

Ceramide profile in hypohidrotic ectodermal dysplasia

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Summary

Background. Hypohidrotic ectodermal dysplasia (HED) is a rare genetic disease. The clinical presentation includes lack of sweating ability, and an often widely spread dermatitis resembling atopic dermatitis (AD). In AD, the skin-barrier defect is partly ascribed to the altered lipid profile in the stratum corneum and partly to mutations of the filaggrin genes. To our knowledge, no data are available about the epidermal lipid profile of HED.

Aim. To compare the ceramide profile for patients with HED and AD.

Methods. The ceramide profile and ceramide/cholesterol ratio were compared between patients with HED ($n = 7$) and patients with AD ($n = 21$), using cyanoacrylate to take biopsy samples from the stratum corneum. Lipids were extracted from the biopsies and analysed using high-performance thin-layer chromatography.

Results. The lipid profiles of HED and AD were similar in distribution, apart from ceramide 1, which was significantly higher in HED ($P = 0.04$).

Conclusions. The increased ceramide 1 level found in HED compared with AD is known to play a role in the structure of the lipid bilayers. However, further studies are needed to identify the functional significance of these observations and thereby elucidate differences in the skin barrier between HED and AD.

Hypohidrotic ectodermal dysplasia (HED) is a rare genetic disease characterized by sparse hair, abnormal and missing teeth, saddle nose, and lack of sweat glands (Fig. 1). Patients often present with a widespread dermatitis, which may be misinterpreted as atopic dermatitis (AD). In recent years, tremendous advances have been made in the genetics of this condition, and at least 64 genes have been ascribed to ectodermal dysplasia.¹ Nevertheless, HED is a very rare disease, and in the literature, it has mostly been described in case reports. To our knowledge, no clinical dermatological research has been published to elucidate the pathogenesis of the disease.^{2,3}

From a clinical point of view, the eczematous characteristics of HED skin resemble those of atopic dermatitis (AD), and treatment regimens are therefore often similar, although the HED-associated dermatitis may at times seem more recalcitrant. The barrier defect in AD is known to derive from at least two apparently independent mechanisms: filaggrin mutations or abnormalities in epidermal lipids.^{4,5} These two mechanisms seem to represent different pathways to impaired barrier function, and to our knowledge, no data are available about either the filaggrin status or the skin lipids of patients with HED. The aim of the present study was to examine the ceramide profile of patients with HED and AD in order to compare the two diseases and provide data on the pathogenesis of HED.

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Methods

The study was approved by the local ethics committee (study no. SJ-13.986), and informed consent was obtained from all participants.

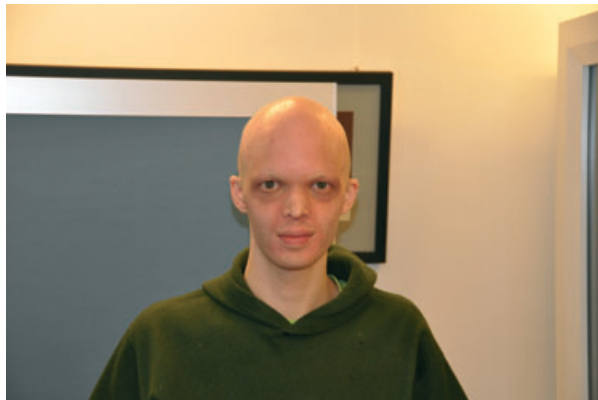


Figure 1 Male participant, with typical HED characteristics like sparse hair and dry skin.

Study design

In total, 7 patients with HED (6 men, 1 woman, median 23 years, range 18–50) and 21 with AD (12 men, 9 women, median 29, range 18–50) were included in the study.

All participants were asked not to use any topical treatment on the day of examination. The recently validated cyanoacrylate stripping method was used to take samples for lipid analysis.⁶ Non-lesional skin on the volar forearm was wiped with acetone to eliminate contamination by surface lipids. A droplet of cyanoacrylate tissue glue (LiquiBand®; Medlogix Global Ltd, Plymouth, UK) was placed at one end of a glass slide and held against the skin until the glue had dried, and the slide was then pulled off. Extraction of lipids and high-performance thin-layer chromatography (HPTLC) was performed as described previously.^{5,6}

Statistical analysis

For comparison between the different ceramides for the two groups of patients, the nonparametric Mann–Whitney *U*-test was used. $P < 0.05$ was considered significant. We did not correct for multiple comparisons, thus the analysis should be considered explorative. Data were analysed using SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA).

Results

We found a significantly higher level of ceramide 1 in subjects with HED compared with subjects with AD ($P = 0.04$). There was no significant difference for other

Table 1 Percentage distribution of ceramides and the ceramide:cholesterol ratio.

	HED	Atopic dermatitis
Ceramide 1 (EOS)	18.0 (13.4–19.3)*	14.5 (11.1–15.4)*
Ceramide 2 + 9 (EOP + NS)	16.6 (13.4–18.8)	19.8 (16.7–21.0)
Ceramide 3 (NP)	17.2 (15.3–19.1)	17.9 (15.1–19.5)
Ceramide 4 (EOH)	5.9 (4.7–6.1)	6.7 (4.4–8.3)
Ceramides 5 + 8 (AS + AH)	19.3 (18.0–21.6)	20.4 (18.6–21.4)
Ceramide 6 (NH)	9.4 (8.7–10.7)	10.2 (8.5–12.8)
Ceramide 7 (AP)	15.6 (12.3–16.7)	12.1 (10.3–12.1)
Ceramide:cholesterol ratio	1.7 (1.4–1.8)	1.6 (1.3–1.8)

A, α -hydroxy fatty acid; EO, ester-linked ω -hydroxy acid; N, nonhydroxy fatty acid; P, phytosphingosine; S, sphingosine; H, 6-hydroxyphingosine; HED, hypohidrotic ectodermal dysplasia. Ceramide levels other than the ceramide:cholesterol ratio are presented as percentages (first to third quartile). * $P < 0.05$.

ceramide subgroups or the ceramide:cholesterol ratio (Table 1).

Discussion

Recently, a study investigating the quality of life for people with ED reported that the skin involvement has the greatest effect on the quality of life for these patients.⁷ From a clinical point of view, the dermatitis seen in HED has many of the eczematous characteristics of AD, and as one important characteristic for AD is the altered ceramide profile, knowledge about the ceramide profile of HED could provide data about the pathogenesis of HED. In the present study, we therefore characterized the ceramide profile and ceramide:cholesterol ratio of patients with HED and compared them with patients with AD.

Patients with AD are known to have an altered ceramide profile compared with healthy people, with lower levels of ceramide 1 and 3, higher levels of ceramide 7, and a lower ceramide:cholesterol ratio compared with healthy controls.^{5,8–10} For patients with HED, we found a ceramide profile similar to that found in AD skin, except for a significantly higher level of ceramide 1. Ceramide 1 has previously been shown to be of key importance for the lamellar organization of the stratum corneum lipids,¹¹ which is in agreement with the deteriorated skin barrier found in patients with AD. As the level of ceramide 1 for patients with HED is significantly higher for patients with AD, this may point to a more normal skin barrier. In fact, data from a previous study by our group, adjusted for age, found that healthy people have levels of ceramide 1 between those of HED and AD, suggesting that patients with HED may have an overabundance of ceramide 1

in their skin.⁵ Future studies will aimed at investigating this and the functional effects of the high ceramide 1 level in HED epidermal-barrier function as measured by transepidermal water loss and irritation tests, among others.

Apart from ceramide 1, the ceramide subgroups and ceramide:cholesterol ratio were similar in distribution between HED and AD. As AD skin differs from healthy skin in ceramides other than ceramide 1, this indicates some similarities in the pathogenesis of HED and AD. From the present knowledge of HED, no explanation for the increased ceramide 1 can be given. Further studies concerning skin barrier function and the enzymatic differences between the two diseases are necessary.

What's already known about this topic?

- The ceramide profile is altered in AD.
- The dermatitis in HED resembles that of AD, therefore the two conditions may have mechanisms in common.

What does this study add?

- The ceramide profiles of the two diseases are similar in distribution apart from ceramide 1, which is significantly higher in HED skin.

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