Association of atopic dermatitis with primary hereditary ichthyoses

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ABSTRACT

Objective: The aim of this study is to find out the association of atopic dermatitis and other atopic features with primary hereditary ichthyosis (PHI) among Saudi patients in King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia.

Methods: From the out-patient Department of Dermatology logbooks, all Saudi patients with clinically and histopathologically confirmed PHI seen between January 1990 and December 1995 were included in this study. Clinical findings regarding the atopic manifestations of PHI were extracted into data collection forms and computer-analyzed, using Statistical Package for Social Sciences.

Results: Over a 6-year study period, 10,455 new patients were seen in our Dermatology Clinics. Of these, 61 had PHI, there were 37 males and 24 females with a ratio of 1.5:1. Atopic dermatitis (AD), diagnosed according to Hanifin and Rajka criteria, was found in 7 (11.5%) patients of PHI; 5 of which were ichthyosis vulgaris and 2 with x-linked recessive ichthyosis. Isolated features of atopy were observed in the form of pruritus 49 (80%), elevated immunoglobulin E 27 (44.3%), dandruff 24 (39%), keratosis pilaris (KP) 15 (25%) and asthma 3 (5%).

Conclusion: In the present study, there was an 11.5% association between AD and PHI. However, isolated features of atopy were found in PHI in variable proportions ranging from 5-80%.

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Primary hereditary ichthyosis (PHI) is a group of genetic disorders of keratinization, which includes the following subdivisions: ichthyosis vulgaris (IV), x-linked recessive ichthyosis (XLRI), epidermolytic hyperkeratosis (EH), and autosomal recessive ichthyosis (ARI). In a study in England, 46% of IV experienced some atopic symptoms and 41% had at least one relative with atopic manifestations, whereas only 7% with sex-linked ichthyosis had some atopic symptoms.[1] Moreover, family history of atopy was found in 30% of IV patients from 17 ethnic origins in Israel.[2] In another study, immunoglobulin (Ig) E levels were elevated in autosomal dominant ichthyosis (ADI) with atopy as compared to ADI without atopy and concluded that the increased level of IgE in ADI is due to atopy.[3] Later, Sakura et al[4] found that 10 of 29 (34.5%) patients of x-linked ichthyosis with steroid sulfatase deficiency (STS gene deletion) had associated allergic disorders, including asthma, rhinitis, and dermatitis. In the above-mentioned studies, a relationship between ichthyosis (mostly IV) and various atopic manifestations have been determined with little emphasis on a purely diagnosed atopic dermatitis. The main objective of this study is to characterize the relation between atopic dermatitis diagnosed according to Hanifin

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and Rajka[5] criteriaand PHI in the Eastern Province of Saudi Arabia. The occurrence of isolated feature of atopy in these PHI patients has also been determined and discussed.

Methods. The logbooks of dermatology clinics in King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia were reviewed, and Saudi patients with clinically and histopathologically confirmed PHI seen in the period between January 1990 and December 1995 were included in the study. All demographic data and pertinent clinical findings including type of ichthyosis as well as atopic manifestations such as elevated IgE, generalized pruritus, asthma, keratosis pilaris (KP) and dandruff were transferred into especially designed protocol forms. The occurrence of various types of PHI was determined first. Patients fulfilled the diagnostic criteria of atopic dermatitis based on Hanifin and Rajka diagnostic features; including family history were discriminated from others, with isolated features of atopy. The occurrence of atopic dermatitis among various types of PHI was estimated using SPSS, besides determination of relationship between other features of atopy and various types of PHI.

Results. ***Occurrence of various types of primary hereditary ichthyosis***. In 6-years study period, 10,455 new patients were seen in Dermatology Clinics. Of 71 diagnosed as PHI, 61 were Saudis and included in the study. The distribution of the clinical types of PHI in this study was demonstrated in **Table 1**. The most common type of ichthyoses was IV (41%), whereas XLRI was found in 11 (18%), EH or bullous ichthyosiform erythroderma in 2 (3%), and autosomal recessive ichthyoses (ARI) in 23 (38%).

Atopic dermatitis and primary hereditary ichthyosis. Of 61 patients with PHI, 7 (11.5%) had atopic dermatitis diagnosed according to Hanifin and Rajka criteria. Five of them had IV (forming 20% of all IV cases) and 2 had ARI (8.7% of all ARI) (**Table 2**).

Other manifestations of atopy. Pruritus was the most frequent (80%) feature of atopy among all 61 patients of PHI, mostly found in IV and ARI. Elevated IgE was found in 44.3%, Dandruff in 39.3%, KP in 24.6% and asthma in 5% (**Table 3**).

Discussion. The association of atopic manifestations with PHI is not clearly identified. Because of the overlap of clinical presentations of both atopic dermatitis and ichthyosis vulgaris, the claim of association remains uncertain at best. Both AD and IV may present with xerosis (dry skin), scaling and KP, which may contribute to itching in

Table 1 - Distribution pattern of types of ichthyoses in 61 Saudi patients.

Type of ichthyoses	N	(%)	Males		Females	
			n	(%)	n	(%)
Ichthyosis vulgaris	25	(41)	20	(80)	5	(20)
X-linked recessive ichthyosis	11	(18)	11	(100)	-	-
Epidermolytic hyperkeratosis	2	(3)	-		2	(100)
Autosomal recessive ichthyosis	23	(38)	6	(26)	17	(74)

Table 2 - Association between atopic dermatitis and various types of ichthyoses.

Type of ichthyoses	N	Atopic dermatitis	
		n	(%)
Ichthyosis vulgaris	25	5	(20)
X-linked recessive ichthyosis	11	0	
Epidermolytic hyperkeratosis	2	0	
Autosomal recessive ichthyosis	23	2	(8.7)
Total	**61**	**7**	**(11.75)**

Table 3 - Occurrence of other features of atopy in various types of ichthyoses.

Type of ichthyoses	N	Pruritus	IgE	Asthma	Dandruff	Keratosis pilaris
Ichthyosis vulgaris	25	21	11	2	9	13
X-linked recessive ichthyosis	11	5	2	1	2	1
Epidermolytic hyperkeratosis	2	2	0	0	0	0
Autosomal recessive ichthyosis	23	21	14	0	13	1
Total (%)	**61 (100)**	**49 (80)**	**27 (44.3)**	**3 (5)**	**24 (39.3)**	**15 (24.6)**

these conditions.[1,6-9] The previous studies reported a higher rate (30-50%) of association between ichthyosis and atopy as compared to the current one (11.5%). This may be due to the fact that previous studies focused mainly on IV and determined association of ichthyosis with isolated features of atopy rather than properly diagnosed AD. Generalized pruritus was encountered in 49 (80%) of PHI, of these 21 patients had IV and another 21 had ARI. It is not rare to find pruritus in patients with ichthyosis.[10] Dry skin, scaling, super imposed infection and stress experienced by patients may contribute to pruritus.[6-8,11] Low percentage of AD (11.5%) encountered in this study suggests that pruritus per se does not signify a manifestation of coexistent AD in ichthyosis.

In the present study, elevated IgE was found in 44.3% of PHI, mostly IV and ARI cases. The elevated IgE in IV is usually attributed to atopy.[3,12,13] In cases of ARI it may be attributed to other factors such as genetic factors, environmental factors and microbial agents, which may invade the skin leading to stimulation of IgE production.[14-16] However, considering properly diagnosed AD in 7 (11.5%) patients of 61 confirm that elevated IgE is not a major criteria for the diagnosis of AD. Moreover, it also suggests that elevated IgE is not a useful criteria for association of AD and ichthyosis. Of the 15 (24.6%) patients with KP, 13 were IV patients. Keratosis pilaris is a common feature of both AD and IV.[8,17,18] Family history of atopy in KP has been found to be 37% in one study.[17] Some authors believe that KP has no diagnostic significance to AD, where it was found more frequent in IV without associated eczema.[13] Keratosis pilaris has been included as one of the minor criterion of AD by Hanifin and Rajka.[5] The present study indicates that KP in ichthyosis may or may not be related to atopy. Low occurrence of asthma in PHI (5%) supports the findings of lower association of AD with PHI in this study (11.5%). On the other hand, higher occurrence of pruritus (80%) and elevated IgE (44.3%) in PHI is more likely being due to other reasons than atopy.

Netherton syndrome (NS) is characterized by ARI and AD and is caused by mutation in SPINK5 gene.[19-20] The association between AD and SPINK5 has been reported in British patients with AD and recently confirmed in Japanese patients with AD.[16] Similarly, there is a possibility of genetic interplay behind the association of AD and autosomal dominant ichthyosis (such as IV) as well as other ichthyoses.

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References

1. Wells RS, Kerr CB. Clinical features of autosomal dominant and sex-linked ichthyosis in the English population. ***Br Med J*** 1966; 1: 947-950.
2. Ziprowski L, Feinstein A. A survey of Ichthyosis vulgaris in Israel. ***Br J Dermatol*** 1972; 86: 1-8.
3. Wursch TG, Wuthrich B. Serum IgE level in autosomal dominant and x-chromosomal recessive ichthyosis vulgaris. ***Z Hautkr*** 1980; 55: 1615-1619.
4. Sakura N, Nishimura T, Ohsaki M, Ogata T. Allergic disease as an association of steroid sulphatase deficiency. ***J Inher Metab Dis*** 1997; 20: 807-810.
5. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. ***Acta Derm Venereol Suppl*** 1980; 92: 44-47.
6. Uehara M, Miyauchi H. The morphologic characteristics of dry skin in atopic dermatitis. ***Arch Dermatol*** 1984; 120: 1186-1190.
7. Goldsmith LA, Thomas NE. Dermatology. 3rd ed. Philadelphia (PA): WB Saunders Company; 1992. p. 1383.
8. Williams ML, Elias PM. Genetically transmitted, generalized disorders of cornification of the ichthyoses. ***Dermatology Clinics*** 1987; 5: 155-178.
9. Rothe MJ, Grant-Kels JM. Atopic Dermatitis: An Update. ***J Am Acad Dermatol*** 1996; 35: 1-13.
10. Griffiths WA, Judge MR, Leigh IM. Disorders of Keratinization. In: Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Textbook of Dermatology. Vol 2. Oxford (UK): Blackwell Science; 1998. p. 1483-1588.
11. Shwayder T, Ott F. All about Ichthyosis. ***Pediatr Clin North Am*** 1991; 38: 835-857.
12. Rabinowitz LG, Esterly NB. Atopic dermatitis and ichthyosis vulgaris. ***Pediatr Rev*** 1994; 15: 220-226.
13. Mevorah B, Marazzi A, Frenk E. The prevalence of accentuated palmoplantar markings and keratosis pilaris in atopic dermatitis, autosomal dominant ichthyosis study control dermatological patients. ***Br J Dermatol*** 1985; 112: 679-685.
14. Ansi S, Mitsuhashi Y, Sasaki K. Netherton's syndrome in siblings. ***Br J Dermatol*** 1999; 14: 1097-1100.
15. Hofer MF, Lester MR, Schlievent PM, Leung DY. Up regulation of IgE synthesis by staphylococcal toxic shock syndrome toxin-1 in peripheral blood mononuclear cells from patient with atopic dermatitis. ***Clin Exp Allergy*** 1995; 25: 1218-1227.
16. Kato A, Fukai K, Oiso N, Hosomi N, Murakami T, Ishii M. Association of SPINK5 polymorphism with atopic dermatitis in the Japanese population. ***Br J Dermatol*** 2003; 148: 665-669.
17. Poskitt L, Wilkinson JD. Natural history of keratosis pilaris. ***Br J Dermatol*** 1994; 130: 711-713.
18. Macharia WM, Anabwani GM, Owili DM. Clinical presentation of atopic dermatitis in negroid children. ***Afr J Med Med Sci*** 1993; 22: 41-44.
19. Chavanas S, Bodemer C, Rochat A, Hamel-Teillac D, Ali M, Irvine AD, et al. Mutations in SPINK5, encoding a serine protease inhibitor, cause Netherton syndrome. ***Nat Genet*** 2000; 25: 141-142.
20. Walley AJ, Chavanas S, Moffatt MF, Esnouf RM, Ubhi B, Lawrence R, et al. Gene polymorphism in Netherton and common atopic diseases. ***Nature Genet*** 2001; 29: 175-178.