

CASE REPORT

Skin bioengineering in the diagnosis of occupational protein contact dermatitis

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Abstract	Protein contact dermatitis (PCD) often presents as chronic hand eczema (CHE) with an immediate hypersensitivity to protein proved by a positive skin prick test or by the presence of specific immunoglobulin E. This is frequently induced by occupational exposure to proteins in food workers, farmers, animal breeders, veterinarians and healthcare professionals. While skin barrier impairment is crucial in the pathogenesis of PCD, methods to assess skin barrier function such as trans-epidermal water loss and stratum corneum hydration are not widely used in clinical settings. We describe the diagnostic workup of occupational PCD due to Argentinean shrimps and discuss how the use of skin bioengineering methods including assessment of corneocytes morphology by Scanning Electron Microscopy provides with insightful information on skin barrier function. Diagnosis of PCD is time-consuming and a multidisciplinary team contributes to early diagnosis and proper occupational rehabilitation.
Key words	Food industry; occupational skin disease; prevention; seafood allergy; skin barrier.

Background

Occupational protein contact dermatitis (PCD), an underdiagnosed and frequent skin condition among food handlers, presents as chronic hand eczema (CHE) that occurs in contact to proteinaceous material [1]. Skin barrier impairment, atopy and skin exposure to irritants are a precondition for the development of PCD as large proteins are unable to penetrate an intact skin barrier [1]. For instance, the stratum corneum (SC) permeability barrier function in terms of transepidermal water loss (TEWL) and SC hydration is rapidly impaired in the pathophysiology of contact dermatitis [2].

Impaired skin barrier such as occurs in atopic dermatitis also presents alterations in the morphology of corneocytes due to numerous nanoscale protrusions on the surface of corneocytes, named 'villus-like projections' (VPs) observable by Scanning Electron Microscopy

(SEM) [3]. These VPs are present in lower amounts or absent in the forearms in healthy skin [4].

We present the diagnostic workup of a chef with occupational CHE and PCD to Argentinean shrimps. We monitored skin bioengineering methods, SEM monitored skin barrier function and the presence of VPs on the surface of corneocytes in a 9-month follow-up period from diagnosis to the clinical improvement.

Case presentation

A 27-year-old male with CHE extending to the wrists, forearms and fingertips not responding to topical corticosteroids, systemic retinoids and phototherapy was referred to the Department of Occupational Medicine. He had no history of atopy, asthma or food allergy. The skin problems started after his first year as a chef in a Thai restaurant, and worsened after a 10-h shift and at the end of each week.

Key learning points

What is already known about this subject:

- Chronic hand eczema is common in food handlers and protein contact dermatitis (PCD) is often underdiagnosed.
- Skin barrier disruption plays a major role in the pathogenesis of PCD, but it is seldom monitored during the diagnostic workup.

What this study adds:

- Diagnosis of occupational PCD is time-consuming.
- Non-invasive skin bioengineering methods can monitor skin barrier function in a clinical setting.
- Structural changes in the morphology of the corneocytes seem to play a role in the skin barrier disruption observed in PCD.

What impact this may have on practice or policy:

- Multidisciplinary collaboration between occupational physician, dermatologist and allergist is essential for early diagnosis and intervention.
- Accessibility to occupational health services and training on glove use and skin care to promote a healthy skin barrier should be encouraged among food handlers.

Daily working activities included cleaning, cutting fish, shrimps, vegetables (cucumber, carrot, onion, ginger, mushrooms, garlic), fruits (avocado, lemon) and spices (green chilli, Thai chilli, Thai basil, Thai coriander, sesame seeds and oil, soy sauce, peanuts, tamarind, coconut) to prepare typical Thai food. He washed, peeled, opened and cut ~120 Argentinean red shrimps (*Pleoticus muelleri*) daily and reported pruritic wheals, tingling, erythema, itchy mouth and throat within 30 min of contact. He washed his hands >20 times daily and used vinyl gloves for >2 h. He changed gloves about every 30 min after the skin problems started because his hands became wet inside the gloves. He reported time pressure and high workload especially during the summer and Christmas season. He was not familiar with Occupational Health Services, even when this service is mandatory for food handlers according to the Norwegian Labour Inspectorate.

Investigations

Patch testing with the European baseline series (Chemotechnique Diagnostics, Vellinge, Sweden) was performed according to the recommendations of the European Society of Contact Dermatitis [5]. Reading showed a weak positive reaction (+) to cobalt 1.0% pet aq. on Day 3, which was not considered clinical relevant for the patient's occupational exposure and history.

Skin prick testing was performed according to international recommendations [6]. Firstly, we performed prick-to-prick tests with fresh vegetables, meat, seafood and sauces that the patient handled at work. An infiltrate of 8 mm diameter to Argentinean shrimps was observed after 15 min. The patient reported intense local itching and vesicles on the test site 1 day after. For ethical reasons we were unable to test eight 'healthy' controls with prick-to-prick testing. We also performed skin prick testing with commercial shrimp extract (Soluprick,

ALK-Abelló, Hørsholm, Denmark) and an infiltrate of 6 mm was observed after 15 min.

Total and specific serum immunoglobulin E (IgE) were determined using the ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden). The total concentration of IgE was within normal limits (55.0×10^3 IU/L; reference $<114 \times 10^3$ IU/L), but increased specific IgE to shrimp (4.0×10^3 IU/L) and crab (0.87×10^3 IU/L) were found (reference $<0.35 \times 10^3$ IU/L).

Biophysical measurements of the skin barrier were performed after 30 min acclimatization in standardized environmental conditions (room temperature, 20–25°C; humidity levels, 30–35%), and all topical therapies, including emollients, were withheld from the patients' upper limbs for 24 h before measurements. TEWL was determined by the open-chamber diffusion technique using a Tewameter 300 (Courage and Khazaka Electronic GmbH, Cologne, Germany). SC hydration down to a depth of ~10–20 µm was quantified in terms of skin capacitance with a Corneometer CM 825 (C+K Electronic, Cologne, Germany).

All measurements were performed by the same investigator and on a clinically affected area of skin, i.e. on the dorsal side of the hand, volar forearm and a clinically unaffected area of the skin, i.e. on the volar side of the arm at the time of diagnosis (baseline) and 9 months after (follow-up). The percentage change in TEWL and skin capacitance between diagnosis and follow-up are presented as relative change between baseline and follow-up [6,7]. Table 1 shows the improvement in TEWL and skin capacitance from baseline to follow-up which was in line with the observed clinical improvement.

SC was sampled from the same skin areas at baseline and follow-up by tape stripping (TS) [8]. Circular adhesive TS (2.2 cm², D-Squame; Monaderm, Monaco, France) was attached to the skin and pressed for 10 s with a constant pressure (150 g/cm²) by using a D-Squame

Pressure Instrument D500 (CuDerm, Dallas, TX, USA). Five consecutive TS were then gently removed after the skin barrier measurements, placed in a closed vial and stored at 4°C until analysis.

The morphology of corneocytes was qualitatively analysed in field emission scanning electron microscope, FESEM SU 6600 (HITACHI, Ibaraki-Ken, Japan). We visualized samples from TS2 to TS5 at 10–11 mm working distance using an acceleration voltage of 12 keV.

Figure 1 shows representative micrographs from TS3 from both clinically unaffected (1A.1, 1A.2) and affected skin at baseline (1B.1, 1B.2) and follow-up (1C.1, 1C.2) taken at secondary electron imaging mode at 1.500× or 10.000× magnifications. The irregular shape of the corneocytes and the presence of VPs on the corneocytes surface of clinically affected skin were remarkable compared to those from unaffected skin. These alterations were still present at follow-up, though the VPs were less

prominent. A similar pattern was observed in TS 2, 4 and 5 (data not shown).

The case was reported to the Labour Inspectorate of Norway and the Norwegian Labour and Welfare Administration who recognized PCD as an occupational disease and offered the patient occupational rehabilitation and re-training as an IT technician. He quit working as a chef after 2 months sick leave. His CHE resolved completely with exposure avoidance, skin phototherapy and regular use of moisturizers.

Discussion

The case meets the specific criteria for PCD [9]:

- Chronic or recurrent eczema caused by contact with high-molecular-weight proteins. The muscle protein tropomyosin has been implicated as a major allergen in shrimps [10].

Table 1. TEWL, skin capacitance and relative change for both skin biophysical measurements at baseline (T₀) and follow-up (T₁)

	TEWL (g/h/m ²) ^a			Skin capacitance (U.A) ^b		
	T ₀	T ₁	Relative change (Δ)	T ₀	T ₁	Relative change (Δ)
Dorsal side hand	14.69	9.44	−35.73 %ΔTEWL	35	52	48.57 %Δ skin capacitance
Volar side forearm	42.11	13.52	−67.89 %ΔTEWL	36	41.66	15.72 %Δ skin capacitance
Volar side upper arm	10.33	9.6	−7.06 %ΔTEWL	32	42	31.25 %Δ skin capacitance

^ag/h/m²: gram per hour per square metre. TEWL (g/h/m²): <25: healthy skin barrier; >25: impaired skin barrier.
^bU.A = arbitrary units. <40: dry skin; >40 moisturized.

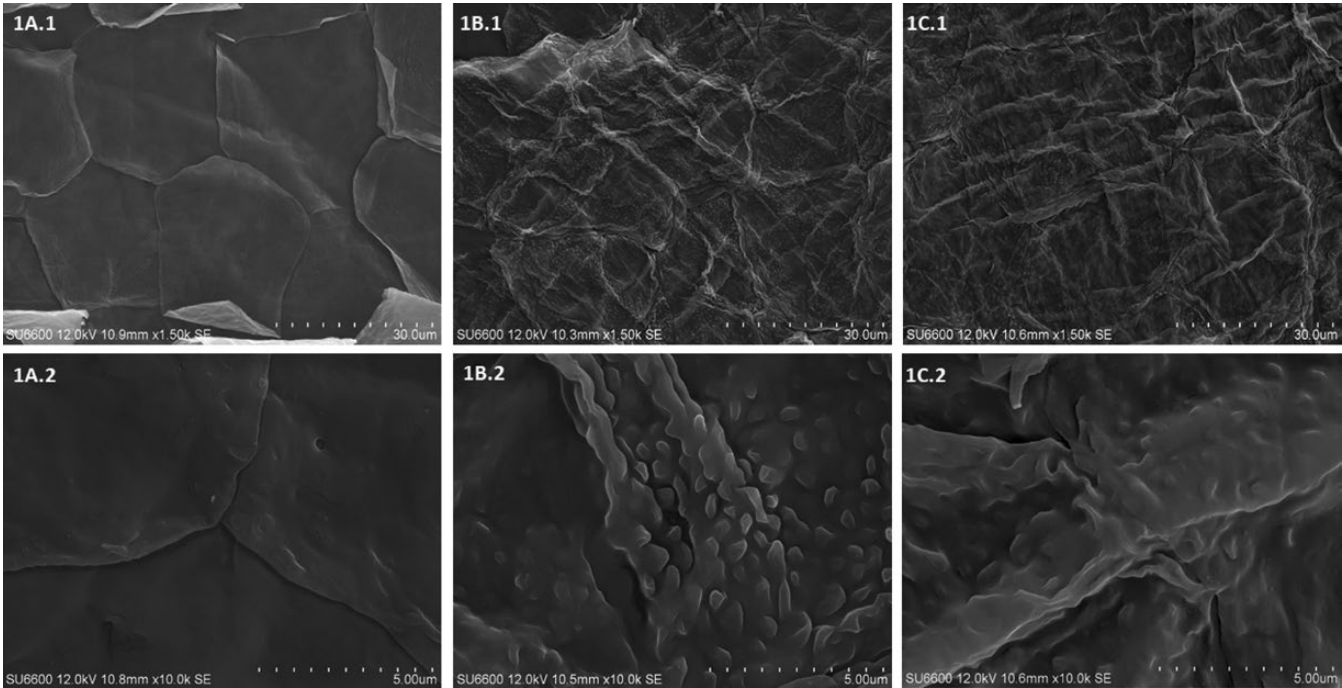


Figure 1. SEM micrographs of corneocytes in clinically unaffected skin from upper arm (1A.1 and 1A.2), clinically affected skin from forearm at baseline (1B.1 and 1B.2) and follow-up (1C.1 and 1C.2). Note the irregular shape and the villous-like projections on the corneocytes surface of clinically affected skin.

- Immediate itching urticarial eruption that occurs within 30 min of contact.
- Positive prick testing to shrimp. To note, the skin reaction to Argentinean shrimps in skin prick-to-prick test was stronger than the reaction to standardized shrimp extract in the regular prick test, which is in line with previous findings reporting that fresh food extracts give a stronger and more sensitive response than commercial extracts [11].
- Additionally, the patient presented increased levels of shrimp-specific IgE.
- Patch test results that are often negative.

By using skin bioengineering methods, our findings support that disruption of skin barrier in terms of TEWL and SC hydration is a part of the pathogenesis of PCD. Although the CHE resolved and skin barrier function, as measured in terms of TEWL and skin capacitance improved after 9 months, the presence of VPs on the corneocytes surface of previously affected skin did not reflect these improvements. This finding may represent a persistent abnormality in a disrupted skin barrier, which also was described for both the acute and convalescent phases of atopic eczema [12].

Primary prevention among seafood handlers can reduce the occurrence of PCD [13]. The patient worked in a high-risk occupation for PCD, but primary preventive measures were not properly implemented. For example, chefs who handle seafood have a higher occurrence of PCD than fishermen due to poorer implementation of skin protection measures [14]. The lack of training in the use of personal protective equipment and wrong glove use (vinyl gloves that break more easily) may have contributed to the development of CHE.

Finally, this case highlights that multidisciplinary work between specialists in dermatology, allergy and occupational medicine is crucial for the diagnosis and occupational rehabilitation [15]. As a result of correct diagnosis, exposure avoidance, recognition of PCD as an occupational disease and retraining the patient improved his quality of life and was able to continue working without hand eczema.

Competing interests

None declared.

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