Exfoliative Dermatitis in Thai Children: 10 Years Review

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ABSTRACT:

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Background: Exfoliative dermatitis is an uncommon, potentially serious skin condition. Thus it might poses a significant challenge to find the underlying etiologies.

Objective: To determine the etiologies, clinical presentations, laboratory findings and outcomes of exfoliative dermatitis in Thai children.

Material and methods: A retrospective study of patients diagnosed of exfoliative dermatitis at the Dermatology Unit, Queen Sirikit National Institute of Child Health during January 2009 to December 2019 was reviewed.

Results: Forty-one patients were identified. Age ranged from birth to12 years, with median age was 5 months (IQR 0-33 months), female to male ratio of 1:1. Clinical findings were pruritus (80.5%), fever (51.2%), failure to thrive (14.6%) and alopecia (12.2%). The most common causative diseases were inflammatory dermatoses in 26 cases (63.4%), including atopic dermatitis in 15 cases (36.6%), psoriasis in 8 cases (19.5%), pityriasis rubra pilaris in 2 cases (4.9%) and pityriasis lichenoides et varioliformis acuta in

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1 case (2.4%). Other causes were genodermatoses in 9 cases (22.0%), primary immunodeficiency syndrome in 2 cases (4.9%), drug allergy in 1 case (2.4%) and unknown causes in 3 cases (7.3%). In neonatal exfoliative dermatitis (N=11), the underlying causes included congenital ichthyosis in 9 cases (81.8%) and Netherton syndrome in 2 cases (18.2%). Skin biopsies were done in 30 cases (73.2%). The follow up of 37 cases (90.2%) revealed good complete recovery in 8 patients (19.5%), chronic dermatoses in 19 patients (46.3%) and persistent exfoliative dermatitis in 10 patients (24.4%). Mortality rate was 2.4% due to severe sepsis.

Conclusion: The clinical features of exfoliative dermatitis are unspecified with few cause-orienting clues. Etiologies of exfoliative dermatitis depend on the patient's age group. In neonatal exfoliative dermatitis are most commonly due to congenital ichthyosis or immunodeficiency syndrome. Likewise, exfoliative dermatitis with infants and childhood onset are most attributed to inflammatory dermatoses.

Key words: Exfoliative dermatitis, children, neonate

Introduction

Exfoliative dermatitis or erythroderma is defined as generalized erythema and scaling involving more than 90% of the body surface area[1-5]. It is a non-specific reaction pattern that can be induced by a variety of different diseases or medications. Exfoliative dermatitis is a rather uncommon situation in the pediatric age group[4-7]. Its overall incidence is found to be 35 per 100,000 amongst the dermatologic out-patient population in a cosmopolitan setting. A sample of 80 patients with exfoliative dermatitis contained only seven patients within the pediatric age group equating to a frequency of 8.8%[6].

Although the clinical picture may appear uniformly similar, the underlying etiology is variable. The underlying diseases range from benign, inflammatory disorders such as atopic dermatitis to fatal diseases such as immunodeficiencies. The etiology of exfoliative dermatitis is frequently difficult to establish, and is usually delayed, owing to the poor specificity of clinical and histological findings. Exfoliative dermatitis in adult age groups has been reported by various authors[8-15]. However there are few studies discussing this problem in children[16-20].

We carried out a retrospective study of 41 pediatric cases of exfoliative dermatitis. Patients were excluded if blistering occurred. The aim of this study is to determine the underlying causes and to analyze retrospectively clinical laboratory data and outcomes of this condition in Thai children.

Patients and methods

This retrospective study was conducted at the Dermatology Unit, Queen Sirikit National Institute of Child Health, Bangkok, Thailand. Forty-one patients (20 boys and 21 girls) with exfoliative dermatitis were attended between the 1st of January 2009 to the 31st of December 2019. The diagnosis of exfoliative dermatitis was based on the clinical features of extensive erythema with scaling affecting more than 90% of the body surface area with or without skin biopsy and less than 15 years old. A detailed history was elicited including personal data, onset of disease, duration, drug history and family history of a similar condition or atopy. The clinical data during each episode such as scaling, pruritus, hair and nail involvement, mucosal involvement, edema, lymphadenopathy and hepatomegaly were also assessed. The patients were seen at different intervals for follow up. This study was approved by The Research Ethic Review Committee of Queen Sirikit National Institute of Child Health.

Laboratory investigations included complete blood count, liver and renal function test, and serum electrolyte. Skin biopsy specimens were obtained from patients during erythrodermic stage. The hematoxylin-eosin (H&E) stained sections were examined to assess the presence of relevant features of the final etiological diagnosis.

Table1 Causative factors of exfoliative dermatitis in children

Etiology	N (%)
Inflammatory dermatoses	26 (63.4)
Atopic dermatitis	15 (36.6)
Psoriasis	8 (19.5)
Pityriasis rubra pilaris	2 (4.9)
Pityriasis lichenoides et varioliformis acuta	1 (2.4)
Genodermatoses (congenital ichthyosis)	9 (22.0)
Congenital ichthyosiform erythroderma	4 (9.8)
Lamellar ichthyosis	4 (9.8)
Ichthyosis, unspecified	1 (2.4)
Primary immunodeficiency syndrome	2 (4.9)
Netherton syndrome	2 (4.9)
Drugs	1 (2.4)
Phenobarbital	1 (2.4)
Unknown	3 (7.3)

Table 2 Causative factors of exfoliative dermatitis according to age group

Age	Etiology	N (%)
Neonate*	Genodermatoses	
	Lamellar ichthyosis	4 (9.8)
	Congenital ichthyosiform erythroderma	4 (9.8)
	Ichthyosis, unspecified	1 (2.4)
	Primary immunodeficiency syndrome	
	Netherton syndrome	2 (4.9)
	Total	11 (26.8)
Infant†	Inflammatory dermatoses	
	Atopic dermatitis	8 (19.5)
	Psoriasis	5 (12.2)
	Unknown	3 (7.3)
	Total	16 (39.0)
Childhood‡	Inflammatory dermatoses	
	Atopic adermatits	7 (17.1)
	Psoriasis	3 (7.3)
	Pityriasis rubra pilaris	2 (4.9)
	Pityriasis lichenoides et varioliformis acuta	1 (2.4)
	Drugs	
	Phenobarbital	
	Total	1 (2.4)
		14 (34.1)

* Neonate 0-1 month, †infant 1-12 months, ‡childhood > 1 year

Results

In the 10-years study period, 41 cases of exfoliative dermatitis in children were included. Twenty patients (48.8%) were male and 21 patients (51.2%) were female, with female: male ratio of 1:1. Age ranged from birth to 12 years, with median age was 5 months (IQR 0-33 months). No family history of exfoliative dermatitis or underlying skin diseases were found. The causative factors of erythroderma were shown in Table1. The most frequent underlying causes were inflammatory

dermatoses in 26 cases (63.4%), in which atopic dermatitis was the most common in 15 cases (36.6%). Other causes were genodermatoses in 9 cases (22.0%), primary immunodeficiency syndrome in 2 cases (4.9%), drug allergy in 1 case (2.4%) and unknown causes in 3 cases (7.3%). According to age onset, the underlying causes were shown in Table 2. Neonatal onset was observed in 11 cases (26.8%), which were 9 cases of congenital ichthyosis and 2 cases of Netherton syndrome.

Table 3 Clinical manifestations according to the groups of etiology

Clinical manifestations	Inflammatory dermatoses, (N=26)	Genodermatoses, (N=9)	Primary immunodeficiency syndrome, (N=2)	Drugs, (N=1)	Unknown cause, (N=3)
Pruritus, N (%)	21 (80.8)	9 (100)	0	1 (100)	2 (66.7)
Pain, N (%)	2 (7.7)	0	0	0	0
Nail involvement, N (%)	1 (3.8)	0	0	0	0
Fever, N (%)	15 (57.7)	0	2 (100)	1 (100)	3 (100)
Ectropion, N (%)	1 (3.8)	5 (55.6)	0	0	0
Alopecia, N (%)	1 (3.8)	2 (22.2)	2 (100)	0	0
Growth failure, N (%)	2 (7.7)	2 (22.2)	2 (100)	0	0
Edema, N (%)	2 (7.7)	0	0	0	0
Hepatomegaly	1 (3.8)	0	1 (50.0)	1 (100)	0

All the patients had erythema and some degree of scaling. Other clinical manifestations were pruritus 33 cases (80.5%), fever in 21 cases (51.2%), ectropion in 6 cases (14.6%), alopecia in 5 cases (12.2%), hepatomegaly in 3 cases (7.3%), pain in 2 cases (4.9%), nail involvement in 1 case (2.4%). There was no mucosal involvement. Table 3 showed clinical manifestations according to the groups of etiology. Other systemic signs revealed failure to thrive in 6 cases (14.6%), delay development in 6 cases (14.6%) and sepsis in 4 cases (9.8%). (Table 4)

Hematologic investigations revealed anemia in 13 patients (31.7%), which was found to be mild anemia (Hb 10-10.9 g/dL) in 7 patients (17.1%) and moderate anemia (Hb 7-9.9 g/dL) in 5 patients (12.2%). One patient (2.4%) had severe anemia with a hemoglobin level of less than 7 g/dL. Eosinophilia was commonly observed in atopic dermatitis (60%) and psoriasis (12.5%). Hypoalbuminemia was observed in 9

patients (22.0%) including atopic dermatitis, psoriasis, pityriasis rubra pilaris, Netherton syndrome and ichthyosis. Detail of laboratory findings are shown in Table 5.

Table 4 Systemic findings in 41 cases of exfoliative dermatitis

Systemic findings	N (%)
Failure to thrive	6 (14.6)
Delay development	6 (14.6)
Sepsis	4 (9.8)
Otitis media	3 (7.3)
Chronic diarrhea	3 (7.3)
Pneumonia	2 (4.9)
Epilepsy	2 (4.9)
Zinc deficiency	1 (2.4)
Arthritis	1 (2.4)
Kwashiorkor	1 (2.4)

Cutaneous biopsy was performed in 30 patients (73.2%). Histologic examination showed nonspecific spongiotic dermatitis in 12 cases (29.2%), psoriasis in 6 cases (14.6%), pustular psoriasis in 2 cases (4.9%), pityriasis rubra pilaris in 2 cases (4.9%) and pityriasis lichenoides et varioliformis acuta (PLEVA) in 1 case (2.4%). Histological examinations in 6 cases (14.6%) of ichthyosis demonstrated focal parakeratosis, mild spongiosis and irregular acanthosis with elongation of rete ridge. There are dilated capillaries and superficial perivascular lymphohistiocyte infiltrative in upper dermis.

Therapy of exfoliative dermatitis was topical and/or systemic medication depending on the etiology. All patients were prescribed emollient for skin hydration. Topical corticosteroids were prescribed in 32 cases (78.0%), and topical calcineurin inhibitors were given in 2 cases (4.9%). Six patients (14.6%) required systemic corticosteroids. Methotrexate and cyclosporine were administered in 2 cases (4.9%) with atopic dermatitis. Acitretin was administered in 12 cases (29.3%) with psoriasis, pityriasis rubra pilaris, lamellar ichthyosis and Netherton syndrome.

We found 1 case (2.4%) who died of severe sepsis, This patient presented with generalized erythema and scaling at 2 months and died of severe sepsis at age of 5 months. The duration of follow-up of this study was from 2 months to 13 years, with a mean of 41.9 ± 41.7 months. The follow up of 37 cases (90.2%) revealed good

complete recovery in 8 patients (19.5%), chronic dermatoses in 19 patients (46.3%) and persistent exfoliative dermatitis in 10 patients (24.4%). Cases of complete recovery were patients with atopic dermatitis, psoriasis, and drug allergy.

Table 5 Laboratory findings in exfoliative dermatitis according to the groups of etiology

Laboratory findings	Inflammatory dermatoses, (N=26)	Genodermatoses, (N=9)	Primary immunodeficiency syndrome, (N=2)	Drugs, (N=1)
Complete blood count				
Thrombocytosis, N (%)	12 (46.2)	0	1 (50)	0
Leukocytosis, N (%)	10 (38.5)	0	1 (50)	0
Anemia, N (%)	5 (19.2)	2 (22.2)	2 (100)	1 (100)
Eosinophilia, N (%)	10 (38.5)	0	0	0
Liver function tests				
Hypoalbuminemia, N (%)	6 (23.1)	0	2 (100)	0
Elevated AST or ALT, N (%)	2 (7.7)	0	2 (100)	1 (100)
Electrolytes				
Hyponatremia, N (%)	7 (26.9)	0	0	0
Hypernatremia, N (%)	0	1 (11.1)	0	0

AST; Aspartate transaminase, ALT; Alanine transaminase

Discussion

The most frequent underlying causes in our study were inflammatory dermatoses (63.4%), which was the same as another study in children[16,18-19]. Atopic dermatitis was the most common inflammatory dermatoses. Previous study in Thai children, Wisuthsarewong et al[19] reported that the common causative factors were preexisting skin diseases and genodermatoses. However, we found primary immunodeficiency syndrome and drug allergy less than previous study. Etiological groups among other studies of exfoliative dermatitis and our study were given in Table 6.

Table 6 Causes of pediatric exfoliative dermatitis in previous studies compared with present study

Author, year, country, total number (N)	Inflammatory dermatoses, N (%)	Primary immunodeficiency syndrome, N (%)	Genodermatoses, N (%)	Drugs, N (%)	Other, N (%)
Present study (41)	26 (63.4)	2 (4.9)	9 (22)	1 (2.4)	3 (7.3)
Wisuthsarewong et al., 2017, Thailand[19] (47)	25 (53.2)	6 (12.7)	5 (10.6)	5 (10.6)	6 (12.8)
Kalsy et al., 2013, India[20] (14)	4 (28.5)	0	3 (21.4)	6 (42.9)	1 (7.1)
Al-Dhalimi et al., 2007, Iraq[16] (42)	18 (42.9)	2 (4.8)	13 (31)	0	7 (16.7)
Pruszkowski et al., 2000, France[17] (53)	10 (18.9)	24 (45.3)	12 (22.6)	5 (9.4)	5 (9.4)
Sarkar et al., 1999, India[18] (17)	7 (41.2)	0	2 (11.8)	5 (29.4)	3 (17.6)

The underlying causes were classified according to whether the onset was neonatal or non-neonatal. In our study, we found that congenital ichthyosis and primary immunodeficiency syndrome were one of the most likely causes of exfoliative dermatitis in neonatal onset. Diagnosis of Netherton syndrome may be difficult and delayed by a few months to years. Hair characteristic (trichorrhexis invaginata) is rather helpful in our case (Figure 1, 2), appears as late as 1 year in one case. Repeated light microscopic examination of the hair was therefore necessary in suspected cases of Netherton syndrome. We also identified mutation in SPINK5 gene to confirm diagnosis of our patients.

One of our patient diagnosed as unspecified ichthyosis presented with collodion baby and neurologic involvement (schizencephaly, right hemiparesis, seizure, mental retardation). The patient was suspected of Sjogren-Larsson syndrome. The diagnosis was not confirmed since she lost to follow up.

Figure 1 Exfoliative dermatitis in a neonate with Netherton syndrome. The erythroderma is not specific

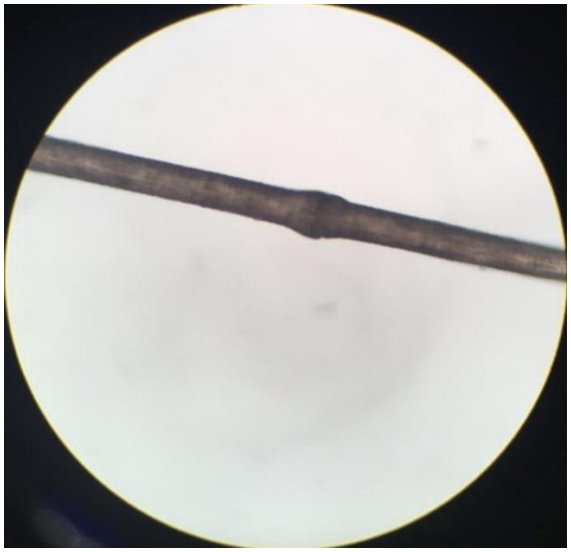

Figure 2 Light microscopy shows trichorrhexis invaginate of our patients

Regardless of the etiology, the clinical features of exfoliative dermatitis were almost identical. Some clinical features may be helpful in identifying causes but no characteristic features or pathognomonic sign were found. Pruritus was the most common complaint similarly to previous studies[16-20]. There was no mucosal involvement in our study. Failure to thrive and alopecia may be related to underlying diseases and severity of exfoliative dermatitis[16]. Nail involvement and arthritis were seen only in cases with psoriasis.

The main complications in our studies were failure to thrive, infection, hypoalbuminemia, hyponatremia and anemia which were attributable to the severity of skin disease and underlying disease. In our study we found failure to thrive in 6 cases (14.6%). It was found in Netherton syndrome (2 cases), ichthyosis (2 cases), atopic dermatitis (1 case) and psoriasis (1 case). These findings are similar to previous literature report[16]. The loss of weight observed with erythroderma appears to be multifactorial. We found that cases of atopic dermatitis who presented with erythroderma, chronic diarrhea, hypoalbuminemia and edema had concomitant cow's milk protein allergy in 4 cases.

Laboratory investigations were generally not helpful in the diagnosis of the underlying causes. Leukocytosis, eosinophilia, anemia and hypoalbuminemia were the common abnormalities found in this condition regardless of etiologies. We observed eosinophilia (26.8%) in a significant proportion of patients, as also observed in the other published studies[16-18]. It has been suggested elsewhere that eosinophilia could be attributed either to an underlying atopy or allergic phenomenon[17,21].

Specific histologic findings that helpful for diagnosis of exfoliative dermatitis were found in 11 cases (36.7%), a percentage similar to those reported in the other studies of adult erythroderma[8,10,22]. Specific cutaneous changes of dermatoses are obscured by the non-specific changes induced by the inflammatory reaction of erythroderma. The best clinicohistologic correlation was found in psoriasis, pityriasis rubra pilaris and PLEVA.

After a follow-up of 3 years (range 2 months-13 years), most patients had chronic dermatoses in 19 cases (46.3%) and persistent exfoliative dermatitis in 10 cases (24.4%), similar to those reported in previous studies[16-17].

Despite its limitations (retrospective design and the missing information in some of the patient's record), this study provided us with interesting information related to clinical features and prognosis of exfoliative dermatitis in children.

Conclusion

Most of the clinical features of exfoliative dermatitis were nonspecific with few cause-orienting clues. Although numerous laboratory values were abnormal, most findings were non-diagnostic and were rather related to inflammatory process, with the exception of skin biopsy. The most common etiology of erythroderma in children was the presence of underlying inflammatory dermatoses, which neonatal onset may indicate congenital ichthyosis or primary immunodeficiency syndrome as underlying etiology.

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