

3. Bonilla FA, Khan DA, Ballas ZK, Chinen J, Frank MM, Hsu JT, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol.* 2015;136:1186–205.
4. Yousefzadegan S, Tavakol M, Abolhassani H, Nadjafi A, Mansouri S, Yazdani R, et al. Systematic investigation for underlying causes of recurrent infections in children: surveillance of primary immunodeficiency. *Eur Ann Allergy Clin Immunol.* 2018;50:72–80.
5. Fischer A, Provot J, Jais JP, Alcais A, Mahlaoui N. Autoimmune and inflammatory manifestations occur frequently in patients with primary immunodeficiencies. *J Allergy Clin Immunol.* 2017;140:1388–93.
6. O'Sullivan MD, Cant AJ. The 10 warning signs: a time for a change? *Curr Opin Allergy Clin Immunol.* 2012;12:588–94.

Claudia Millán-Longo^a, Paula Rodríguez Molino^a,
Teresa del Rosal Rabes^a, Dolores Corral Sánchez^b,
Ana Méndez Echevarría^{a,*}

^a *Servicio de Pediatría Hospitalaria, Enfermedades Infecciosas y Tropicales, Hospital Infantil Universitario La Paz, Instituto de Investigación IdiPAZ, Madrid, Spain*
^b *Servicio de Hemato-Oncología Pediátrica, Hospital Infantil Universitario La Paz, Madrid, Spain*

* Corresponding author.

E-mail address: amendezes@yahoo.es

(A. Méndez Echevarría).

<https://doi.org/10.1016/j.anpede.2018.12.010>
2341-2879/

© 2019 Published by Elsevier España, S.L.U. on behalf of Asociación Española de Pediatría. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Cold urticaria and coeliac disease in a paediatric patient[☆]



Urticaria por frío y enfermedad celiaca en paciente pediátrico

Dear Editor:

Cold urticaria (CU) is a chronic form of urticaria that may be associated with various systemic disorders. Coeliac disease (CD) is also commonly associated with other disorders, usually of the immune system.

To date, there have been several descriptions of the association between CD and chronic idiopathic urticaria in children,¹ but we only found 1 case in the reviewed literature with diagnosis of CD in a patient with a previous history of CU where the cutaneous manifestations improved after excluding gluten from the diet.²

Given the current scarcity in the literature of data on the association between these two conditions, we considered that the description of this case of diagnosis of CD in the context of CU would be of interest.

The patient was a boy aged 5 years assessed due to episodes of urticaria in areas of the body exposed to environmental coldness with onset 2 months prior, manifesting with nasal itching in the absence of other mucosal, cutaneous, respiratory or gastrointestinal symptoms, and improving on returning to warmer settings. The episodes occurred in the absence of previous exercise, intake of drugs or intercurrent infection. The patient did not experience symptoms after bathing in the sea or a pool. The personal and family histories were unremarkable except for a history of rhinitis, hay fever and penicillin allergy in the mother.

The patient had a positive ice cube challenge and received a diagnosis of CU. Further tests included a com-

plete blood count and chemistry panel, measurement of basal tryptase, C-reactive protein, thyroid-stimulating hormone, free thyroxine, anti-thyroid stimulating immunoglobulin and total IgE, total complement test (C3, C4 and C1 inhibitor) and determination of immunoglobulins, antinuclear antibodies, rheumatoid factor and cryoglobulins, all with normal results. The salient findings were serum levels of deamidated antigliadin (DMG) IgG antibodies of 7.3 AU/mL, anti-transglutaminase antibodies (ATA) IgA 11.6 AU/mL and anti-thyroid peroxidase (anti-TPO) antibodies of 63 IU/mL. The patient was instructed to take measures to avoid the cold and to maintain his usual diet without restrictions.

Three months later the patient remained free of gastrointestinal or systemic manifestations and occasionally exhibited very mild facial urticaria after exposure to cold. Laboratory tests revealed levels of DMG IgG of 58 AU/mL, ATA IgA of 66 AU/mL, ATA IgA greater than 200 AU/mL, with a positive result for detection of anti-endomysial antibodies (EMA) (titre of 1:160) and molecular detection of HLA DQ2 (DQA1*05 B1*02) suggestive of sensitivity to gluten. The thyroid function was normal, with a negative result for anti-TSI and a level of anti-TPO of 54 IU/mL.

The patient received a diagnosis of CD and was prescribed a gluten-free diet, after which he exhibited a progressive decrease in the antibody levels, reaching normal values at 10 months, with improvement of cutaneous symptoms.

Cold urticaria is the fourth most frequent cause of chronic urticaria, with an estimated incidence of 0.05%. It can develop at any age, with a higher prevalence between ages 18 and 25 years and a predominance of the female sex (2:1). The diagnosis is based on a compatible history with development of symptoms on exposure to cold stimuli (environment, oral intake, contact) and a positive ice cube challenge. It can be inherited or acquired, and primary or secondary to systemic disorders (such as cryoglobulinemia, vasculitis, infection, hypothyroidism or blood disorders).³

Coeliac disease mainly affects individuals with a genetic predisposition (HLA DQ2/DQ8) and is frequently associated with other immune disorders, such as chronic idiopathic urticaria, diabetes type 1 or autoimmune thyroiditis, among others. In the case presented here, the diagnosis of CD was made based on the ESPGHAN5 criteria (presence of

[☆] Please cite this article as: Méndez Sánchez A, Pascual Pérez AI, Vázquez Piñera MA, Fernández González P. Urticaria por frío y enfermedad celiaca en paciente pediátrico. *Arch Bronconeumol.* 2019;91:410–411.

symptoms, HLA DQ2 haplotype, an ATA IgA value more than tenfold the upper limit of normal and a second positive marker [EMA]) without performance of a biopsy.

Our patient exhibited typical clinical features of CU without manifestations suggestive of CD. Subsequent follow-up evaluations detected a progressive increase in serum markers of CD, which improved after exclusion of gluten from the diet. The pattern of cutaneous symptoms paralleled the changes in serum markers of CD.

The immune mechanisms underlying chronic urticaria and CD are different (Th2 and Th1 responses, respectively).^{4,5} A hypothesis proposed to explain cases where both disorders are associated is that the increased bowel permeability secondary to inflammatory infiltration in CD would allow passage of antigens to the blood and the formation of circulating immune complexes believed to be involved in the pathogenesis of chronic urticaria. Additional mechanisms have been proposed, such as the formation of anaphylatoxins triggered by the production of antibodies, which in turn induce the degranulation of mast cells and basophils.⁵

Recent reviews of cases of chronic urticaria have concluded that routine performance of a broad array of diagnostic tests offers a poor yield for diagnosis of associated diseases, and that performance of tests based on the findings of the history taking and/or the physical examination is more useful.⁶

This case study, along with other reported cases, encourage considering the addition of screening for CD in children with CU to the history taking and physical examination, and other diagnostic tests in case of suggestive findings.

References

1. Caminiti L, Passalacqua G, Magazzù G, Comisi F, Vita D, Barberio G, et al. Chronic urticaria and associated coeliac disease in children: A case-control study. *Ped Allergy Immunol*. 2005;16:428–32.
2. Pedrosa Delgado M, Martín Muñoz F, Polanco Allué I, Martín Esteban M. Cold urticaria and celiac disease. *J Investig Allergol Clin Immunol*. 2008;18:123–5.
3. Hochstadter EF, Ben-Shoshan M. Cold-induced urticaria: challenges in diagnosis and management. *BMJ Case Rep*. 2013;8, <http://dx.doi.org/10.1136/bcr-2013-010441>.
4. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, et al. European society for pediatric gastroenterology hepatology, and nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr*. 2012;54:136–60.
5. Peroni DG, Parola G, Tenero L, Fornaro M, Bodini A, Pollini F, et al. Chronic urticaria and celiac disease: a case report. *Pediatr Dermatol*. 2010;27:108–9.
6. Kozel MM, Bossuyt PM, Mekkes JR, Bos JD. Laboratory tests and identified diagnoses in patients with physical and chronic urticaria and angioedema: a systematic review. *J Am Acad Dermatol*. 2003;48:409–16.

Alejandra Méndez Sánchez^{a,*}, Alicia Isabel Pascual Pérez^b,
 María Antonia Vázquez Piñera^a,
 Porfirio Fernández González^a

^a *Unidad de Alergia Infantil, Área de Gestión Clínica de Pediatría, Hospital Universitario Central de Asturias, Oviedo, Spain*

^b *Unidad de Gastroenterología Infantil, Área de Gestión Clínica de Pediatría, Hospital Universitario Central de Asturias, Oviedo, Spain*

*Corresponding author.

E-mail address: amendezarbolea@gmail.com

(A. Méndez Sánchez).

<https://doi.org/10.1016/j.anpede.2019.01.017>
 2341-2879/

© 2019 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Takayasu arteritis of atypical presentation. Tocilizumab as an alternative therapeutic option[☆]



Arteritis de Takayasu de presentación atípica. Tocilizumab como alternativa terapéutica

Dear Editor:

Takayasu arteritis (TA) is a granulomatous large vessel vasculitis that is infrequent in children. It usually has onset with headache, fever, abdominal pain or hypertension (HTN). In rare cases, onset occurs with heart failure, which has only been described in 18% of paediatric cases. There has been

recent evidence of the involvement of interleukin-6 (IL-6) in its pathogenesis, whose levels appear elevated in serum and the arterial wall.¹

The diagnosis of TA requires the presence of angiographic abnormalities in addition to at least 1 out of 5 criteria (EULAR/PRINTO/PRES criteria, [Table 1](#)).² Although computed tomography angiography (CTA) is the gold standard of imaging, as it allows visualization of blood flow and the extent of collateralization, it does not provide any information about the arterial wall. Thus, a magnetic resonance angiography (MRA) is also useful to assess abnormalities of the vessel wall, and its results correlate to clinical manifestations and inflammatory marker levels. Positron emission tomography/computer tomography (PET-CT) is not indicated for routine assessment, but it may be useful in patients with negative inflammatory markers.²

Treatment is delivered in 2 phases: induction and maintenance. In case of haemodynamic instability, the induction phase consists of steroids delivered by intravenous pulse initially followed by oral administration combined with an immunosuppressive agent (cyclophosphamide or methotrexate).³ The agents used in the maintenance

[☆] Please cite this article as: Cubiles Arillo Z, Núñez Cuadros E, Martínez Rivera V, González Gómez JM, Cuenca Peiró V. Arteritis de Takayasu de presentación atípica. Tocilizumab como alternativa terapéutica. *An Pediatr (Barc)*. 2019;91:411–413.