

Short communication

Clinical features and natural history of physical urticaria in children

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Physical triggers are the most common precipitating factors for chronic urticaria in childhood. We investigate the natural history of physical urticaria (PU) and attempt to identify prognostic features. A retrospective study covering a 3 yr period (1999–2002) identified 82 children with PU seen in a tertiary referral centre. Parents of 53 children with PU responded to follow up by questionnaire and were included in the data analysis. The questionnaire ascertained symptom severity, remission status, effects of treatment and prognostic factors in determining resolution of the urticaria. Not all parents answered every question. Fisher's exact test was used to compare the remission and non-remission groups and Kaplan–Meir survival analysis was used to derive estimates of time to achieve remission. All 53 children with PU had chronic urticaria, with dermatographic, cholinergic and mixed subtypes of PU forming over 70% of the subtypes. Overall, 13% (6/45) of the children reported respiratory symptoms with the episodes of urticaria, and 67% (35/52) reported associated angioedema. In univariate analysis, a history of other allergic conditions in the child was associated with a greater chance of non-remission ($p = 0.007$). No significant difference in the age of onset of urticaria and duration of individual bouts was noted between the remission and non-remission groups. Episodes of urticaria were significantly less frequent ($p = 0.02$) in the remission group (monthly/weekly/daily – 70%/30%/0%) than the non-remission group (38%/34%/28%). Among the 20 children achieving remission, on average this occurred 30 months after onset of symptoms. In the survival analysis, the number of children becoming urticaria free was 11.6% (95% CI: 5.4%–23.9%) at 1 yr post-onset and 38.4% (95% CI: 25.9%–54.3%) 5 yr post-onset. In conclusion, based on this selected tertiary population, the prognosis for PU may not be as benign as has previously been reported. A history of allergic conditions and more frequent episodes of urticaria were associated with a poorer prognosis.

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Chronic urticaria, defined as urticaria lasting longer than 6 wk, affects 0.1–0.3% of children in the UK. Physical urticaria (PU) has been reported as the cause of 6–17% of chronic urticaria (1). PU is divided into several subtypes with dermatographic urticaria being the commonest form of PU in children and adults – in some pediatric studies accounting for up to 24% of the sample (Table 1) (2–5).

There is very limited literature regarding the natural history of PU, and most relates to the adult population (3). A search of PubMed up to 2006 revealed 19 publications since 1983, only five of which included any pediatric data (1, 3, 6–8).

The aim of the current study is to investigate the natural history of PU in a pediatric population seen in a tertiary referral pediatric allergy clinic. The different subtypes of PU and their

Table 1. Classification of physical urticaria

Type	Usual triggers
Dermatographic	Minor trauma
Aquagenic	Hot or cold water
Cholinergic	Emotion, exercise
Cold	Cold water, cold environment
Delayed pressure	Tight clothing, jogging, sitting
Solar	Sunshine
Vibratory	Vibrating tools
Exercise	Physical exertion

prevalence are assessed, as is the age of onset and, if applicable, resolution. Data relating to frequency of the episodes and associated symptoms are also presented. Prognostic factors for remission vs. non-remission are analyzed.

Subjects and Methods

The study was carried out at the Department of Pediatric Allergy, Asthma and Immunology at St Mary's Hospital, London, a tertiary referral centre serving West London and surrounding areas. The Department patient database was searched retrospectively for patients over a 3 yr period (September 1999 to August 2002), using a number of keywords to identify the cases (i.e., PU, names of subtypes, chronic urticaria). The relevant medical records were then reviewed to confirm the diagnosis of PU. Follow-up data was obtained using a questionnaire sent out between January and March 2003.

Our search identified a total number of 410 cases diagnosed with all types of urticaria during the study period. A total of 82 patients with PU were finally identified. Only patients with urticaria solely generated by physical stimuli were included. All patients were sent a questionnaire with specific questions referring to the condition's progress. The parents of these children were asked about the presence and nature of symptoms, age of onset and, where applicable, age of resolution. Other questions aimed to reveal the frequency of the episodes, their average duration, treatment, and the presence of any associated swelling or difficulty in breathing. Finally, the parents were questioned regarding any first degree family history of allergy or allergies in the affected child (asthma, eczema, perennial rhinitis, hay fever, pet allergy, food allergy). The data were analyzed using STATA 8 (9).

Results

There were 53 respondents (M:F 25:28), a response rate of 65%. Not all respondents

answered every question. There were no significant demographic differences between the questionnaire responders and the 29 non-responders.

The subtypes of PU reported were as follows: dermatographic ($n = 20$, 38%), cholinergic ($n = 10$, 19%), mixed physical subtypes ($n = 9$, 17%), pressure ($n = 5$, 9%), cold ($n = 5$, 9%), heat ($n = 1$, 2%), unspecified ($n = 2$, 4%) and subtype not declared ($n = 1$, 2%). Among the mixed group, the combination of cholinergic and dermatographic urticaria was the commonest.

All children exhibited chronic urticaria as their symptoms lasted for more than 6 wk. In 35 out of 52 patients (67%) there was associated angioedema during the urticarial episodes. The frequency of respiratory symptoms during bouts of urticaria was low, comprising only six out of 45 patients (13%).

For the purposes of the survival analysis, the cohort was divided into 'remission' and 'non-remission' groups, with remission being defined as the absence of any urticaria for at least three consecutive months and until the time of follow up. At the time the study was performed, the condition had resolved in 38% of the patients ($n = 20$, M:F 13:7). The profiles of the remission group and non-remission group are summarized in Table 2. No statistically significant differences were found in the age of onset and duration of bouts between the remission and non-remission groups. However, the increased frequency of exacerbations seen in the non-remission group was statistically significant ($p = 0.02$). Children in non-remission were also more likely to have a history of allergic conditions ($p = 0.007$).

A Kaplan-Meier plot was produced to assess the natural history of PU among the children going into remission (Fig. 1). Of those going into remission, 50% had done so approximately 2 yr post-onset.

The survival analysis of the whole cohort presents a less optimistic picture: the number of children becoming urticaria free was 11.6% (95% CI: 5.4%–23.9%) at 1 yr post-onset and 38.4% (95% CI: 25.9%–54.3%) 5 yr post-onset. However, it is important to note that a considerable number of the non-remitting children are censored in the survival analysis (i.e., have not been followed up for a prolonged period) – 25% had had their urticaria for 30 months or less at the time of the questionnaire.

Discussion

This is the largest reported study of physician diagnosed PU in children. Overall, 38% of our

Table 2. Comparison of remission and non-remission children

	Remission group (n = 20)	Non-remission group (n = 33)	p-value
Age of onset (yr)	4.4	4.1	0.75*
Sex (Male:Female)	13:7	14:19	0.16†
Mean duration of PU in months (inter-quartile range)	30.1 (12–39)	56.7 (30–78)	0.003*
Frequency of episodes			
Monthly	70% (14/20)	38% (11/29)	0.02‡
Weekly	30% (6/20)	34% (10/16)	
Daily	0%	28% (8/29)	
Duration of episodes (days)	2.2	1.6	0.17*
Associated features			
Angioedema	65% (13/20)	69% (22/32)	1.0†
Breathing difficulty	6% (1/16)	17% (5/29)	0.40†
Personal history of other allergic conditions	50% (10/20)	89% (24/27)	0.007†
Family history of other allergic conditions	80% (16/20)	96% (27/28)	0.15†
Family history of urticaria/angioedema	32% (6/19)	20% (6/30)	0.50†

*Student's *t*-test; †Fisher's exact test; ‡Chi-squared test.

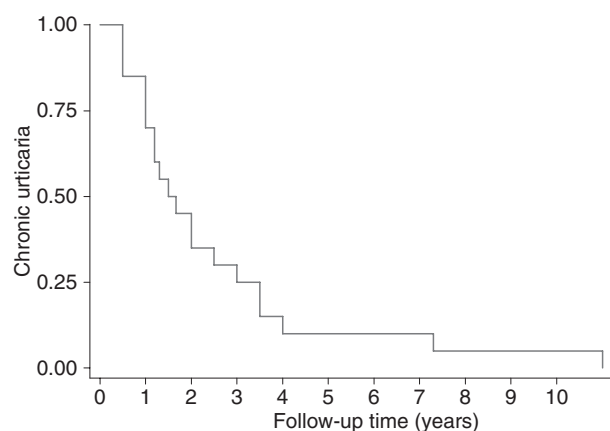


Fig. 1. Kaplan–Meier plot of time to remission for the subgroup achieving remission.

patients were free of symptoms at the time of the study and the mean duration of symptoms was 30 months among those achieving remission. In the adult study of Kozel et al. (6), the remission rate for PU at 1 yr follow up was 16.4%, whereas in our cohort it was 11.6%. Humphreys and Hunter (3) found that symptoms were persistent for more than 5 yr in 5% of children with PU and 13% of adult patients. However, in our study the average duration of urticaria for all the children was 47 months suggesting a significantly poorer prognosis and only 38.4% were urticaria free 5 yr post-onset. Participation bias may account for some of the difference in the poorer prognosis in this study compared to previous studies with respondents perhaps being more likely to have on-going urticaria than non-respondents. Selection bias may also be an issue in that the population studied was derived from a specialist tertiary referral allergy clinic, and therefore is likely to represent the more severe end of the spectrum of PU.

All the children had chronic urticaria. There was no male or female predominance in children suffering from PU in this study, although adult studies have shown that about two-thirds of the affected people are women (3). The dermatographic, cholinergic and mixed subtypes of PU represented the commonest types of PU, in that order, and together accounted for over 70% of all cases. The frequencies of the different subtypes are in keeping with other researchers' results (1, 3, 6).

In the current study, 67% of the children had angioedema associated with their urticaria, and 13% reported respiratory involvement. The study of Sackesen et al. (1) included a very small number of children, and reported that associated angioedema occurred in 59% of the cases.

Children with PU can present at any age. The mean age of onset in the remission and non-remission groups is very similar, which from a clinical perspective means that age alone will not discriminate who will achieve remission. In contrast, frequent episodes (daily) and a history of allergic conditions suggest a poorer prognosis.

In conclusion, PU is a relatively common cause of chronic urticaria in childhood and almost always affects quality of life. The prognosis in this cohort would appear to be less favorable than has been previously reported, and prognostic factors are relatively few.

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