

OCCUPATIONAL AIRBORNE AND HAND DERMATITIS TO HOP (*HUMULUS LUPULUS*) WITH NON-OCCUPATIONAL RELAPSES

Radosław Śpiewak, Jacek Dutkiewicz

Department of Occupational Biohazards, Institute of Agricultural Medicine, Lublin, Poland

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Abstract: We report a case of a 57-years-old female farmer with occupational airborne dermatitis and hand dermatitis to hop (*Humulus lupulus*). The disease appeared at the age of 46, after 30 years of working with hop without any health problems. The patient had skin erythema of the face, neck and décolleté, oedema of the eyelids, conjunctivitis, as well as acute dermatitis of the hands. The symptoms were provoked both by fresh and dried hop, appeared after half-an-hour of working and persisted over 1–2 days. There were no other skin or allergic problems. Skin tests were carried out with hop leaves (saline extract: prick positive, patch negative; glycerol extract: prick positive, patch negative) and hop cones (saline extract: prick positive, patch negative; glycerol extract: prick negative, patch positive after 48 and 72 hours). Despite discontinuing work, the patient experienced several relapses of her dermatitis. We identified new sources of hop allergens: a beauty cream and a herbal sedative, both containing hop extract. During the next hop cultivation period it also turned out that sleeping in one bed with her husband was provoking relapses of the patient's dermatitis. The husband admitted that sometimes he felt too tired to wash thoroughly after working on the plantation. Our case shows that connubial contacts with husband working in the same workplace may cause relapses of occupational dermatitis. To our knowledge, this is the first report on the concurrent occupational and connubial dermatitis to hop.

Address for correspondence: Radosław Śpiewak, MD, Instytut Medycyny Wsi, ul. Jaczewskiego 2, 20-090 Lublin, Poland. E-mail: spiewak@galen.imw.lublin.pl

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INTRODUCTION

During the hop harvest in August and September 2000 we carried out a field study on work-related skin diseases among hop farmers in eastern Poland, which has been described previously [21]. Among 73 farmers examined, 11 complained of skin symptoms when working with hop. In one of the farmers, we suspected a severe, invalidating occupational dermatitis. This diagnosis was later confirmed at our department. Interestingly, after cessation of work the patient suffered from relapses of her dermatitis after using cosmetics and herbal medicines containing hop extracts, and when sleeping in one bed

with her husband who had worked with hop. This case is described in the present report.

CASE DESCRIPTION

On-site examination. The 57-years old woman was seen for the first time in September 2000, during the previously mentioned study of hop farmers [21]. On the study day, she was feeding a machinery that separates hop cones from stems and leaves. During this process, she was placing stems of hop cut on the plantation into a chain which pulls them into the machinery. She was also removing the debris of stems and leaves from the belt

transporting separated hop cones to the dryer. At the time of our inspection, the patient had intense skin erythema of the face, neck and décolleté, oedema of the eyelids and conjunctivitis, as well as acute dermatitis of the hands (erythema and desquamation of the entire skin on the hands, small oozing papules and vesicles, mostly on the sides of the fingers).

Patient's history. The patient had worked on the farm from the age of 16, since when she had been regularly involved in hop production. Every year she took part in cultivating and harvesting hop, separating hop cones, drying and packing them into special bags in which hops are sold to breweries. For more than 30 years she did not have any skin problem. The first symptoms of dermatitis occurred at the age of 46, during a harvesting season. She had erythema and intense pruritus on uncovered skin areas, including the hands, face and neck. Since then, the disease appeared always when working with hop (green parts of the plant or hop cones). The symptoms appeared typically after half-an-hour of working and persisted over 1–2 days after cessation of work. The dermatitis recurred in every hop harvesting period, and each year was more intense. Also handling dried hops provoked similar skin symptoms.

The farmer was invited for further testing and reported to institute after the hop harvest. At that time, there were no visible skin changes. Two weeks later, she collected samples of dried hops for examinations. Subsequently, moderate dermatitis appeared on her hands. Besides the symptoms related to hop, she denied ever having had any other skin or allergic problems in her life.

Routine allergy tests. Skin prick tests were carried out with a series of farm-specific allergens including grain, straw, and hay dusts, farm animal epithelia and feathers, flours, bran and pollens of cultivated plants (Allergopharma, Germany and Biomed, Poland). There were only weak immediate wheal-and-flare reactions (+) to moulds *Penicillium notatum* and *Botrytis cinerea*, and a late reaction to *Pantoea agglomerans* (reddish, palpable infiltration found the following day). Patch tests with European Standard, Plant Series, Rubber Series, *Dermatophagoides* Mix (Chemotechnique, Sweden) and the Pesticides Series (Institute of Agricultural Medicine in Lublin, Poland) revealed only a weak reaction to *Dermatophagoides* Mix after 48 hours. The measurements of total IgE and IgE specific to farm animal allergens and storage mites were carried out using UniCAP 100 (Pharmacia and Upjohn, Sweden), and showed a normal total IgE value (21.4 kU/l) and no specific IgE detectable in serum. Using the double gel immunodiffusion (Ouchterlony), the presence of precipitating antibodies specific to Gram-negative bacterium *Pantoea agglomerans* (syn. *Erwinia herbicola*) and yeast-like fungus *Candida albicans* was detected.

Aimed allergy tests. As the most probable cause of the dermatitis was hop, a series of prick and patch tests was

Table 1. Results of skin prick tests and patch tests with hop extracts

Allergen	Prick	Patch
Hop leaves - saline extract	+	–
Hop leaves - glycerol extract	+	–
Hop cones - saline extract	+	–
Hop cones - glycerol extract	–	D3(+), D4(+)

D3 - reading of skin reaction after 48 hours, D4 - reading after 72 hours.

carried out in order to verify the casual relationship. The hop extracts for skin tests were prepared in our laboratory. Fresh cones and leaves of hop (*Humulus lupulus*) were cut into small pieces, and each extracted with glycerol and saline (0.85% NaCl) in the hop to solvent proportion of 1:2 (w/w) for 48 hours at 4°C. Subsequently, the extracts were centrifuged for separation of clear supernatants, which were then sterilised by filtering, checked for sterility and lack of toxicity, and stored at 4°C until usage. These extracts had already been used for testing in our previous study [21]. The skin prick tests were carried out on the anterior surface of the forearm using standardised lancets (Allergopharma, Germany), with reading of skin reaction after 20 minutes. Wheals on test sites with a diameter equal or greater than ½ of the diameter of histamine control wheal were regarded as positive results. Patch tests were carried out with the same hop extracts. Small pieces of filter paper were soaked in the extracts and subsequently fixed for 48 hours on the patient's back using IQ Chambers (Chemotechnique, Sweden). The reading of skin reaction was carried out after 48 hours (D3) and 72 hours (D4). The results of skin tests with hop extracts are shown in Table 1. A control patch test was carried out on 4 healthy volunteers – none of them had a positive reaction.

The patient suggested yet another possible cause of her dermatitis – the pesticide Confidor® (imidacloprid) which for some years had been regularly used on her plantation. Therefore, we also patch tested 0.01% and 0.1% solutions of the pesticide, however, with negative results after 48 and 72 hours.

Diagnosis and further observations. Based on the above results, the diagnosis of occupational allergic airborne and hand dermatitis to hop was established, and eventually accepted by the State Sanitary Authority, and compensated for by the farmer's insurance institution. However, even after work cessation, the patient experienced several relapses of her dermatitis. Each time, a new source of the same allergen could be identified. For the first time, a "natural" beauty cream caused contact dermatitis on the face of the patient. On the product label, hop extract was listed among the ingredients. For the second time, the patient had dermatitis flare after taking one tablet of a herbal sedative, which also contained hop extract.

During the following vegetation period the patient no longer took part in the work; however, hop production on

her farm continued. Interestingly, further relapses of the patient's dermatitis were provoked by sleeping in the same bed with her husband who was taking part in the hop harvest. The man admitted that after a whole day of work on the plantation, sometimes he felt too tired to take shower or bathe, and went to bed soiled with hop sap.

DISCUSSION

The first description of contact dermatitis from hop was published by Badham in 1834 (cited after [6]). In 1952, in Herefordshire, UK, occupational dermatitis to hop was observed in 22 individuals. From this group, 11 hop-pickers were forced to change their occupation due to intensity of the disease [6]. In the 1970s, Newmark described 2 cases of hop allergy: a chemist who developed urticaria, rhinitis, conjunctivitis and asthma after 6 months work as a hop selector for a brewery [15], and a hop farmer with occupational respiratory disorder [16]. Another case of a laboratory worker who developed conjunctivitis, rhinitis, bronchitis and dermatitis to hops was described by Raith and Jäger [18]. A case of contact urticaria to dried hops has been reported recently by Estrada and colleagues [10].

Probably the first systematic study on hop-related skin diseases was carried out by Tsykrunov [25], who published in 1978 data on 156 Ukrainian hop-workers; 15% of them were found to have hop-related skin diseases. In our study of 73 eastern-Polish hop farmers [19, 21], 8 farmers (11%) complained of skin symptoms provoked by contact with hop. Four of them suffered from airborne dermatitis, 2 farmers had hand eczema, and the remaining 2 complained of intense pruritus of uncovered skin when working with hop. Two of the 8 farmers have had positive prick tests with hop extracts.

In the case reported here, the results of skin tests were consistent with the patient's history and indicated that the dermatitis was of allergic nature. We observed positive skin reactions to hop extracts, both in prick test (immediate wheal and flare reaction) and patch test (delayed eczematous reaction). An overlap of type I and type IV allergy is typically seen in occupational protein contact dermatitis [11]. In our case, however, it remains unclear whether type I and type IV responses were triggered by the same allergen, because reactions on both tests were induced by different extracts, as shown in Table 1. We have previously described a similar case of occupational airborne contact dermatitis to *Phaseolus vulgaris*; in that case, patch tests with *Phaseolus* leaves gave positive results, but prick tests remained negative [20].

In the present case, allergy to hop seems to be a well-documented and most convincing cause for the skin disease. However, we also observed another immunological phenomenon which deserves discussion. As mentioned previously, there was a late skin reaction to the allergen of the bacterium *Pantoea agglomerans* on skin prick tests; we did not observe an immediate reaction; however, on the next day a reddish, palpable infiltration was found on

the test site. This kind of reaction is thought to be typical of type III allergy [1, 24], which is consistent with the presence of precipitating antibodies specific to *P. agglomerans* in the serum of the patient. *Pantoea agglomerans* (synonyms *Erwinia herbicola*, *Enterobacter agglomerans*) is a Gram-negative bacterium present abundantly on surfaces of cultivated plants [9], thus we can easily assume that our patient was heavily exposed to it. Although the role of precipitins in skin eczema is not known, there is an interesting observation by Bünger and co-workers [3] who have found a significantly increased frequency of skin diseases among compost workers; in most cases skin symptoms coexisted with increased levels of IgG specific to actinomycetes *Saccharopolyspora rectivirgula* and *Streptomyces thermovulgaris*. In our previous study of farming students [23], we found that all students with specific cellular reactivity to microbes typical of farm environment (including *P. agglomerans*) had work-related symptoms (vs. 27.7% of those non-reactive, $p = 0.001$); allergic skin diseases were also more frequent in this group (40% reactive vs. 9.2% non-reactive, $p = 0.009$). These observations indirectly indicate the possible role of microbial antigens in etiopathogenesis of work-related skin diseases. In the presented case, however, allergy to hop seems to be the most convincing explanation for the disease. Bacterial antigens would at best play a secondary role, if any. Plants may also cause symptoms through a non-immunologic, irritating effect, as we have shown in the case of thyme [22].

Some allergens which primarily sensitise through the skin are later capable of inducing dermatitis flare after ingestion. This phenomenon has been documented in allergy to metals [28, 30], balsam of Peru [29], and corticosteroids [5]. Moreover, in 2 cases of occupational protein contact dermatitis to meat and fish, oral challenge with the responsible allergens caused extracutaneous symptoms [2]. Regarding the airways, similar mechanism has been reported in 2 bakers, who first developed occupational asthma and subsequently also food intolerance to flour [14]. Nevertheless, in more recently published cases [12, 13], such a phenomenon was not observed, possibly due to degradation of the high-molecular weight allergens in the alimentary tract. In our patient, taking one tablet of a herbal sedative containing hop extract caused a relapse of her dermatitis. This shows that the hop allergen responsible for contact allergy was also capable of inducing dermatitis when ingested. We were interested whether ingestion of beer would also cause any skin symptoms, which would tell us whether the responsible allergen is heat-stable (in Poland all beers are pasteurised). Unfortunately, the patient never drank beer.

The term "connubial dermatitis" refers to dermatitis caused by substances to which one is exposed secondarily through physical contact with the spouse, typically when sleeping together in the same bed. The contact is not necessarily related to sexual activities, thus connubial dermatitis is not confined solely to the genitals [27]. Wilkinson used this term in an even broader sense,

describing 2 cases of dermatitis in which exposure resulted from sharing a household or a car [31]. In the literature there are a few reports on connubial dermatitis in which the identified causes were mostly topical drugs [4, 26], cosmetics [8], and fragrances [7]. We are aware of 2 previous case reports of connubial dermatitis to an occupational substance. In 1975, Wilkinson reported on connubial photodermatitis to chlorpromazine and prometazine in a veterinary surgeon's wife. She was exposed when using her husband's car in which he carried his veterinary drugs [31]. In 1987, Newton and White described another case of dermatitis caused by the antihelminthic morantel in the wife of a pharmaceutical company's worker who was employed at production of this drug [17]. Our case shows that when sensitisation takes place in occupational conditions, contact with the husband working in the same workplace may be responsible for relapses of dermatitis after cessation of work. There were also non-occupational sources of the hop allergen: a beauty cream and an oral herbal sedative containing hop extracts.

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