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Article type : Letter to the Editor

Dermatographism and urticaria in a paediatric population

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Running Title: Dermatographism and urticaria in children

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Word count: 1190

Table count: 1

Figure count: 2

Disclosure statement: The authors declare that there are no conflicts of interest regarding the publication of this paper.

Financial support: The authors received no specific funding for this work.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/PAI.13209](#)

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To the Editor,

Dermatographism is a transient linear cutaneous wheal produced after applying a force or scratching the skin. Wheals usually appear in about 5 to 10 minutes and persist for 15 to 30 minutes. Simple dermatographism must be differentiated from "symptomatic dermatographism" where patients suffer itching or a burning sensation together with the erythematous wheal [1,2]. Dermatographism is the most common expression of physical urticaria [3] with a prevalence estimated as 2-5% in the general population, with a higher prevalence in the paediatric population of about 24% [4]. The pathophysiology is explained as an exaggeration of the triple response of Lewis, where mechanical trauma activates vasoactive mediators released from mast cells following antigen interaction to the bound IgE; other mediators like histamine, leukotrienes, bradykinin, heparin, kallikrein, substance P are also most likely implicated [1]. Simple dermatographism is transient and does not usually require treatment. Stroking the skin with an object that can produce a linear pressure helps in diagnosing dermatographism, however the action is operator-dependent and has inter-individual variations [5]. For this reason, an appropriate validated method to elicit dermatographism has recently been developed and the authors of two studies described their results with this instrument, called the FricTest, or friction test dermographometer (Charité Hospital, Berlin, Germany) [2,6]. Both studies included adult patients. The aim of this study was to evaluate dermatographism in a paediatric population and investigate its correlation with urticaria and atopy. To our knowledge, this is the first study to examine a possible link between dermatographism and urticaria, and also to specifically focus on children.

Materials and methods

From April 2018 to March 2019, 100 children with history of urticaria, evaluated in the Allergy Unit of Anna Meyer Children's Hospital, were consecutively enrolled as "cases". A parallel group of 100 children without a history of urticaria were enrolled as "controls". At the hospital admission and according to the hospital ethic committee form, all children's parents signed an informed consent to the processing of clinical data for research studies. Patients who did not give the consent were excluded from the present study. We recorded their demographic characteristics (age, sex), family history of urticaria, associated symptoms (rhinitis, atopic dermatitis, asthma). In children with a history of urticaria, we reported the type of urticarial manifestation (acute, chronic) and possible causes (physical, foods, drugs, infectious diseases). Urticaria was defined as "acute" when children reported a single episode or several episodes over a period of weeks or months, but always isolated and with rapid resolution; "chronic" when they had recurrent episodes lasting longer than 6 weeks with continuous disease activity [7]. In case of physical urticaria, we reported the specific trigger based on the clinical history (heat, cold, pressure, cholinergic). When urticaria occurred without a specific cause it was defined as spontaneous/idiopathic. The aetiology of urticaria was based on the clinical history; patients with suspected food or drug hypersensitivity (with urticaria as the primary symptom) underwent subsequent allergy investigations but the final diagnosis falls outside the aim of this paper.

All patients underwent skin prick tests (SPTs) with common inhalants and in case of suspected food allergy, also with the culprit food. The SPT result was considered positive if the mean wheal diameter was ≥ 3 mm compared with the negative control [8]. Depending on the SPT results, patients were divided into two groups, "atopic" and "non-atopic".

During the visit, a provocation test with the FricTest was performed to evaluate the presence and degree of dermatographism. A FricTest 4.0 (Moxie, Berlin, Germany) was applied perpendicular to the skin of the volar forearm with a pressure ensuring complete contact of all the pins. The instrument has four pins with different lengths of 3 – 3.5 – 4 – 4.5 mm respectively, allowing for simultaneous testing of 4 shear force strengths, which is ideal for threshold testing [9]. A wheal with a width of ≥ 3 mm measured 10 min after provocation was considered a positive response. When all the pins elicited the wheals, it was considered "severe" dermatographism [2].

Statistical analysis

The chi-square test was used to assess the relationship between the different forms of urticaria and dermatographism and between atopy and dermatographism. Moreover, positive family history of

urticaria was calculated in the cases and controls. A p-value equal or inferior to 0.001 was considered statistically significant. Statistics were performed using SOFA Statistics version 1.5.0.

Results

During the enrolment period, 200 patients were included, 100 cases and 100 controls. Among the cases, 61 children had negative SPTs (non-atopic) and 39 had positive SPTs for inhalants and/or foods (atopic). Among the controls, 62 children were non-atopic and 38 were atopic. Mean age was 8.3 years. A family history of urticaria (in a first-degree relative) was reported in 26% of cases and 7% of controls, respectively ($p < 0.01$). Other symptoms (rhinitis, wheezing/asthma, atopic dermatitis) were recorded for the two groups. The demographic characteristics are summarised in Table 1.

Among the cases, 77% had a history of acute urticaria and 23% of chronic urticaria.

Overall, dermatographism was elicited in 73/200 (36.5%) of children, in 51% of cases and in 22% of controls. Among the cases, dermatographism was present in 23/51 (45%) of atopic and 28/51 (55%) of non-atopic children, respectively. Investigating the degree of dermatographism, severe dermatographism was present in 17/92 (18.5%) patients with dermatographism and in particular in 16 cases and 1 control. Figure 1 illustrates the presence of dermatographism among patients with different types of urticaria: 39/77 (50.6%) in children with acute urticaria and 12/23 (52.2%) in children with chronic urticaria. As regards severe dermatographism (Figure 2), it was elicited in 16% of patients with urticaria and in particular, in 26% with chronic urticaria.

Regarding the correlation between dermatographism and atopy, we found that overall, dermatographism was present in 32/77 (41.5%) atopic patients and 41/123 (33.3%) non-atopic patients. The statistical analysis showed a significant correlation ($p < 0.001$) between dermatographism and urticaria and between severe dermatographism and urticaria. There was a statistically significant difference in the family history of urticaria between the cases and controls. Conversely, there was no association between dermatographism and atopy.

Discussion and conclusion

Dermatographism is considered the most common form of physical urticaria, in most patients it is idiopathic [4], however it has also been reported in association with hypereosinophilic syndrome, drug-induced urticaria, reactive polyarthritis with *Helicobacter pylori*, and endocrinopathies like hyperthyroidism, hypothyroidism, diabetes mellitus etc.

Martorell et al [4] investigated dermatographism in a paediatric population and its correlation with atopy, reporting that 38% of children with dermatographism had positive skin tests, lower than our rate (32 atopic patients out of 73 with dermatographism - 43.8%). Moreover, in their study 47 out of 100 children with atopy had dermatographism, similar to our data (32 patients with dermatographism out of 77 atopic children – 41.5%).

There are no studies in literature that evaluate the relationship between dermatographism and urticaria. For the first time our pilot study has shown a statistically significant correlation between urticaria and dermatographism in a paediatric population, without any differences between the acute and chronic forms. Consequently, dermatographism could be related to urticaria per se and not only to the chronic inducible form, suggesting a unique intrinsic marker in all forms of urticaria.

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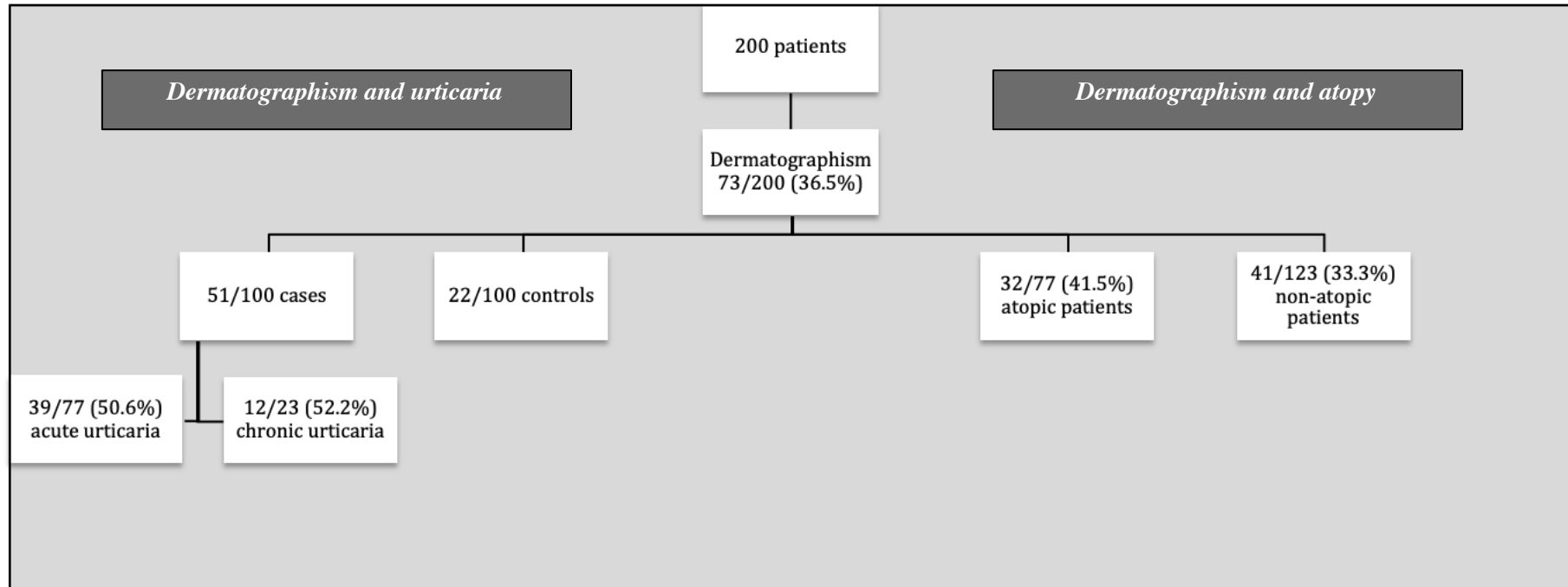
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Figure 1. Evidence of dermatographism associated with urticaria and atopy.

Figure 2. Severe dermatographism (on the left)

Table 1. Demographic characteristics of patients

<i>PATIENTS</i>	Number		Mean age (y)	Sex	Family history of urticaria	Rhinitis	Wheezing/ asthma	Atopic dermatitis
<i>Cases (urticaria)</i>	100		8.5	45 M/55 F (0.8)	26/100	31/100	19/100	30/100
	Acute	77						
	Chronic	23						
<i>Atopic</i> <i>Non-atopic</i>	39	61						
<i>Controls</i>	100		8.1	51 M/49 F (1)	7/100	46/100	28/100	18/100
<i>Atopic</i> <i>Non-atopic</i>	38	62						
<i>TOT</i>	200		8.3	96 M/104 F (0.9)	33/200 (16%)	77/200 (38%)	47/200 (23.5%)	48/200 (24%)





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