Protein Contact Dermatitis: Review of 27 Cases

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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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Dermatitis de contacto por proteínas. Revisión de 27 casos

Introduction

The term protein contact dermatitis (PCD) was coined by Hjorth and Røed-Petersen 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 allergens 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. 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 dorsal 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). The allergy type can determine the most appropriate diagnostic technique (patch tests, skin tests, or both). 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.

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. The face was affected in 5 of our patients, probably as a result of contact with contaminated hands. 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. Atopy is also a risk factor, 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). Diagnosis is based on clinical findings, mainly the location of the lesions and occupational risk, which is assessed using skin tests. 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. 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. In isolated cases, this may be the only positive diagnostic test, 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.

To improve prognosis, the first step is to avoid the allergen, 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. 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

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Profession</th>
<th>Latency Period</th>
<th>Atopy</th>
<th>Location</th>
<th>Time Since Onset</th>
<th>Other Diagnoses</th>
<th>Patch Tests</th>
<th>Prick-by-Prick Test</th>
<th>Specific Immunoglobulin E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>Man</td>
<td>Cook</td>
<td>12 mo</td>
<td>Yes</td>
<td>Hands (dorsum and palm) Forearms</td>
<td>Face</td>
<td>–</td>
<td>–</td>
<td>Fish (hake)</td>
<td>Chicken, Pork, Class 3 hake, Class 3 megrim</td>
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<tr>
<td>2</td>
<td>42</td>
<td>Woman</td>
<td>Cuttlefish cleaner</td>
<td>2 y</td>
<td>Yes</td>
<td>Hands (dorsum) Forearms OAS</td>
<td>2 y</td>
<td>–</td>
<td>–</td>
<td>Fish Ink and digestive tract of cuttlefish Garlic</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>Woman</td>
<td>Cook</td>
<td>2 y</td>
<td>No</td>
<td>Hands (dorsum and palm) Forearms</td>
<td>–</td>
<td>Contact dermatitis, Diallyl disulfide, Thimerosal (RU)</td>
<td>–</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>Woman</td>
<td>Cook</td>
<td>6 y</td>
<td>No</td>
<td>Hands (dorsum, fingers, and palm) Forearms</td>
<td>10 y</td>
<td>Contact dermatitis, Contact urticaria</td>
<td>–</td>
<td>Thiamin mix, Nickel (PaR), Cobalt (PaR), Class 1 megrim</td>
<td>ND</td>
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<tr>
<td>5</td>
<td>28</td>
<td>Man</td>
<td>Chemist</td>
<td>2 y</td>
<td>No</td>
<td>Hands (dorsum and periungual area)</td>
<td>1 y</td>
<td>–</td>
<td>–</td>
<td>Alcohols, wool (RU), Latex</td>
<td>Class 1 latex</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>Woman</td>
<td>Cuttlefish cleaner</td>
<td>4.5 y</td>
<td>Yes</td>
<td>Forearms Face (eyelids) OAS</td>
<td>6 mo</td>
<td>–</td>
<td>Nickel (PaR)</td>
<td>Fish Ink and digestive tract of cuttlefish Potato Latex Eggplant</td>
<td>Class 1 hake, Class 1 megrim</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>Woman</td>
<td>Cook</td>
<td>-</td>
<td>Yes</td>
<td>Eczema Hands (fingers)</td>
<td>3 y</td>
<td>Atopic eczema on hands</td>
<td>–</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>Woman</td>
<td>Hairdresser</td>
<td>2 mo</td>
<td>No</td>
<td>Hands (dorsum) Forearms</td>
<td>6 y</td>
<td>Irritant dermatitis</td>
<td>Nickel (PaR)</td>
<td>Latex, Rup test on affected area (+)</td>
<td>ND</td>
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<tr>
<td>9</td>
<td>49</td>
<td>Man</td>
<td>Builder</td>
<td>1 y</td>
<td>No</td>
<td>Hands (dorsum, fingers) Forearms</td>
<td>23 y</td>
<td>Contact dermatitis</td>
<td>–</td>
<td>Dichromate (PR), Latex</td>
<td>Class 0 latex</td>
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<tr>
<td>10</td>
<td>53</td>
<td>Woman</td>
<td>Homemaker</td>
<td>-</td>
<td>No</td>
<td>Hands (palm) Forearms</td>
<td>2 y</td>
<td>Dyshidrotic eczema, Contact dermatitis</td>
<td>–</td>
<td>Dichromate (PR), Qobalt (PR), PPDA (RU)</td>
<td>Class 0 latex</td>
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<tr>
<td>11</td>
<td>19</td>
<td>Woman</td>
<td>Cook</td>
<td>6 mo</td>
<td>No</td>
<td>Hands (dorsum, fingers, and sides)</td>
<td>6 mo</td>
<td>Chronic irritative dermatitis, Dyshidrotic eczema</td>
<td>–</td>
<td>Latex, Rup test on affected area (+)</td>
<td>Class 0 latex</td>
</tr>
<tr>
<td>12</td>
<td>35</td>
<td>Woman</td>
<td>Poultry slaughterhouse worker</td>
<td>3 mo</td>
<td>Yes</td>
<td>Hands Forearms</td>
<td>3 mo</td>
<td>Contact dermatitis</td>
<td>Thiamin mix (PR), Nickel (PaR) (liver, sweetbreads, and heart)</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>Age</td>
<td>Sex</td>
<td>Profession</td>
<td>Latency Period</td>
<td>Atopy</td>
<td>Location</td>
<td>Time Since Onset</td>
<td>Other Diagnoses</td>
<td>Patch Tests</td>
<td>Prick-by-Prick Test</td>
<td>Specific Immunoglobulin E</td>
</tr>
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</tr>
<tr>
<td>13</td>
<td>33</td>
<td>Man</td>
<td>Baker</td>
<td>15 y</td>
<td>Yes</td>
<td>Hands (sides and dorsum of fingers and hands)</td>
<td>1 y</td>
<td>Atopic eczema on hands</td>
<td>(-)</td>
<td>Wheat flour</td>
<td>Class 4 wheat</td>
</tr>
<tr>
<td>14</td>
<td>24</td>
<td>Woman</td>
<td>Fishmonger (halibut)</td>
<td>6 mo</td>
<td>No</td>
<td>Hands (dorsum and palms) Forearms</td>
<td>18 mo</td>
<td>Psoriasis (PASI 2)</td>
<td>Thimerosal (RU) PPDA (RU)</td>
<td>Fish (halibut)</td>
<td>Class 2 hake Class 2 megrim</td>
</tr>
<tr>
<td>15</td>
<td>30</td>
<td>Woman</td>
<td>Cook</td>
<td>4 mo</td>
<td>Yes</td>
<td>Hands (dorsum and fingers) Forearms Face (upper eyelids)</td>
<td>13 y</td>
<td>Atopic dermatitis</td>
<td>Nickel (PA) Cobalt (PA)</td>
<td>Potato Chicken (meat)</td>
<td>ND</td>
</tr>
<tr>
<td>16</td>
<td>34</td>
<td>Woman</td>
<td>Cook</td>
<td>2 mo</td>
<td>Yes</td>
<td>Hands (dorsum and fingers) Forearms OAS</td>
<td>3 y</td>
<td>Ethylene-diamine (RU)</td>
<td>FishGlass</td>
<td>2 hake Class 2 megrim</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>40</td>
<td>Woman</td>
<td>Food handler</td>
<td>6 y</td>
<td>No</td>
<td>Hands (dorsum of the fingers and finger pads) Forearms Face (upper eyelids)</td>
<td>2 y</td>
<td>Contact dermatitis</td>
<td>Thiuram mix (PR)</td>
<td>Fish (tuna)</td>
<td>ND</td>
</tr>
<tr>
<td>18</td>
<td>28</td>
<td>Woman</td>
<td>Cuttlefish cleaner</td>
<td>18 mo</td>
<td>No</td>
<td>Hands (dorsum) Forearms</td>
<td>2 y</td>
<td>Nickel (PA)</td>
<td>Fish Ink and digestive tract of cuttlefish Squid</td>
<td>Class 3 hake Class 3 megrim</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>22</td>
<td>Man</td>
<td>Cook</td>
<td>18 mo</td>
<td>Yes</td>
<td>Hands (finger pads) Forearms</td>
<td>12 mo</td>
<td>Dyshidrotic pulpitis</td>
<td>(-)</td>
<td>Class 3 squid</td>
<td>Class 0 squid</td>
</tr>
<tr>
<td>20</td>
<td>30</td>
<td>Woman</td>
<td>Cook</td>
<td>2 y</td>
<td>No</td>
<td>Hands Forearms (wrist’s)</td>
<td>1 y</td>
<td>Contact dermatitis</td>
<td>Formaldehyde (PR) Bronopol (PR)</td>
<td>Eggplant</td>
<td>ND</td>
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<tr>
<td>21</td>
<td>29</td>
<td>Man</td>
<td>Pizza chef</td>
<td>4.5 y</td>
<td>Yes</td>
<td>Hands (fingers) Forearms Face (eyelids)</td>
<td>18 mo</td>
<td>Atopic eczema on hands</td>
<td>(-)</td>
<td>Wheat flour</td>
<td>Class 1 wheat</td>
</tr>
<tr>
<td>22</td>
<td>38</td>
<td>Man</td>
<td>Builder</td>
<td>-</td>
<td>Yes</td>
<td>Hands (dorsum)</td>
<td>14 y</td>
<td>Atopic eczema on hands</td>
<td>(-)</td>
<td>Latex (-) Rub test on affected area (+)</td>
<td>Class 0 latex</td>
</tr>
<tr>
<td>23</td>
<td>44</td>
<td>Woman</td>
<td>Baker</td>
<td>27 y</td>
<td>Yes</td>
<td>Hands (dorsum, fingers)</td>
<td>1 y</td>
<td>Contact dermatitis</td>
<td>Benzoyl peroxide (PR)</td>
<td>Wheat flour α-amylase</td>
<td>ND</td>
</tr>
</tbody>
</table>
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.
Acknowledgments

Dr. Hernández-Bel is grateful to Dr. Jesús de la Cuadra for teaching him all he knows about contact dermatitis and skin allergy.

References


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.