



Occupational asthma due to tampico fiber bystander exposure in a brush production company – case report and literature review

Monika Raulf · Ingrid Sander · Thomas Brüning · Silke König

Received: 9 August 2018 / Accepted: 3 September 2018
 © Springer Medizin Verlag GmbH, a part of Springer Nature 2018

Abstract

Background A female machine operator in a brush factory presented for an expert medical examination due to suspected occupational obstructive pulmonary disease. She reported the occurrence of severe respiratory distress whenever colleagues in the same working area processed tampico fibers or a mixture of tampico fibers and bassine. The challenge posed in terms of the expert appraisal was to either prove or rule out occupational causality and IgE-mediated (IgE, immunoglobulin E) sensitization in relation to the reported workplace-related symptoms.

Methods As part of the further diagnostic work-up, tampico fibers were isolated from the workplace and the proteins biotinylated and coupled to a streptavidin ImmunoCAP for specific IgE testing. The material taken from the workplace was checked for mite allergen contamination. In addition, a systematic literature search was conducted in PubMed on “agave-/tampico fibers and diseases.”

Results Tampico-specific IgE antibodies (10.5 kU/l and immunoblot labeling of protein bands in the 25-kDa range) were detected in the patient’s serum. The

inhibition assay showed that mite-allergen contamination of the tampico materials was not responsible for the IgE reactivity.

Conclusion Tampico fibers are robust fibers obtained from the leaves of the Mexican *Agave lechugilla*. The literature describes several cases of skin reactions in the form of irritant contact dermatitis due to occupational exposure to agave leaves or contact with agave sap. In the present case, the asthma symptoms of a female worker in a brush factory were attributed to inhalant bystander exposure to tampico fibers in the workplace. The unequivocal evidence of sensitization to tampico fibers met the medical requirements for the recognition of an occupational disease (BK 4301).

Keywords Occupational allergy · Tampico fiber · IgE detection · Occupational exposure · Allergen identification

Abbreviations

CCD	Cross-reactive carbohydrate determinant
ELISA	Enzyme-linked immunosorbent assay
FeNO	Fractional exhaled nitric oxide
ICS	Inhalant corticosteroid
IgE	Immunoglobulin E
kDa	Kilodalton
kU	Kilounit
LABA	Long-acting beta agonists
ppm	Parts per million
SABA	Short-acting beta agonists
SDS-PAGE	Sodium dodecyl sulfate polyacrylamide gel electrophoresis
sIgE	Specific immunoglobulin E

Background and objective

A 45-year-old female presented for an expert medical examination due to suspected occupational ob-

Dr. I. Sander · Prof. Dr. T. Brüning
 Institute for Prevention and Occupational Medicine of the
 German Social Accident Insurance, Institute of the
 Ruhr-University Bochum (IPA), Bochum, Germany

Dr. S. König
 Department of Occupational Lung and Respiratory
 Diseases, Statutory Accident Insurance Clinic Falkenstein,
 Falkenstein, Germany

Prof. Dr. M. Raulf (✉)
 Institute for Prevention and Occupational Medicine
 of the German Social Accident Insurance,
 Institute of the Ruhr University Bochum (IPA),
 Bürkle-de-la-Camp-Platz 1, 44789 Bochum, Germany
raulf@ipa-dguv.de

structive respiratory disease. She had been working for 4 years as a machine operator in a brush factory where she produced brushes made of polypropylene. The patient reported severe respiratory distress and throat irritation in conjunction with the agents tampico fibers and bassine, despite the fact that she did not work with these materials herself, but was exposed to them via coworkers that handled the materials on the same premises.

Tampico fibers (synonyms: agave fibers, Mexican fibers, ixtle, and natural fibers) are robust fibers obtained from the leaves of the Mexican *Agave lechugilla*. Agave leaves are harvested on plantations three to four times a year once they reach the age of 3 years. The finished fiber often bears the trade name tampico fiber, after the port town Tampico in Mexico. It is considered to be acid, alkali, and heat resistant, is elastic, and absorbs water.

The fiber is often used in combination with bassine. Bassines are extremely coarse fibers that are obtained from the Palmyra palm (also referred to as sago palm, *Areaceae* family), primarily in East India. Both fibers are used in the production of brushes (e.g., scrubbing brushes).

Establishing whether the patient exhibited type-1 sensitization to tampico fibers was of particular importance in the context of the occupational health appraisal on causality.

Case report

Occupational exposure

The patient had been working full-time since 02/2013 at a brush factory in the punching and finishing department, where she performed all necessary tasks, including the operation of a drilling and filling machine. She also performed some tasks in the packing and dispatch department in the adjacent hall. When operating the drilling and punching machines, the patient came into contact with wood dust and the polypropylene brush material processed there. Her colleagues processed tampico fibers and a material made up of a mixture of tampico fibers and bassine in the same department. According to the information provided by the supplier, these natural substances always have a certain dustiness; particularly the fibers of the Mexican agave are sometimes used as polishing materials. This is due to microcrystalline silica particles contained in the cells of the plant fibers. The supplier ruled out the possibility of mold infestation of the agave materials.

Patient history

The patient had been known to suffer from seasonal allergic rhinoconjunctivitis since the age of 13; this was treated with systemic antihistamines, eye drops, and nasal spray in the pollen season only.

The onset of respiratory symptoms occurred approximately 6 months after starting work at the brush factory. The patient reported sneezing attacks, a dry cough, and dyspnea. According to the information she provided, pronounced dyspnea occurred when colleagues in the same department processed tampico fibers and a material made from a mixture of tampico fibers and bassine. The patient reported that her symptoms had worsened over time and that she experienced dyspnea even when only one coworker in the room started processing these materials. She experienced respiratory problems even when these materials were worked with at a distance of more than 10 m. Coughing and dyspnea occurred ever more frequently over time. No respiratory problems occurred when she operated the drilling and punching machines, which involved contact with wood dust and the polypropylene brush material processed there.

Medical findings and diagnostic allergy testing

The patient was initially treated with antibiotics by her general practitioner for suspected acute bronchitis. Upon first presentation to a pulmonary specialist in 06/2015, lung function analysis revealed no obstructive respiratory disorder. Inhalation challenge testing with methacholine showed pronounced bronchial hyperreactivity. The pulmonary specialist initiated inhalant treatment with an inhalant corticosteroid (ICS), long-acting beta agonists (LABA), and short-acting beta agonists (SABA). While on this treatment, acute dyspnea occurred increasingly frequently during working hours as a result of bystander exposure to tampico fibers; the lung specialist treated this with intravenous cortisone. Despite the workplace-related symptoms, no peak-flow measurements have been made at the workplace as yet.

At the time of the examination for the expert appraisal (05/2017), the patient was in good general health and no clinically abnormal findings were made. Overview chest X-rays revealed normal cardiac and pulmonary findings. Detailed lung function analysis showed a medium- to high-grade obstructive respiratory disorder, which was partially to fully reversed with two doses of salbutamol. Blood gas analysis at rest and during exertion revealed no partial respiratory failure. Spiroergometry was performed, showing slightly reduced performance due to a lack of training and an early latent gas exchange disorder. Exhaled nitrogen monoxide (FeNO) was significantly elevated at 122 ppm (parts per million).

As part of the diagnostic allergy work-up, the patient tested positive in the skin prick test to early- and late-flowering grass and cereal pollen, weed pollen, as well as *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. Friction testing with the brush material (tampico fibers) produced no skin reaction.



Fig. 1 Tampico fiber material taken from the patient's workplace (used to produce the extract)

Serological diagnosis revealed a total IgE level within the normal range (63.3 kilounit[kU]/l), as well as specific IgE to early- and late-flowering grasses and *D. farinae* and *D. pteronyssinus* (each CAP class 3).

Further diagnostic procedures

The challenge posed in terms of the expert appraisal was to either prove or rule out occupational causality and IgE-mediated sensitization in relation to the reported workplace-related symptoms and concomitant type-1 sensitization to grass pollen and house dust mites as competing factors for the onset of bronchial asthma. Commercial extracts to test sensitization to tampico fibers were not available. The severity of the disease prevented workplace-related challenge testing.

In order to conduct further diagnostic tests, tampico fibers from the workplace were extracted (Fig. 1). After determining the protein content in the supernatant (0.68 mg protein/g material; protein determination according to Bradford [1]), protein biotinylation and binding to a streptavidin ImmunoCAP (Thermo Fisher Scientific, Phadia AB, Uppsala, Sweden) was performed [2]. These ImmunoCAPs enabled specific IgE antibody levels to tampico fibers of 10.5 kU/l (CAP class 3) to be determined in the patient's serum (ImmunoCAP system).

The level of IgE antibodies to horseradish peroxidase to rule out binding to cross-reactive carbohydrate structures (cross-reactive carbohydrate determinant, CCD) was 0.02 kU/l (CAP class 0). Protein separation of the tampico protein extract using SDS-PAGE (Sodium dodecyl sulfate polyacrylamide gel electrophoresis) and subsequent Coomassie staining showed two protein bands in the 25-kilodalton (kDa) range (Fig. 2). In subsequent immunoblot analysis, the IgE antibodies in the patient's serum marked a sharp band in the 25-kDa range, while three other

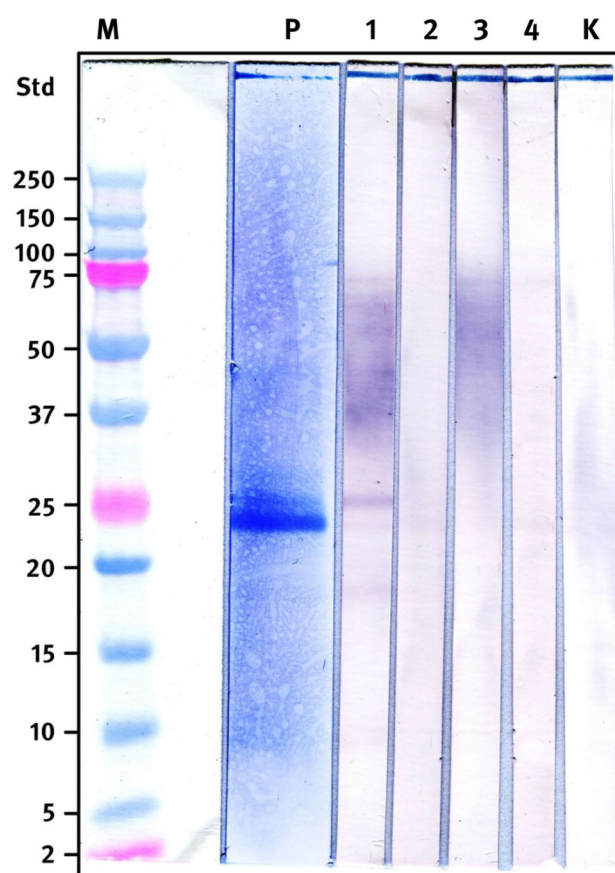


Fig. 2 Protein separation of the tampico fiber extract using SDS gel, Coomassie protein staining, and IgE immunoblotting. *M* protein standard: Bio-Rad Precision Plus Protein Dual Xtra Prestained (Laboratories GmbH, München, Germany), *P* Tampico protein (Coomassie-protein stained), *1-K* IgE immunoblotting, *1* patient serum, *2-4* sera from control subjects with comparable total IgE, *K* second antibody control (puffer instead of serum)

sera with comparable total IgE levels showed no IgE reactivity in this range.

Since the patient was also sensitized to mites (sIgE to *D. pteronyssinus* 6.29 kU/l and *D. farinae* 5.09 kU/l), the tampico protein extract was analyzed for mite antigens in the domestic mite Enzyme-linked immunosorbent assay (ELISA) (antibody-based detection method) [3]. A concentration of 15.8 ng domestic mite antigen per gram of material was detected. In order to rule out the possibility that IgE binding to the tampico material was caused by reactivity to *D. farinae*, inhibition testing was performed with the tampico protein ImmunoCAP as solid phase and *D. farinae* (1.3 mg protein/ml) as inhibitor. While the addition of *D. farinae* extract did not cause inhibition of IgE binding to the tampico protein ImmunoCAP, complete autoinhibition was seen with the tampico fiber extract (Table 1).

Table 1 Inhibition testing with patient serum

Solid phase	Inhibitor	Inhibition	
		kU _A /l	%
Tampico fibers bg417	PBS (reference value)	6.78 ^a	0
Tampico fibers bg417	Tampico extract (1.8 mg protein/ml)	0.08	99
Tampico fibers bg417	<i>Dermatophagoides farinae</i> (Allergopharma) (1.3 mg protein/ml)	6.83	–1

PBS phosphate-buffered saline, kU kilounit

^aThe tampico-specific IgE concentration in undiluted serum was 10.5 kU/l. For the inhibition experiment, 50 µl serum was mixed with 10 µl PBS or inhibitor

Table 2 Literature overview of diseases/symptoms caused by contact with tampico fibers or the agave plant

Reference/country	Collective	Type of exposure	Type of investigation	Symptoms	Conclusion
Brenner et al. (1998); Israel [5]	12 patients (10 m, 2 f); 11 of whom were soldiers	Skin contact with fresh sap from <i>Agave americana</i> while cutting lower leaves	Dermatological examination, biopsies in some cases, clinical laboratory tests	Extreme itch, redness and erythematous patches on the forearm; 10 patients showed systemic signs and symptoms, 8 fever and abnormal laboratory values	Contact dermatitis with, e. g., systemic symptoms; treated with saline compresses and oral antihistamines; systemic manifestations resolved after 24 h; exanthema subsided after several days; scaling and hyperpigmentation persisted for 7–10 days
Ricks et al. (1999); Texas/USA (case report) [6]	Male patient	Cutting/sawing agave plants during landscape management	Dermatological examination, biopsy	Palpable purpura in linear and tortuous patterns, pruritus	Direct toxic effect of calcium oxalate crystals and saponins in agave sap
Salinas et al. (2001); Mexico [7]	26 male workers on an agave plantation 46 male workers at a tequila distillery	Frequent skin contact with fresh agave plants or parts of plants	Questionnaire; query about irritation upon agave contact	50% of workers in the distillery reported current and 30% historical symptoms. Only one third of plantation workers reported no symptoms	Irritant contact dermatitis, localized to the forearm, neck and abdomen; cause: raphide bundles in the extruded sap of agave leaves; suitable protective clothing recommended
High (2003); Texas/USA (case report) [8]	Male patient	Cutting/sawing agave plants during landscape management	Dermatological examination, biopsy	Burning and itching immediately following contact with plant sap; symptoms resolved following removal with water; erythematous papules on exposed sites the following morning	Acute irritant contact dermatitis; biopsy revealed epidermal spongiosis, superficial perivascular inflammatory infiltrates; resolved after 7 days without treatment
Quirce et al. (2008); Spanien [9]	2 brush makers affected; 5 workers in total examined	Foreman/assistant foreman in a brush factory (brothers); in contact with tampico fibers for 13 and 10 years, respectively	FeNO measurement, challenge testing with aqueous tampico extract, sputum analysis, skin testing with tampico extract, immunoblotting	Both patients suffered from workplace-related rhinitis and asthma; one patient additionally from contact urticaria upon contact with tampico fibers	Inhalation and contact with tampico fibers triggered an IgE-dependent mechanism

m Male, f female, FeNO fractional exhaled nitric oxide, IgE immunoglobulin E

Discussion

There are a number of reports in the literature on skin reactions in the form of irritant contact dermatitis induced by occupational exposure while processing the leaves, or coming into contact with the sap, of the succulents *Agave americana* and *Agave tequilana* ([4]; Table 2, literature review). This dermatitis is known as “mal de agaveros” in Mexico, particularly among workers on agave plantations and in tequila production [7]. These, however, are not allergic reactions. Instead, raphide bundles, with their fine, monoclinic crystal needles of calcium oxalate, have been identi-

fied as the cause of the burning pain and protracted skin inflammation.

Exposure to tampico fibers as the cause of occupational rhinitis and asthma symptoms in two brush makers in a factory was first described by Quirce et al. [9]. At the time of that investigation, the two brush makers had been occupationally exposed to tampico for 13 and 10 years, had experienced symptoms of rhinitis for 10 and 8 years, and asthma symptoms for 2 and 5 years, respectively. Three other workers at the same company reported no symptoms. At 44 and 83 ppm, exhaled nitric oxide levels were elevated in

the two symptomatic patients, while in the normal range (<23 ppm) in the other patients.

Both symptomatic patients tested positive to skin prick testing with a tampico extract, as well as to specific provocation testing with a nebulized aqueous tampico extract. A marked increase in eosinophilic granulocytes was seen in induced sputum obtained 24 h following provocation. The non-symptomatic workers tested negative to skin prick testing with tampico extract. Three IgE-binding protein bands in the range of 31, 38, and 43 kDa were detected in the tampico extract with the sera from the two patients. The authors summarized these findings as an IgE-dependent mechanism of upper and lower respiratory tract symptoms induced by tampico fibers.

The present case report also documents IgE-mediated sensitization in workers involving severe respiratory distress and irritative cough, even upon indirect exposure to tampico fibers in a brush factory. In contrast to the investigation by Quirce et al. [9], quantitative detection of tampico fiber-specific IgE was achieved in the present case. Immunoblotting confirmed IgE recognition of tampico protein. However, the clearest reaction band was in the 25-kDa range. The inhibition experiment was able to dispel the suspicion that IgE reactivity was caused by mite-allergen contamination of the tampico material used for extraction: tampico fiber-specific IgE binding of the patient's serum could not be reduced by the addition of *D. farinae* allergens.

Although the worker did not process the tampico fibers herself, and thus no direct contact took place, inhalative bystander exposure to evidently highly allergenic tampico fiber dust in the workplace appears to be sufficient to cause workplace-related symptoms and sensitization to this unequivocal occupational allergen source. Inhalation provocation testing with methacholine revealed pronounced bronchial hyperreactivity in the patient. The high FeNO level of 122 ppm in the patient's exhaled air supports the suspected diagnosis of allergic asthma and suggests type 2 respiratory inflammation [10]. Due to the severity of the disease, it was not possible to perform workplace-related provocation testing in the patient. In line with the "Reichenhaller Recommendation" [11], the indication for specific bronchial provocation testing and/or workplace-based inhalation testing is not mandatory in the case of unequivocal exposure-related patient history and clear evidence of sensitization—both of which were present in this particular case.

The medical criteria for BK 4301—"obstructive airway diseases (including rhinopathy) caused by allergenic substances and which result in an individual being forced to cease all activities that were or could be causal to the onset, exacerbation, or recurrence of the disease"—were recognized in the case presented here. Since the insured individual still works at the factory, it has not been possible as yet to recognize her dis-

ease as an occupational disease (BK 4301), since this requires cessation of work activity. A change of workplace within the company is currently being looked into. The steps taken to date have not yet resulted in an improvement, since the new workplace is unlikely to be allergen-free.

Although brush manufacturing jobs and exposure to materials such as tampico fibers are comparatively rare in Germany, sensitization and respiratory symptoms can occur even as a result of bystander exposure and should be taken into consideration. In vitro diagnostic methods are also available for future cases requiring the serological detection of sensitization to tampico fibers in the context of expert appraisals (www.ipa-dguv.de).

Conflict of interest M. Raulf has received lecture fees from ThermoFisher Scientific, Astellas, and HAL. I. Sander, T. Brünig, and S. König declare that they have no competing interests.

References

1. Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem.* 1976;72:248–54.
2. Sander I, Kespohl S, Merget R, Goldscheid N, Degens PO, Brünig T, et al. A new method to bind allergens for the measurement of specific IgE antibodies. *Int Arch Allergy Immunol.* 2005;136:39–44.
3. Sander I, Zahradnik E, Kraus G, Mayer S, Neumann HD, Fleischer C, et al. Domestic mite antigens in floor and airborne dust at workplaces in comparison to living areas: a new immunoassay to assess personal airborne allergen exposure. *PLoS ONE.* 2012;7:e52981.
4. Crawford GH, Eickhorst KM, McGovern TW. Botanical briefs: the century plant—Agave Americana L. *Cutis.* 2003;72:188–90.
5. Brenner S, Landau M, Goldberg I. Contact dermatitis with systemic symptoms from Agave Americana. *Dermatology.* 1998;196:408–11.
6. Ricks MR, Vogel PS, Elston DM, Hivnor C. Purpuric agave dermatitis. *J Am Acad Dermatol.* 1999;40:356–8.
7. Salinas ML, Ogura T, Soffchi L. Irritant contact dermatitis caused by needle-like calcium oxalate crystals, raphides, in Agave tequilana among workers in tequila distilleries and agave plantations. *Contact Dermatitis.* 2001;44:94–6.
8. High WA. Agave contact dermatitis. *Am J Contact Dermat.* 2003;14:213–4.
9. Quirce S, Fernández-Nieto M, Pastor C, Sastre B, Sastre J. Occupational asthma due to tampico fiber from agave leaves. *Arerugi.* 2008;63:943–5.
10. Buhl R, Bals R, Baur X, Berdel D, Criée CP, Gappa M, et al. S2k-Leitlinie zur Diagnostik und Therapie von Patienten mit Asthma. 2017. https://www.awmf.org/uploads/tx_szleitlinien/020-009l_S2k_Asthma_Diagnostik_Therapie_2017-11_1.pdf.
11. Deutsche Gesetzliche Unfallversicherung (DGUV), editor. Reichenhaller Empfehlung. Empfehlung für die Begutachtung der Berufskrankheiten der Nummern 1315 (ohne Alveolitis), 4301 und 4302 der Anlage zur Berufskrankheiten-Verordnung (BKV). 2012. <http://publikationen.dguv.de/dguv/pdf/10002/reichenhallneu.pdf>.