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ORIGINAL ARTICLE

Protein Contact Dermatitis: Review of 27 Cases

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Protein contact dermatitis;
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Abstract

Background: Protein contact dermatitis (PCD) is a rare and underdiagnosed condition that many dermatologists fail to recognize. Nevertheless, increasing awareness of the condition and the substances responsible has led to a rise in the number of published cases in recent years.

Objective: To determine the clinical characteristics and allergens implicated in PCD in our setting.

Material and methods: A retrospective observational study of all patients diagnosed with PCD in the last 10 years was undertaken in the Skin Allergies Unit of the Department of Dermatology at Hospital General Universitario in Valencia, Spain. All patients were assessed by skin-prick test with the standard GEIDAC allergen panel and by prick-by-prick test with foods or other products that were linked to immediate skin symptoms following handling.

Results: Twenty-seven patients (8 men and 19 women) were diagnosed with PCD, and 26 of the cases were occupational in origin. The mean age of the patients was 32.3 years and 51.8% had a history of atopy. The latency period varied from 2 months to 27 years. The most commonly affected areas were the backs of the hands and the forearms. Four patients had an oral allergy syndrome. In order of frequency, the substances responsible for PCD were fish (9 patients, 33.3%), latex (8 patients, 29.6%), potato (4 patients, 14.8%), chicken (3 patients, 11.1%), flour (3 patients, 11.1%), alpha amylase (2 patients, 7.4%), aubergine (2 patients, 7.4%), pork (1 patient, 3.7%), garlic (1 patient, 3.7%), and *Anisakis* (1 patient, 3.7%).

Conclusions: PCD is a clinically relevant condition that dermatologists should include in the differential diagnosis of chronic dermatitis affecting the hands or forearms in patients at high occupational risk, particular those in the food preparation industry.

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PALABRAS CLAVE

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Látex;
Prick-by-prick test

Dermatitis de contacto por proteínas. Revisión de 27 casos

Introducción: La dermatitis de contacto por proteínas (DCP) es una patología infrecuente, poco conocida por el dermatólogo e infradiagnosticada. Recientemente el número de casos publicados de DCP ha ido en aumento por un mayor conocimiento de esta entidad, así como del espectro de sustancias responsables de la misma.

Objetivo: Estudiar las características clínicas y los alérgenos implicados en la DCP en nuestro entorno.

Material y métodos: Se trata de un estudio observacional y retrospectivo de todos los pacientes diagnosticados de DCP en los últimos 10 años en la Sección de alergia cutánea del Servicio de Dermatología del Hospital General Universitario de Valencia. Todos los pacientes fueron estudiados mediante pruebas epicutáneas con la batería estándar del GEIDAC y mediante pruebas cutáneas con los alimentos y/o productos que al manipularlos relacionaban con síntomas cutáneos inmediatos.

Resultados: Un total de 27 pacientes (8 varones y 19 mujeres) fueron diagnosticados de DCP, 26 de los cuales fueron de origen laboral. La edad media fue de 32,3 años, y el 51,8% tenían historia personal de atopia. El tiempo de sensibilización fue variable, entre dos meses y 27 años. Las áreas más frecuentemente afectadas fueron el dorso de las manos y los antebrazos. Cuatro pacientes presentaron un síndrome oral de alergia. Las sustancias responsables de la DCP fueron, por orden de frecuencia, pescados (9/27, 33,3%), látex (8/27, 29,6%), patata (4/27, 14,8%), pollo y harina (3/27, 11,1%), alfa-amilasa y berenjena (2/27, 7,4%) y carne de cerdo, ajo y anisakis (1/27, 3,7%).

Conclusiones: La DCP es una entidad de relevancia clínica que el dermatólogo debe considerar en el diagnóstico diferencial de una dermatitis crónica de las manos y/o antebrazos en pacientes con alto riesgo ocupacional, particularmente manipuladores de alimentos. © 2010 Elsevier España, S.L. y AEDV. Todos los derechos reservados.

Introduction

The term protein contact dermatitis (PCD) was coined by Hjorth and Foed-Petersen¹ in 1976 to describe a new form of chronic and recurrent occupational contact dermatitis. The authors reported 10 patients with allergic contact dermatitis that could not be diagnosed with patch tests; in addition, the allergen went undetected unless skin tests for immediate allergy (scratch tests) and radioallergosorbent tests for serum immunoglobulin (Ig) E were applied. Since then, several reports of new cases of PCD have been published, although these generally describe isolated reactions.²⁻³³ The list of causative agents is constantly increasing. PCD is usually induced by substances belonging to 4 groups of products related mainly to foods, namely, animal proteins, vegetable proteins, cereal grains and flours, and enzymes. Although some reviews have been published, very few specific wide-ranging series of patients with PCD are available.

We present the cases of PCD diagnosed in our department during 2000-2009. We describe the occupation of the patients, the clinical characteristics of the condition, the diagnostic yield of the tests used, and the allergens currently responsible for PCD in our setting.

Patients and Methods

We performed a retrospective observational study of patients diagnosed with PCD at the Skin Allergies Unit

of the Department of Dermatology at Hospital General Universitario in Valencia, Spain between January 2000 and December 2009. We identified 27 patients from electronic clinical records. During this period, we performed patch tests on 3174 patients using the standard series of the Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC); specific series were used in some patients depending on their profession (eg, hairdressers and bakers).

Those patients who consulted for dermatitis on the hands or forearms and whose history reflected immediate pruritus on contact with specific substances were simultaneously assessed using skin tests: prick-by-prick test in the case of allergy to foods and prick test in the case of allergy to latex, alpha amylase, or *Anisakis*. If the results of these tests were negative and the suspicion well founded based on the clinical history, we performed a rub test by applying the food to the affected or previously affected area or a glove-use test in the case of immediate reaction to rubber gloves.

PCD was suspected in those patients who reported intense pruritus, stinging, or a burning sensation a few minutes after touching specific foods, except for acidic foods (eg, lemon, tomato) or very irritant foods. Patients attended our clinic with the suspect foods (natural and fresh) in order to undergo prick-by-prick test. In the case of latex, alpha amylase, and *Anisakis*, we performed prick testing with commercial extracts (Alk-Abelló).

Serum specific IgE was analyzed using a chloramphenicol enzyme-linked immunosorbent assay when available. PCD

was diagnosed as the main cause or as a complication of previous or concomitant dermatitis depending on follow-up and total or partial cure of eczema on the hands, forearms, or face.

The data recorded were age and sex, profession, personal history of atopic disease (dermatitis, asthma, or rhinitis), latency period, location of lesions, time since onset, results and relevance of positive results in skin tests (present, past, or unknown), results of skin tests (prick-by-prick test and/or rub test), and determination of specific IgE.

Results

PCD was diagnosed in 27 patients (8 men and 19 women) (Table 1), all of whom had symptoms of eczema. Eczema was occupational in 26 cases (mainly cooks [10], cuttlefish or fish cleaners [3], and bakers [3]). Mean age was 32.3 years (range, 19-53 years). Fourteen patients (51.8%) had a history of atopic disease. The latency period ranged from 2 months to 27 years. The presenting complaint was subacute or chronic dermatitis (Figure 1), except for the 2 patients who presented with acute exudative lesions 24 hours after returning to work following a long sick leave (Figure 2). The skin lesions affected the hands in 26 of the 27 cases (96.3%), mainly on the dorsum and fingers, the forearms in 20 cases (74%), and the face in 5 cases (18.5%). Four patients who were allergic to fish proteins had symptoms of oral allergy syndrome on ingestion. The time since onset ranged from 3 months to 25 years, with a mean of 4.75 years. PCD was considered the main diagnosis (Table 1) in 15 cases (55.5%); in the remaining 12 cases (44.5%), it was considered a complication of other skin diseases (Table 1). Patch testing revealed positive results to an allergen in 17 cases (63%); in 10 cases (37%) this was of present relevance, particularly to thiuram mix (4 cases, 14.8%), and associated with exposure to protective rubber gloves.

The skin tests (prick test and/or rub test) (Figure 3) revealed the following sensitizations: proteins from several types of fish (both oily and white, 9 cases [33.3%]), latex (8 cases, 29.6%), potato (4 cases, 14.8%), chicken and flour (3 cases, 11.1%), alpha amylase and eggplant (2 cases, 7.4%), and pork, garlic, and *Anisakis* (1 case, 3.7%). None of the 3 cuttlefish cleaners were allergic to cuttlefish meat, but rather to the fish commonly found in the digestive tract of cuttlefish. Similarly, a kitchen assistant who gutted anchovies was not sensitized to the fish itself, but to the *Anisakis* found in its digestive tract.

Specific IgE to allergens was analyzed in 15 patients and correlated well with the prick test results in 10 of these cases.

Discussion

According to the Gell and Coombs classification, contact skin allergy may be due to delayed sensitization (type IV) or immediate sensitization (type I).^{1,2} The allergy type can determine the most appropriate diagnostic technique

(patch tests, skin tests, or both).³⁻⁶ PCD is an immediate-type reaction, as is contact urticaria. Both diseases are characterized by immediate pruritus on contact with the allergen; however, the lesions in PCD are eczematous, unlike the wheals of contact urticaria.⁷⁻¹⁰

Clinically, PCD manifested in our patients as subacute or chronic eczema on the hands or forearms and could not be distinguished from irritant or allergic contact dermatitis.¹⁷ The face was affected in 5 of our patients, probably as a result of contact with contaminated hands.¹⁸ Four patients with PCD due to fish reported pruritus in the mouth and edema or dermatitis on the lips after ingestion. This oral allergy syndrome appeared after the PCD lesions.

Occupations involving food handling (cooks, cuttlefish cleaners, fishmongers, and bakers) were most-often associated with PCD in our series; however, in the case of latex allergy, other professions (eg, hairdressers and chemists) were also affected.

Several factors favor the development of skin lesions, for example, repeated exposure to the allergen, chronic scratching, moisture, or previous irritant or allergic contact dermatitis.¹⁶ Atopy is also a risk factor,⁹⁻¹⁶ as we observed in more than 50% of our patients.

Lesions normally resolve during vacation time or sick leave and recur immediately on return to work. We feel that obtaining this information from the patient history is of the utmost importance when PCD is clinically suspected (Figures 1 and 2).³⁰ Diagnosis is based on clinical findings, mainly the location of the lesions and occupational risk, which is assessed using skin tests.²⁹ The fastest, easiest, and most sensitive method of confirming the diagnosis is the prick-by-prick test with the foods causing immediate itching on contact.²⁵ In PCD, the rub test is positive when applied to the affected or previously affected area (Figure 3). However, this test gives a negative result on healthy skin, thus enabling PCD to be distinguished from contact urticaria.³³ In isolated cases, this may be the only positive diagnostic test,^{26,27} as we observed with latex in our series. Specific serum IgE titers correlate well with the results of prick tests, although the assay is not always commercially available and a negative result does not rule out a diagnosis.²⁴

To improve prognosis, the first step is to avoid the allergen,³⁰ which, for financial reasons, is not always feasible for some food industry workers. Two such patients received 0.1% topical tacrolimus, which produced a much better symptomatic response than topical corticosteroids.³¹ Using rubber gloves led to contact dermatitis with thiuram mix in 4 cases; therefore, plastic gloves are recommended. Leaving their job was the only possible alternative to ensure a total cure of the lesions in some of our patients. In at least 2 of the cuttlefish cleaners, PCD was legally classed as an occupational disease that gave the patients the right to compensation.

Fish proteins were the most common cause of PCD in our setting. The latex proteins in rubber gloves should also be included as a relevant causative agent, although immediate hypersensitivity to latex more commonly manifests as immune contact urticaria. In the future, we will become aware of more PCD allergens as our experience with this condition increases.

Table 1 Protein Contact Dermatitis

Case	Age	Sex	Profession	Latency Period	Atopy	Location	Time Since Onset	Other Diagnoses	Patch Tests	Prick-by-Prick Test	Specific Immunoglobulin E
1	31	Man	Cook	12 mo	Yes	Hands (dorsum and palm) Forearms	Face	-		(-)	Fish (hake) Chicken Pork
2	42	Woman	Cuttlefish cleaner	2 y	Yes	Hands (dorsum) Forearms OAS	2 y		(-)	Fish Ink and digestive tract of cuttlefish	Class 3 hake Class 3 megrim
3	22	Women	Cook	2 y	No	Hands (dorsum and palm) Forearms		Contact dermatitis	Diallyl disulfide (PR) Thimerosal (RU)	Garlic	ND
4	36	Woman	Cook	6 y	No	Hands (dorsum, fingers, and palm)	10 y	Contact dermatitis	Thiuram mix (PR) Nickel (PaR) Cobalt (PaR)	Potato Latex Eggplant	ND
5	28	Man	Chemist	2 y	No	Hands (dorsum and periungual area)	1 y	Contact urticaria	Alcohols, wool (RU)	Latex	Class 1 latex
6	22	Woman	Cuttlefish cleaner	4.5 y	Yes	Forearms Face (eyelids) OAS	6 mo		Nickel (PaR)	Fish Ink and digestive tract of cuttlefish	Class 1 hake Class 1 megrim
7	35	Woman	Cook	-	Yes	Eczema Hands (fingers)	3 y	Atopic eczema on hands	(-)	Potato	ND
8	23	Woman	Hairdresser	2 mo	No	Hands (dorsum) Forearms	6 y	Irritant dermatitis	Nickel (PaR)	Latex (-) Rub test on affected area (+)	ND
9	49	Man	Builder	1 y	No	Hands (dorsum, fingers) Forearms	23 y	Contact dermatitis	Dichromate (PR)	Latex	Class 0 latex
10	53	Woman	Homemaker	-	No	Hands (palm) Forearms	2 y	Dyshidrotic eczema	Dichromate (PR) Cobalt (PR) PPDA (RU)	Latex (-) Rub test on affected area (+)	Class 0 latex
11	19	Woman	Cook	6 mo	No	Hands (dorsum, fingers, and sides)	6 mo	Contact dermatitis Chronic irritative dermatitis Dyshidrotic eczema	(-)	Latex (-) Rub test on affected area (+)	Class 0 latex
12	35	Woman	Poultry slaughterhouse worker	3 mo	Yes	Hands Forearms	3 mo	Contact dermatitis	Thiuram mix (PR) Nickel (PaR)	Chicken (liver, sweetbreads, and heart)	ND

Table 1 (Continuation)

Case	Age	Sex	Profession	Latency Period	Atopy	Location	Time Since Onset	Other Diagnoses	Patch Tests	Prick-by-Prick Test	Specific Immunoglobulin E
13	33	Man	Baker	15 y	Yes	Hands (sides and dorsum of fingers and hands)	1 y	Atopic eczema on hands	(-)	Wheat flour	Class 4 wheat
14	24	Woman	Fishmonger (halibut)	6 mo	No	Hands (dorsum and palm) Forearms	18 mo	Plaque psoriasis (PAS, 2)	Thimerosal (RU) PPDA (RU)	Fish (halibut)	Class 2 hake Class 3 megrim
15	30	Woman	Cook	4 mo	Yes	Hands (palm) Forearms Face (upper eyelids)	13 y	Atopic dermatitis	Nickel (PaR) Cobalt (PaR)	Potato Chicken (meat)	ND
16	34	Woman	Cook	2 mo	Yes	Hands (dorsum and fingers) Forearms OAS	3 y		Ethylene-diamine (RU)	Fish Class	2 hake Class 2 megrim
17	40	Woman	Food handler	6 y	No	Hands (dorsum of the fingers and finger pads) Forearms Face (upper eyelids)	2 y	Contact dermatitis	Thiuram mix (PR)	Fish (tuna)	ND
18	28	Woman	Cuttlefish cleaner	18 mo	No	Hands (dorsum) Forearm OAS	2 y		Nickel (PaR)	Fish Ink and digestive tract of cuttlefish Squid	Class 3 hake Class 3 megrim Class 0 squid
19	22	Man	Cook	18 mo	Yes	Hands (finger pads) Forearms	12 mo	Dyshidrotic pulpitis	(-)		
20	30	Woman	Cook	2 y	No	Hands Forearms (wrists)	1 y	Contact dermatitis	Formaldehyde (PR) Bronopol (PR)	Eggplant	ND
21	29	Man	Pizza chef	4.5 y	Yes	Hands (fingers) Forearms Face (eyelids)	18 mo	Atopic eczema on hands	(-)	Wheat flour	Class 1 wheat
22	38	Man	Builder	-	Yes	Hands (dorsum)	14 y	Atopic eczema on hands	(-)	Latex (-) Rub test on affected area (+)	Class 0 latex
23	44	Woman	Baker	27 y	Yes	Hands (dorsum, fingers) Forearms	1 y	Contact dermatitis	Benzoyl peroxide (PR)	Wheat flour α -amylase	ND

Table 1 (Continuation)

Case	Age	Sex	Profession	Latency Period	Atopy	Location	Time Since Onset	Other Diagnoses	Patch Tests	Prick-by-Prick Test	Specific Immunoglobulin E
24	23	Man	Baker	5 y	No	Hands (dorsum, fingers)	2 y	Contact dermatitis	Benzoic acid and octyl gallate (PR) Benzoyl peroxide (PR) (-)	α -amylase	ND
25	45	Woman	Waitress	-	Yes	Hands (palm) Forearms	25 y	Contact dermatitis Contact Urticaria	Thiuram mix (PR) Mercury (PR) (-)	Latex Potato	Class 4 latex
26	33	Woman	Cook	1 y	No	Hands (dorsum, fingers, and finger pads) Forearms	3 y	Contact dermatitis	(-)	Squid	ND
27	26	Woman	Kitchen assistant (anchovies)	1.5 y	Yes	Hands (dorsum) Forearms	6 mo	Contact dermatitis	(-)	Anisakis	Class 3 Anisakis

Abbreviations: ND, not done; OAS, oral allergy syndrome; PaR, Psoriasis Area Severity Index; PASI, Psoriasis Area Severity Index; PPDA, paraphenylenediamine; PR, present relevance; RU, relevance unknown.



Figure 1 Subacute dermatitis typically located on the dorsum of the hands.

In conclusion, PCD is a clinically relevant condition that Spanish dermatologists must suspect and, above all, learn to diagnose, since, in our opinion, it is currently underdiagnosed. Almost all the cases in our series had been assessed previously—albeit with patch tests only—by specialists from their occupational health insurance company, allergy specialists, or dermatologists. This is the first reported series of patients diagnosed with PCD in Spain and one of the most recent series in the international literature.

Conflict of Interest

The authors declare that they have no conflict of interest.



Figure 2 Fish cleaner who presented acute dermatitis 24 hours after returning to work following sick leave.

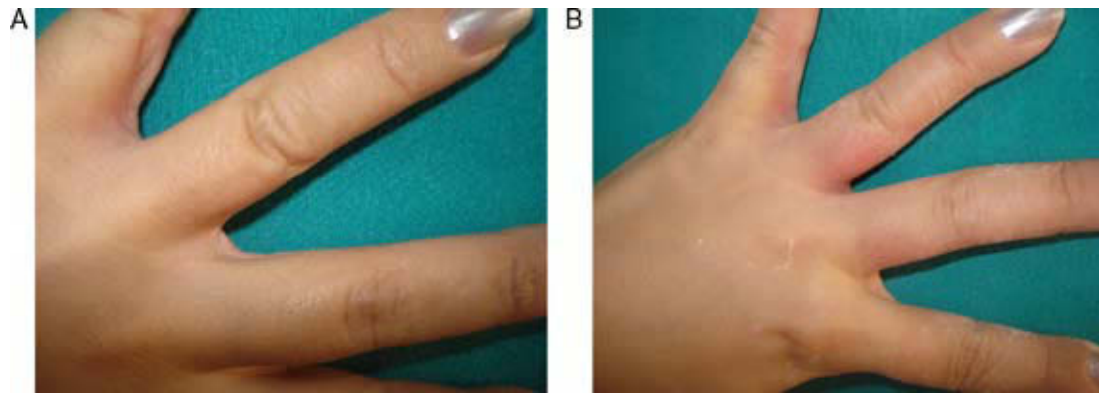


Figure 3 Rub test with foods or use test with a latex glove causes immediate eczematous lesions on an area previously affected by dermatitis. A, Before the test. B, Acute dermatitis 20 minutes after putting on a latex glove.

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