = 0.775$), IgG GAF-3X ($p = 0.256$) in the blood serum between the studied groups (Tab. 2). Positive antibodies in the 20-person study group were found respectively in: IgA tTG — 2/20 (10%); IgG tTG — 2/20 (10%); IgA GAF-3X — 3/20 (15%); IgG GAF-3X — 3/20 (15%) patients. In the studied population, no correlation between the coexistence of antibodies characteristic of CD and no correlation with a positive family history of autoimmune diseases (chi-square test) were observed. In the study group, there was a correlation found between the presence of IgA-tTG antibodies and IgG-tTG antibodies and the age of onset of first symptoms and the age of diagnosis of VLS — avarage age of symptoms onset [12.0 years vs 6.53 years

Table 2. Frequency of the presence of characteristic antibodies for celiac disease in the study population

	IgA-tTG (n)	IgG-tTG (n)	IgA-GAF-3X (n)	IgG-GAF-3X (n)
Study group (n = 20)	2	2	3	3
Control group (n = 35)	0	0	3	1
P (Chi-squared test)	0.247 (NS)	0.247 (NS)	0.775 (NS)	0.259 (NS)

(p = 0.042)] and VLS diagnosis [13.5 years vs 7.63 years (p = 0.044)] in girls with antibodies to celiac disease is higher than in girls with no antibodies. A small number of patients (2 persons in the study group) with a positive result of antibodies characteristic for celiac disease is the basic limitation of the clinical trial conducted.

DISCUSSION

The etiopathogenesis of VLS remains unknown and is probably multifactorial. The evidence collected indicates that VLS has an autoimmune aetiology. Antibodies against the basement membrane zone have been found in the sera of patients with vulvar lichen sclerosus and a high proportion of patients have specific antibodies targeting extracellular matrix protein-1 [8, 9].

As it was mentioned before, the pathogenesis is currently not fully understood, but it is hypothesized that a genetic predisposition leads to the development of an immune response. Histopathology shows a thin epidermis, dermal edema, and a bandlike infiltrate of lymphocytes at the dermoepidermal junction. Morrel et al. in 2020 [10] investigated biopsies of 100 juvenile cases of VLS and analyzed the presence or absence of the most salient histopathological characteristics of vulvar lichen sclerosus that are described in the literature. They confirmed that the histopathology of VLS in juveniles encompasses the entire range of features attributed to VLS in general. This includes the presence of histopathological features associated with autoimmune diseases. There is a known association with the human leukocyte antigen (HLA) type 2 genes on DQ7, 8, and 9 [11]. Simpkin et al. [12] found that 48% of patients with VLS present active tissue autoantibodies, whereas thyroid disorder was found in 19% of patients. A large, retrospective review of 532 LS patients comprised of both men and women by Kreuter et al. [13] revealed that while 82% of the total cohort had at least one type of autoimmune disease, more women significantly ($p < 0.0001$) showed comorbidity for an autoimmune disease compared to men (18.9% vs 5.1%). Such findings further confirmed prior case-control reports by Harrington and Dunsmore and Cooper et al. citing 34% and 28.4% of LS women having comorbidity with at least one other autoimmune disease compared to healthy controls, respectively [14, 15]. These figures are comparable to case series studies exclusive to women, citing 21.5–25% of VLS female patients with at least one other autoimmune disease [16, 17]. In stark contrast, only 3–7% LS male patients presented comorbidity with an autoimmune disease, with figures comparable to the prevalence of autoimmune diseases in populations without LS [18–20]. This suggests there is a strong, positive association between LS and autoimmune disease in women and in contrast, a weak association in men [21]. Bieber et al. [22] identified 10,004 women with VLS and 21,672,016 female control individuals without VLS from 2015 to 2017 in the United States. In the LS population, the prevalences were as follows: autoimmune thyroid diseases, 6.11%; vitiligo, 1.95%; psoriasis, 5.12%; and vulvar carcinoma, 1.9%. All comorbidities were more likely to occur in patients with LS compared to control individuals. The most associated autoimmune disease was hypothyroidism, with a prevalence of 4.26%. Notably, vulvar carcinoma was 26 times more likely, and vitiligo was 12 times more likely to occur in patients with LS [22]. According to Balakirski et al. [23], the likelihood of developing related autoimmune diseases is less common in children than in adults, and they are observed mainly in girls: vitiligo, morphea, alopecia areata and autoimmune thyroiditis in progress on first place.

The prevalence of CD has significantly increased over the past 50 years. There has been a substantial increase in the numbers of new cases, partly due to better diagnostic tools and thorough screening of individuals considered to be at high risk for the disorder [24, 25]. In western countries, the prevalence is around 0.6% histologically confirmed and 1% in serological screening of the general population. The female-to male ratio ranges from 1:3 to 1.5:1 [26]. The risk of having CD is much greater in first-degree relatives (5–10%) but lesser in second-degree relatives, as well as in individuals with type 1 diabetes mellitus (T1DM) and other autoimmune diseases, Down syndrome, and several other associated diseases [27, 28]. CD may present in many ways. Traditionally patients with CD presented with malabsorption dominated by diarrhoea, steatorrhea, weight loss or failure to thrive. However, CD can present with a wide range of symptoms and signs, including anaemia, vague abdominal symptoms (often similar to IBS), reflux oesophagitis, eosinophilic oesophagitis, neuropathy, ataxia, depression, short stature, osteomalacia and osteoporosis, unexplained liver transaminitis, adverse pregnancy outcomes and even lymphoma [29]. If left untreated, or if misdiagnosed, there may be serious repercussions for patients with either disease [30]. Although the typical presentation of CD generally includes gastrointestinal symptoms, more individuals are present-

ing with extraintestinal manifestations. A wide variety of dermatologic associations have been described, including alopecia, dermatitis herpetiformis, dermatomyositis, and enamel hypoplasia [31].

As we mentioned before, the relationship between CD and other autoimmune disorders remains unclear. It is likely that it is multifactorial, including genotype predisposition, with untreated CD possibly leading to the onset of additional autoimmune conditions [32]. Literature data on the correlation between the incidence of lichen sclerosus in girls and celiac disease are very scarce.

In 2014, Jacobs et al. [30] described three girls with CD, ages 3–5 years, who presented with skin findings, as well as perivaginal and perianal pruritus consistent with a diagnosis of lichen sclerosus. In 2012, Kupfer et al. [33] in their review article discussed the pathophysiology of CD — more specifically, the link with HLA class II genes HLA-DQ2 and HLA-DQ8. Given the common HLA association between CD and LS, we could search for a similar genetic predisposition to developing both diseases [30]. There have been case reports describing resolution of vitiligo in children with CD after instituting a gluten-free diet [34]. Nevertheless, in the cases of the above three children, starting a gluten-free diet did not appear to change the course of the LS.

CONCLUSIONS

The presented work is a pioneering project in which we tried to elucidate a possible relationship between celiac disease and lichen sclerosus in girls. Our investigation assesses a cohort of patients with VLS taking into consideration their baseline characteristics. The second aim of the research was to study the antibodies characteristic of celiac disease in girls with VLS and the assessment, whether the presence of antibodies specific to celiac disease affects the frequency and course of VLS in children. Literature data on this issue are very scarce. In the PubMed database, we found only one work that was directly related to the topic. It is therefore legitimate to conduct further research aimed at clarifying the mutual correlations between the analyzed antybodies in the group of girls with vulvar lichen sclerosus and celiac disease in order to find the mutual correlations between the analyzed antibodies and the onset and course of VLS in girls. The finding of a positive correlation between the coexistence of VLS and CD may prevent potentially serious, long-term complications.

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

1. Jensen LS, Bygum A. Childhood lichen sclerosus is a rare but important diagnosis. Dan Med J. 2012; 59(5): A4424, indexed in Pubmed: 22549488.
2. Powell JJ, Wojnarowska F. Lichen sclerosus. Lancet. 1999; 353(9166): 1777–1783, doi: 10.1016/s0140-6736(98)08228-2, indexed in Pubmed: 10348006.
3. Wallace HJ. Lichen sclerosus et atrophicus. Trans St Johns Hosp Dermatol Soc. 1971; 57(1): 9–30, indexed in Pubmed: 5570266.
4. Ismail D, Owen CM. Paediatric vulval lichen sclerosus: a retrospective study. Clin Exp Dermatol. 2019; 44(7): 753–758, doi: 10.1111/ced.13894, indexed in Pubmed: 30623460.
5. Folk JE, Finlayson JS. The epsilon-(gamma-glutamyl)lysine crosslink and the catalytic role of transglutaminases. Adv Protein Chem. 1977; 31: 1–133, doi: 10.1016/s0065-3233(08)60217-x, indexed in Pubmed: 73346.
6. Gujral N, Freeman HJ, Thomson ABR. Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World J Gastroenterol. 2012; 18(42): 6036–6059, doi: 10.3748/wjg.v18.i42.6036, indexed in Pubmed: 23155333.
7. Proost S, Schlumberger W, Meyer W, et al. EUROIMMUN AG. Europlus - eine Biochip-Kombination aus Gewebeschnitten und Einzelantigenen für die indirekte Immunfluoreszenz: Endomysium/Gliadin, AMA/M2 und Parietalzellen/Intrinsic-Faktor. Poster zum Kongress für Laboratoriumsmedizin 1996 der Deutschen Gesellschaften für Laboratoriumsmedizin und für Klinische Chemie, 17. bis 20. November 1996 in Düsseldorf. J Lab Med. 1996; 20: 670.
8. Howard A, Dean D, Cooper S, et al. Circulating basement membrane zone antibodies are found in lichen sclerosus of the vulva. Australas J Dermatol. 2004; 45(1): 12–15, doi: 10.1111/j.1440-0960.2004.00026.x, indexed in Pubmed: 14961902.
9. Oyama N, Chan I, Neill SM, et al. Autoantibodies to extracellular matrix protein 1 in lichen sclerosus. Lancet. 2003; 362(9378): 118–123, doi: 10.1016/S0140-6736(03)13863-9, indexed in Pubmed: 12867112.
10. Morrel B, Ewing-Graham PC, van der Avoort IAM, et al. Structured analysis of histopathological characteristics of vulvar lichen sclerosus in a juvenile population. Hum Pathol. 2020; 106: 23–31, doi: 10.1016/j.humpath.2020.09.003, indexed in Pubmed: 32971127.
11. Azurdia RM, Luzzi GA, Byren I, et al. Lichen sclerosus in adult men: a study of HLA associations and susceptibility to autoimmune disease. Br J Dermatol. 1999; 140(1): 79–83, doi: 10.1046/j.1365-2133.1999.02611.x, indexed in Pubmed: 10215772.
12. Simpkin S, Oakley A. Clinical review of 202 patients with vulval lichen sclerosus: a possible association with psoriasis. Australas J Dermatol. 2007; 48(1): 28–31, doi: 10.1111/j.1440-0960.2007.00322.x, indexed in Pubmed: 17222298.
13. Kreuter A, Kryvosheyeva Y, Terras S, et al. Association of autoimmune diseases with lichen sclerosus in 532 male and female patients. Acta Derm Venereol. 2013; 93(2): 238–241, doi: 10.2340/00015555-1512, indexed in Pubmed: 23224274.
14. Harrington CI, Dunsmore IR. An investigation into the incidence of auto-immune disorders in patients with lichen sclerosus and atrophicus. Br J Dermatol. 1981; 104(5): 563–566, doi: 10.1111/j.1365-2133.1981.tb08172.x, indexed in Pubmed: 7236515.
15. Cooper SM, Ali I, Baldo M, et al. The association of lichen sclerosus and erosive lichen planus of the vulva with autoimmune disease: a case--control study. Arch Dermatol. 2008; 144(11): 1432–1435, doi: 10.1001/archderm.144.11.1432, indexed in Pubmed: 19015417.
16. Marren P, Yell J, Charnock FM, et al. The association between lichen sclerosus and antigens of the HLA system. Br J Dermatol. 1995; 132(2): 197–203, doi: 10.1111/j.1365-2133.1995.tb05013.x, indexed in Pubmed: 7888355.
17. Meyrick Thomas RH, Ridley CM, McGibbon DH, et al. Lichen sclerosus et atrophicus and autoimmunity--a study of 350 women. Br J Dermatol. 1988; 118(1): 41–46, doi: 10.1111/j.1365-2133.1988.tb01748.x, indexed in Pubmed: 3342175.
18. Virgili A, Borghi A, Toni G, et al. Prospective clinical and epidemiologic study of vulvar lichen sclerosus: analysis of prevalence and severity of clinical features, together with historical and demographic associations. Dermatology. 2014; 228(2): 145–151, doi: 10.1159/000356163, indexed in Pubmed: 24516059.
19. Edmonds EVJ, Hunt S, Hawkins D, et al. Clinical parameters in male genital lichen sclerosus: a case series of 329 patients. J Eur Acad Dermatol Venereol. 2012; 26(6): 730–737, doi: 10.1111/j.1468-3083.2011.04155.x, indexed in Pubmed: 21707769.
20. Kantere D, Alvergren G, Gillstedt M, et al. Clinical features, complications and autoimmunity in male lichen sclerosus. Acta Derm Venereol. 2017; 97(3): 365–369, doi: 10.2340/00015555-2537, indexed in Pubmed: 27671756.
21. Tran DA, Tan X, Macri CJ, et al. Lichen Sclerosus: an autoimmunopathogenic and genomic enigma with emerging genetic and immune

targets. Int J Biol Sci. 2019; 15(7): 1429–1439, doi: 10.7150/ijbs.34613, indexed in Pubmed: 31337973.
22. Bieber AK, Steuer AB, Melnick LE, et al. Autoimmune and dermatologic conditions associated with lichen sclerosus. J Am Acad Dermatol. 2021; 85(1): 228–229, doi: 10.1016/j.jaad.2020.08.011, indexed in Pubmed: 32777320.
23. Balakirski G, Grothaus J, Altengarten J, et al. Paediatric lichen sclerosus: a systematic review of 4516 cases. Br J Dermatol. 2020; 182(1): 231–233, doi: 10.1111/bjd.18267, indexed in Pubmed: 31260081.
24. Ludvigsson JF, Murray JA. Epidemiology of celiac disease. Gastroenterol Clin North Am. 2019; 48(1): 1–18, doi: 10.1016/j.gtc.2018.09.004, indexed in Pubmed: 30711202.
25. Catassi C, Gatti S, Fasano A, et al. The new epidemiology of celiac disease. J Pediatr Gastroenterol Nutr. 2014; 59 Suppl 1: S7–S9, doi: 10.1097/01.mpg.0000450393.23156.59, indexed in Pubmed: 24979197.
26. Al-Toma A, Volta U, Auricchio R, et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. United European Gastroenterol J. 2019; 7(5): 583–613, doi: 10.1177/2050640619844125, indexed in Pubmed: 31210940.
27. Rubio-Tapia A, Van Dyke CT, Lahr BD, et al. Predictors of family risk for celiac disease: a population-based study. Clin Gastroenterol Hepatol. 2008; 6(9): 983–987, doi: 10.1016/j.cgh.2008.04.008, indexed in Pubmed: 18585974.
28. Book L, Zone JJ, Neuhausen SL. Prevalence of celiac disease among relatives of sib pairs with celiac disease in U.S. families. Am J Gastroenterol. 2003; 98(2): 377–381, doi: 10.1111/j.1572-0241.2003.07238.x, indexed in Pubmed: 12591058.
29. Mulder CJJ, Cellier C. Coeliac disease: changing views. Best Pract Res Clin Gastroenterol. 2005; 19(3): 313–321, doi: 10.1016/j.bpg.2005.01.006, indexed in Pubmed: 15925838.
30. Jacobs L, Gilliam A, Khavari N, et al. Association between lichen sclerosus and celiac disease: a report of three pediatric cases. Pediatr Dermatol. 2014; 31(6): e128–e131, doi: 10.1111/pde.12402, indexed in Pubmed: 25382799.
31. Addolorato G, Parente A, de Lorenzi G, et al. Rapid regression of psoriasis in a coeliac patient after gluten-free diet. A case report and review of the literature. Digestion. 2003; 68(1): 9–12, doi: 10.1159/000073220, indexed in Pubmed: 12949434.
32. Fasano A. Systemic autoimmune disorders in celiac disease. Curr Opin Gastroenterol. 2006; 22(6): 674–679, doi: 10.1097/01.mog.0000245543.72537.9e, indexed in Pubmed: 17053448.
33. Kupfer SS, Jabri B. Pathophysiology of celiac disease. Gastrointest Endosc Clin N Am. 2012; 22(4): 639–660, doi: 10.1016/j.giec.2012.07.003, indexed in Pubmed: 23083984.
34. Rodríguez-García C, González-Hernández S, Pérez-Robayna N, et al. Repigmentation of vitiligo lesions in a child with celiac disease after a gluten-free diet. Pediatr Dermatol. 2011; 28(2): 209–210, doi: 10.1111/j.1525-1470.2011.01388.x, indexed in Pubmed: 21504457.