

ORIGINAL ARTICLE

Characteristics of persistent diaper dermatitis in children with food allergy

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Abstract

Background/Objectives: Diaper dermatitis is often caused by irritant contact occurring beneath the diaper of an infant, and it is aggravated by factors such as dampness, friction, urea, and feces. Food-allergic patients are known to exhibit various skin lesions ranging from urticaria to eczema. This study aims to determine the relationship between persistent diaper dermatitis and food allergy.

Methods: A retrospective chart review was conducted of pediatric patients with a diagnosis of persistent diaper dermatitis between August 2015 and November 2017.

Results: The study included 157 patients diagnosed with persistent diaper dermatitis (67 male, 72 female; median age: 13 months). Diaper dermatitis was more common and included the whole perineum in children who had multiple food allergies ($P = 0.001$). In children with multiple food allergies, the course of diaper dermatitis was more severe, and the condition did not respond to topical treatment ($P = 0.025$). A longer elimination diet was required for patients with Type I reactions and persistent diaper dermatitis ($P = 0.018$). In patients with Type II and mixed reactions, diaper dermatitis was more diffuse and covered the whole perineum ($P = 0.025$). In patients with Type II and mixed reactions, diaper dermatitis was more severe and did not respond to topical treatment ($P = 0.025$).

Conclusions: Persistent diaper dermatitis lasting longer than a month may be associated with food allergy. The diaper rash may also be the only indicator of the food allergy. Elimination of the responsible food may allow these patients to recover from persistent diaper dermatitis.

KEYWORDS

allergy, diaper dermatitis

1 | INTRODUCTION

Food allergy is defined as “an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.”¹ Food allergies can arise in infancy and early childhood, with onset occurring with the introduction of nonmaternal food into the diet.² The most common allergenic foods in early childhood are

cow's milk, eggs, peanuts, hazelnuts, and sesame, while the most common allergenic foods in older children are peanuts, hazelnuts, and seafood.³

Clinicians use the term diaper dermatitis (DD) to describe any of the various cutaneous eruptions appearing in the diaper area. It may provide clues to the diagnosis of a more significant systemic disease or local infection.⁴ The incidence of DD has been shown to peak

between the ages of nine and 12 months.⁵ Its etiology is multifactorial, and impaired barrier function is the underlying pathology. Skin overhydration, diarrhea, oral antibiotics, and prolonged exposure to urine, feces, and microorganisms can all contribute to DD.⁶ This study aims to examine the association between persistent (lasting for more than 1 month) DD and food allergy.

2 | MATERIALS AND METHODS

This retrospective study was conducted at the Gaziosmanpasa Taksim Education and Research Hospital's Pediatric Allergy and Immunology Department and at the İnönü University Medical Faculty's Department of Pediatric Allergy and Immunology between August 2015 and November 2017. Patients admitted to the pediatric allergy and immunology polyclinic with a complaint of persistent DD were included in the study. Patient files were reviewed retrospectively.

One hundred fifty-seven patients with persistent DD (aged 2-89 months) were included in the study. Patients who had DD lasting for at least a month with or without treatment were considered as having persistent DD. Demographic data such as the age of onset of DD, diagnosis age, regular breastmilk intake, duration of DD, accompanying atopic disease, family history of atopy, the nutrient responsible for food allergy, type of food allergy, follow-up DD improvement, recovery time from DD, localization of DD, topical treatment application, topical treatment application time, and response to topical treatment were obtained from the electronic files of the patients. The laboratory result data including total IgE and allergen-specific IgE were obtained from patient files. In addition, the results of skin prick and atopy patch testing were reviewed. The patients were divided into three groups according to the classical findings of food allergy:⁷ Type I (IgE-mediated), Type II (non-IgE-mediated), and mixed type. In addition, the patients were classified in two groups as having a single food allergy or multiple food allergies, and statistical comparisons were performed. The outcomes of food elimination diet were examined.

2.1 | Statistics

We performed statistical analysis using Statistical Package for Social Sciences (SPSS) 21.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as frequency and percentage for categorical variables, whereas quantitative data were expressed as median for non-normally distributed data and as mean for normally distributed data. We used the Mann-Whitney *U*-test to compare the two groups, used the Kruskal-Wallis test to compare the three groups, and used the chi-square test to compare the categorical variables.

2.2 | Ethical considerations

Ethical approval was granted in decision no. 2018/3-9 (dated 30 January 2018) by İnönü University's Ethics Committee of Medical Research.

3 | RESULTS

The study included 157 patients diagnosed with persistent diaper dermatitis (67 male, 72 female; median age: 13 months). The persistent DD of 74.5% of the patients completely or partially disappeared with the elimination diet. No statistically significant differences were

TABLE 1 Demographic of children with persistent diaper dermatitis

	n (%)
Male	85 (54.1)
Female	72 (45.9)
Age at diagnosis, median, (min-max) month	13 (2-89)
Age at onset of diaper dermatitis, median, (min-max) month	2 (0-84)
Duration of diaper dermatitis, median, (min-max) month	8 (1-48)
Family history of atopy	82 (52.2)
Breastfed	90 (57.3)
Atopic disease, in patient	123 (78.3)
Allergic rhinitis	70 (44.6)
Atopic eczema	68 (43.3)
Asthma/wheezing	67 (42.7)
Drug allergy	9 (5.7)
Responsible food	
Cow's milk	96 (61.1)
Egg	32 (20.4)
Wheat	3 (1.9)
Multiple	26 (16.6)
Type of food allergy	
Type 2 (Non-IgE-mediated)	61 (38.9)
Mixed	54 (34.4)
Type 1 (IgE-mediated)	42 (26.8)
Eosinophilia	61 (38.9)
Serum IgE level elevation	44 (28.0)
Follow-up diaper dermatitis improvement	114/153 (74.5)
Recovery time of diaper dermatitis, week, (min-max)	6 (2-8)
Localization of diaper dermatitis	
Whole perineum	105 (66.9)
Local redness	52 (33.1)
Topical treatment application	157 (100.0)
Topical treatment application time, month (min-max)	4 (1-47)
Response of topical treatment	
Responded but repeats	97 (61.8)
No response	60 (38.2)
Oral food challenge for diagnosis	70 (44.5)
Patients with only persistent diaper dermatitis	10 (6.3)
Total	157 (100.0)

TABLE 2 Clinical signs of children with persistent diaper dermatitis

	n (%)
Gastrointestinal system	123 (78.3)
Diarrhea	39 (24.8)
Bloody mucus stool	18 (11.5)
Vomiting	11 (7.0)
Weight loss	7 (4.5)
Constipation	5 (3.2)
Abdominal pain	3 (1.9)
Dyspepsia	1 (0.6)
Skin	110 (70.1)
Urticaria	88 (36.9)
Eczema	57 (36.3)
Pruritis	44 (28.0)
Rash around the mouth	12 (7.6)
Angioedema	7 (4.5)
Flushing	5 (3.2)
Respiratory system	16 (10.2)
Cough	7 (4.5)
Shortness of breath	7 (4.5)
Wheezing	7 (4.5)
Nasal discharge	2 (1.3)
Stridor	0 (0.0)
Cardiovascular system	2 (1.3)
Hypotension	1 (0.63)
Syncope	1 (0.63)
Palpitation	0 (0.0)
Bradycardia	0 (0.0)
Weakness	0 (0.0)
Anaphylaxis	2 (1.3)

found between the healed and unhealed groups in terms of eosinophilia, specific IgE value of food, prick test induration diameter, or serum IgE level ($P > 0.05$). Gastrointestinal symptoms were found in 78.3% of the patients. The demographic and clinical characteristics of the patients diagnosed with DD are summarized in Tables 1 and 2, respectively.

The patients with diaper dermatitis were divided into two groups: those with a single food allergy and those with multiple food allergies. No statistically significant differences were found between singly sensitive and multiply sensitive patients in terms of gender, diagnosis age, DD onset age, duration of DD, atopy in the family, co-existing atopic disease, eosinophilia, follow-up DD improvement, recovery time from DD, or serum IgE level ($P > 0.05$). In the multiple-food-allergy group, having been breastfed for < 6 months was a risk factor ($P = 0.001$). Diaper dermatitis was found to be more common in patients with multiple food allergies, where it was found to include the whole perineum ($P = 0.001$). In addition, DD was found to be more severe in patients with multiple food allergies and in that group it did not respond to topical treatment ($P = 0.025$). The

TABLE 3 Comparison of patients with single and multiple food allergies

	Single food allergy n (%)	Multiple food allergy n (%)	P
Male	67 (51.9)	18 (69.2)	0.091
Diagnosis age, median, (min-max) month	13 (2-89)	11 (4-48)	0.269
Diaper dermatitis onset age, median, (min-max) month	2 (0-84)	3 (039)	0.668
Duration of diaper dermatitis, median, (min-max) month	9 (1-48)	6 (1-48)	0.112
Breastfed (< 6 mo)	84 (64.1)	6 (23.1)	0.001
Family history of atopy	64 (48.9)	18 (69.2)	0.057
Atopic disease, in patient	101 (77.1)	22 (84.6)	0.395
Eosinophilia	51 (38.9)	10 (38.5)	0.964
Serum IgE level elevation	38 (29.0)	6 (23.1)	0.539
Follow-up diaper dermatitis improvement	96 (75.0)	18 (72.0)	0.742
Recovery time of diaper dermatitis, week (min-max)	6 (2-8)	6 (3-8)	0.968
Localization of diaper dermatitis, whole perineum	80 (61.1)	25 (96.2)	0.001
Response of topical treatment, no response	45 (34.3)	15 (57.7)	0.025

Bolded P -values indicate statistical significance.

statistical data of patients with singly sensitive and multiply sensitive allergy are summarized in Table 3.

In addition, patients with DD were placed in three groups according to the classical symptoms of food allergy as Type I, Type II, and mixed type. No statistically significant differences were found among the three groups in terms of gender, diagnosis age, DD onset age, comorbid atopic disease, atopy in the family, eosinophilia, specific IgE value of food, prick-test induration diameter, follow-up DD improvement, or serum IgE level ($P > 0.05$). Type I reactions were found to be more frequent ($P = 0.001$) in patients who had been breastfed for < 6 months. Type II reactions required an elimination diet of longer duration ($P = 0.018$). In Type II and mixed reactions, DD was found to be more diffuse, and it covered the whole perineum ($P = 0.025$). In addition, in Type II and mixed reactions, DD was found to be more severe, and it did not respond to topical treatment ($P = 0.025$). The statistical data of patients with Type I, Type II, and mixed reactions are summarized in Table 4.

4 | DISCUSSION

Diaper dermatitis is the most frequent skin disease in infants, generally developing in months 8-12 and in 7%-35% of infants. The incidence of DD does not differ in terms of race and gender.⁸ Breastfeeding plays an important role in the prevention of DD because the feces of exclusively breastfed infants have a lower pH

TABLE 4 Comparison of patients by type of food allergy

	Type I n (%)	Type II n (%)	Mixt n (%)	P
Male	26 (61.9)	32 (52.5)	27 (50.0)	0.484
Diagnosis age, mean ± SD, month	16.3 ± 11.36	17.08 ± 13.55	13.5 ± 8.68	0.336
Diaper dermatitis onset age, mean ± SD, month	5.19 ± 9.16	7.67 ± 12.94	4.5 ± 5.5	0.101
Duration of diaper dermatitis, mean ± SD, month	11.1 ± 8.3	9.30 ± 7.57	8.69 ± 8.17	0.12
Breastfed (> 6 mo)	8 (19.0)	30 (49.2)	29 (53.7)	0.001
Family history of atopy	19 (45.2)	39 (63.9)	24 (44.4)	0.066
Atopic disease, in patient	30 (71.4)	48 (78.7)	45 (83.3)	0.374
Eosinophilia	16 (38.1)	22 (36.1)	23 (42.6)	0.769
Serum IgE level elevation	15 (35.7)	13 (21.3)	16 (29.6)	0.266
Specific IgE value of food, mean ± SD	4.01 ± 7.97	2.83 ± 11.4	3.2 ± 9.3	0.085
Prick test induration diameter, mean ± SD, mm	3.16 ± 2.65	1.82 ± 1.89	2.04 ± 2.06	0.023
Follow-up diaper dermatitis improvement	29 (69.0)	50 (84.3)	35/52 (67.3)	0.067
Recovery time of diaper dermatitis, mean ± SD, week	6.72 ± 2.01	5.43 ± 2.31	5.38 ± 2.19	0.018
Localization of diaper dermatitis, whole perineum	21 (50.0)	44 (72.1)	40 (74.1)	0.025
Response of topical treatment, no response	9 (21.4)	29 (47.5)	22 (40.7)	0.025
Total	42 (100.0)	61 (100.0)	54 (100.0)	

and lower protease and lipase activity, making it less irritating.⁹ Thus, the disease is less common in children who are breastfed compared with those fed with prepared food or cow's milk.⁸ Approximately 40% of patients with food allergy have experienced a life-threatening allergic reaction, and 30% of children with food allergy have multiple food allergies.¹⁰ In our study, having been breastfed for < 6 months was a risk factor in patients with multiple food allergies. DD was more common in patients with multiple food allergies and covered the whole perineum. In addition, DD was found to have a more severe course in those patients, and it did not respond to topical treatment. Among our patients with Type I reactions, only two had a history of anaphylaxis. A great number of our patients presented urticaria, which developed within the first 2 hours. Thus, mothers continued to use milk products despite the reaction.

Food allergy is defined "as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food." The term allergy is not limited to IgE-mediated immunologic reactions but is used to connote the induction of clinical signs and symptoms, as opposed to sensitivity, which indicate the presence of IgE antibodies in a food, often in the absence of clinical symptomatology.⁷ The most common cause of DD is irritant DD, triggered by prolonged contact between the skin and urine and feces. Irritant DD is most prominent in areas where the diaper is in direct contact with the skin, particularly on the convex surfaces, typically sparing the inguinal creases and gluteal cleft. At the same time, an increasingly common location for irritant DD is the perianal skin, where, in the presence of frequent stools or diarrhea, the diaper is not able to adequately wick away feces. When severe, this can cause erosions. Clinical manifestations are variable and include redness, papules, scaling, superficial erosions, and, less commonly, elevated papules or nodules, referred to as "pseudoverrucous papules and nodules (PVPN)." Allergic contact dermatitis (ACD) also occurs in

the diaper area. Some children are allergic to dyes, adhesives, rubber, and other components of disposable diapers. Clues to this etiology of diaper rash include rash only in areas the allergen contacts, such as linearly arranged pink patches or plaques corresponding to areas of skin contact with elastic diaper components (typically waistline and upper thighs). More generally, rash in the areas in contact with the diaper, but not in protected areas, can point to ACD as the etiology of DD.¹¹ With the elimination diet, 74% of the DD patients, who had experienced the condition for months and even years, recovered. Of our patients, 26% did not benefit from the elimination diet. No elimination was made in unhealed patients except food. There was no statistically significant difference in laboratory values and skin prick tests between healed and unhealed patients. This may be due to lack of data in some patients due to the retrospective study. One possible reason for not healing may be that these patients had food hypersensitivity rather than food allergy. Another reason could be that there was another cause of the DD.

Although food allergy is most often caused by IgE-mediated reactions, it can also result from reactions that are immunologic but through non-IgE-induced mechanisms (eg, food-protein-induced enteropathy and some allergic gastrointestinal disorders, such as allergic colitis and proctocolitis). Some disorders, such as atopic dermatitis and eosinophilic esophagitis, are categorized as mixed-IgE and non-IgE-mediated conditions.⁷ In our study, patients with Type I reactions required a longer elimination diet for DD. In Type II and mixed reactions, DD was more common and covered the whole perineum. In addition, in Type II and mixed reactions, DD had a more severe course and had not responded to previous topical treatments.

Fifty to 70% of food allergies occur with dermatological findings, while 50%-60% occur with gastrointestinal system findings and 20%-30% occur with respiratory system findings.¹² Many of our patients (78.0%) had gastrointestinal symptoms. Diarrhea was prominent in

this group. According to these data, patients with persistent DD and gastrointestinal symptoms are more likely to have food allergy, and an elimination diet of that food resulted in an improvement of the dermatitis (and perhaps other gastrointestinal symptoms). These patients should be considered for allergy evaluation.

The primary function of the skin barrier is to restrict water loss and to prevent entry of irritants, allergens, and skin pathogens. The outermost layer of the skin, called the stratum corneum, is critical to the integrity of the skin barrier, with the protein filaggrin being a key element in the stratum corneum's structure and formation. Loss of function mutations in filaggrin has been implicated in up to 50% of patients with moderate to severe atopic dermatitis. Also, in children with atopic dermatitis, the prevalence of food allergy is approximately 30%-40%.¹³ In our study, there was atopic dermatitis in 36.3% of the patients. In these patients, atopic dermatitis may lead to the development of a disrupted skin barrier and DD.

The global prevalence of all types of food allergy seems to be increasing.¹⁴ Food allergy prevalence has been found to be 6.7% in children.¹⁵ In our study, some of the patients referred only with a complaint of persistent DD. These patients did not have the classical symptoms of food allergy. This shows that patients with food allergy can refer with persistent DD alone. This result suggests that the food allergy prevalence in children is higher than reported.

In conclusion, persistent diaper dermatitis lasting for longer than a month may be associated with food allergy. The elimination of the responsible food brings about recovery from persistent DD in these patients. Thus, in children with persistent DD, especially those with gastrointestinal symptoms, food allergy should be considered and an appropriate workup performed.

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