

Extrinsic allergic alveolitis due to inhaled molds in occupational onion and potato processing: onion- and potato-sorter alveolitis

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Key words

extrinsic allergic alveolitis – hypersensitivity pneumonitis – mold allergy – occupational disease – interstitial lung disease – pulmonary fibrosis – IgG antibodies

Abstract

Background: Only one case of occupational extrinsic allergic alveolitis due to mold inhaled during the sorting and transportation of onions and potatoes has been described in the literature to date. While having been exposed for one year the disease had healed up completely. *Penicillium* and *Fusarium* molds could be identified as cause of the extrinsic allergic alveolitis. We observed the second such patient albeit with more pronounced symptoms. We describe the patient's severe symptoms as well as his broader range of antibodies.

Methods: Assessment of comprehensive documentation as part of the medical examination, interview of former attending physicians, and additional IgG antibody investigations by ELISA and CAP-FEIA technique in order to detect more than the thus far known antigens.

Results: A 53-year-old male non-smoker of German descent, who had worked in the sorting and transportation business of onions and potatoes for more than 20 years was diagnosed with an occupational extrinsic allergic alveolitis. Possible triggers are the molds *Penicillium chrysogenum*, *Aspergillus fumigatus*, *Fusarium proliferatum*, and *Cladosporium herbarum*—against all of which IgG antibodies were

detected in the patient's serum. After antigen avoidance symptoms improved. Interstitial lesions visible on X-ray, a significant diffusion impairment, and a pulmonary hypertension have persisted, though. The disease was accepted as a occupational disease.

Conclusions: Sorting onions and potatoes not only can elicit moderate symptoms of an allergic alveolitis that heal without consequences, but can also lead to irreversible lung fibrosis associated with pulmonary hypertension. According to our findings, in addition to *Penicillium*, *Fusarium*, and *Aspergillus* molds *Cladosporium herbarum* is a possible antigen, too. Thus, this type of extrinsic allergic alveolitis is a serious notifiable occupational disease.

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Background

Only one case of occupational extrinsic allergic alveolitis (EAA, or hypersensitivity pneumonitis) due to mold inhaled during the sorting and transportation of onions and potatoes has been described in the literature to date. In 2008, Germany-based Merget and co-workers described a 42-year-old female of Tamil origin with extrinsic allergic alveolitis due to *Penicillium* and *Fusarium* molds [1].

Case report

We observed the same clinical picture in a 53-year-old male of German descent exhibiting an allergic reaction to the same occupational activity, also in Germany, with the same (albeit more pronounced) symptoms to an almost identical range of antigens.

Personal patient history

The patient reported that he had never been a smoker. He had suffered multiple fractures due to an accident 14 years previously. He had been affected by recurrent respiratory infections. In addition, he had undergone paranasal sinus surgery 10 years previously and had also developed a pollen allergy of the upper airways 2 years previously. According to the patient's medical record, skin prick testing to grass pollen had been equivocally positive. Furthermore, he reported living in normal housing conditions with no indication of exposure to domestic mold. He also had not contact with animals.

In the 6 months prior to diagnosis, the patient had been affected by a chronic cough with sputum production, exertional dyspnea, chest pains, and shivering at night. Treatment with initially 20 mg prednisolone daily resulted in symptom improvement and prompted suspicion of occupational EAA. This suspicion was further supported by the patient's occupational history.

Occupational patient history

The 53-year-old patient, who lived and worked in southern Germany, had completed an apprenticeship as a bricklayer in his youth. He had then worked as a security guard and, as such, had not been exposed to allergens. This was followed by a 1.5-year period as a production assistant in the potato industry. He subsequently worked as a production assistant in the sorting and transportation of onions and potatoes. More specifically, his activities included operating equipment to clean, cut (strip and peel), and pack (the cut) onions. As part of these activities, he was often also required to climb into machinery for cleaning purposes. This resulted in particularly high dust exposure. **Fig. 1** shows an example of this type of machinery. The patient was also exposed to



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Fig. 1: The patient was subject to particularly high exposure to mold dust when cleaning the onion peeling machine.

dust when driving forklift trucks. He had also been employed in the potato goods-in-and-goods-out department, where dusty conditions prevailed.

Clinical findings

Rales were detected at two initial examinations in the lungs. The other clinical findings were normal.

Radiography: Dorso-ventral chest X-ray showed a reticulonodular pattern throughout the lungs. CT revealed generalized ground-glass opacities and nodules, hilar lymph nodes, and localized fibrosis of the right upper lobe. Ground-glass opacities and lymph nodes regressed in the further course under allergen avoidance and systemic corticosteroid therapy, while fibrosis persisted.

Laboratory investigations: Laboratory values revealed a slightly elevated C-reactive protein (CRP) level (5.7 mg/l). Immunoglobulin A, E, G, and M levels were in the normal range. The same applied to the interleukin-2 receptor level. Antinuclear antibody testing was negative. Tracheal aspirate was negative for acid-fast bacilli. Nucleic acid amplification testing for the *Mycobacterium tuberculosis* complex was also negative. Legionella bacteria were not isolated on culture.

ECG: The echocardiogram (ECG) was normal, with the exception of an incomplete right bundle branch block.

Cardiac ultrasound: Ultrasound revealed stage-1 tricuspid valve insufficiency, as well as mild pulmonary hypertension (systolic pulmonary artery pressure [sPAP] of 30 mmHg).

Lung function and blood gases: Lung function and blood gas analysis yielded the following findings: At 76 % of the normal value, vital capacity was mildly impaired. No obstruction was present. Methacholine challenge testing was normal, consistent with undetectable bronchial hyperresponsiveness under corticosteroid therapy (1 mg/day) at the time of testing. Recurrent severe partial respiratory insufficiency (pO₂ values in the range of 63 mmHg) was seen. Diffusing capacity for carbon monoxide (CO) was markedly impaired (DLCOc SB at 31 % of the normal value).

Immunology: The initial investigation detected a high level of serum IgG antibodies to *Aspergillus fumigatus* and *Cladosporium herbarum* (> 200 mgA/l) using the Phadia ImmunoCAP® system (Sennekamp laboratory, Bonn, Germany). After 10-month allergen avoidance, *Aspergillus fumigatus* had dropped to 184 mgA/l (normal, < 64 mgA/l) [2] (**Tab. 1**). In addition, strongly positive IgG antibodies in blood to *Penicillium chrysogenum* (169 mgA/l; normal, < 64 mgA/l), weakly positive antibodies to *Fusari-*

um proliferans (62 mgA/l; normal, < 46 mgA/l), and equivocally positive IgG antibodies to *Absidia corymbifera* and *Mucor racemosus* were found. At the same time, no IgG antibodies to the farmer's lung antigen, *Saccharopolyspora rectivirgula*, or to the *Bacillus subtilis*, found in soil, were detected [3].

Allergy testing on the skin: Under medication (1 mg prednisolone/day), intradermal testing (allergens from Allergopharma®, Merck) showed a moderately positive reaction (++) to *Aspergillus fumigatus*, a weakly positive reaction (+) to *Penicillium notatum*, and an equivocally positive reaction (±) to *Alternaria tenuis*. Skin prick testing (allergens from Allergopharma®, Merck) yielded an equivocally positive reaction (±) to potato. Due to the lack of an allergen extract, it was not possible to test onion. A weakly positive reaction (+) was induced with pollen from trees, grasses, cereal, and herbs. However, no skin reaction was seen to dog, cat, or horse dander, or to the house dust mites *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*.

Measurements in the workplace: In order to determine actual dust exposure, measurements were conducted at the workplace. These yielded a value of 8.1 mg/m³ (normal, < 10 mg/m³) for respirable

Tab. 1: The patient's serum IgG antibodies (mgA/l) over time

Date	25.09.2013	15.05.2014	26.09.2014
<i>Aspergillus fumigatus</i>	> 200 (+++)*	177 (+++)*	184 (+++)*
<i>Penicillium chrysogenum</i>			169 (+++)*
<i>Cladosporium herbarum</i>	> 200 (+++)*	99 (+)*	
<i>Fusarium proliferans</i>			62 (+)*
<i>Aureobasidium pullulans</i>		32 (+)*	
<i>Mucor racemosus</i>		Negative*	13 (+)*
<i>Penicillium casei</i>			(+)**
<i>Absidia corymbifera</i>			(+)**
<i>Sporobolomyces</i>		Negative*	
<i>Thermoactinomyces vulgaris</i>		Negative*	
<i>Saccharopolyspora rectivirgula</i>		Negative*	Negative*
<i>Bacillus subtilis</i>			Negative**

*Antibody analysis using the quantitative ImmunoCAP® system by Phadia/Thermo Fisher Scientific

**Antibody analysis using semi-quantitative ELISA, hence no numerical data

dust. However, this exposure to respirable dust was considered elevated, since the onion sorting machine had been out of operation for 2 h on the day of measurement. Analysis of workplace air yielded a value (derived from three measurements) of 10,391,534 colony-forming units per cubic meter (CFU/m³). For the purposes of comparison: local outdoor air measured 1,314 CFU/m³. The endotoxin concentration in workplace air was 2.381 endotoxin units per cubic meter (EU/m³) compared with 1.370 EU/m³ in local outdoor air. On balance, values measured by the medical service ("Medizinischer Dienst", MTD) were rated as markedly elevated in terms of both molds and endotoxins.

Diagnosis

The diagnosis was ultimately established on the basis of the diagnostic criteria of EAA in **Tab. 2**. The following relevant diagnostic criteria were fulfilled: Antigen contact and inhalation exposure to mold documented to be elevated; exposure-related symptoms; IgG antibodies in serum; rales; typical radiological findings; marked diffusion impairment; as well as improvement of multiple symptoms under avoidance. These corresponded to the six diagnostic criteria required for the diagnosis of extrinsic allergic alveolitis [4]. The diagnosis was further confirmed by positive skin tests to *Aspergillus fumigatus* and *Penicillium notatum* [5, 6], as well as restrictive lung function impairment and pulmonary hypertension [6].

Treatment

The patient was initially treated with 20 mg prednisolone/day, followed by a stepwise reduction to 1 mg prednisolone. Long-term oxygen therapy (2 l oxygen/min) was also administered. Although the patient wished to resume work for financial reasons, it was possible to impress upon him that allergen avoidance was strictly required.

Discussion

Plant allergens in onion and potato are capable of eliciting IgE-mediated allergies. In general, it is extremely rare for plant allergens to induce extrinsic allergic alveolitis. Fine particulate wood, cereal, or soy dust can be involved. This accumulates or is created during wood processing or when flour is obtained from cereal grains or soybeans. During onion and potato processing, however, no fine plant particles are produced, hence nor is respirable dust. Thus, the skin prick test that was only equivocally positive to potato cannot be interpreted as an indication of either an IgE- or an IgG-mediated allergy. Unfortunately, it was not possible to perform skin prick tests for onion in this patient. However, as shown by the bacterial count at the patient's work-

Tab. 2: The German diagnostic criteria for extrinsic allergic alveolitis (EAA) [4]

1. Antigen exposure
2. Exposure- and/or time-dependent symptoms
3. End-inspiratory crepitations (crackles)
4. Specific serum IgG antibodies
5. Radiological signs of EAA, possibly on HRCT
6. Reduced pO₂ at rest and/or during physical exertion or impaired DLCO

The diagnosis of EAA is made if all six criteria are met. If one of the above-mentioned criteria is not met, it can be replaced by one of the following:

- Lymphocytosis in BAL fluid
- Histopathological findings in the lung consistent with EAA
- Positive avoidance test
- Positive inhalation exposure or challenge testing

EAA is diagnosed if a total of six criteria are met

HRCT, high-resolution computed tomography; pO₂, oxygen partial pressure; DLCO, carbon monoxide diffusing capacity; BAL, bronchoalveolar lavage

place, mold mycelia in and on onions, potatoes, and the soil coating them release large quantities of respirable spores.

The molds *Fusarium solani*, two *Penicillium* species, *Aspergillus niger*, *Rhizopus oryzae*, and the yeast fungus *Candida guilliermondii* – but not *Aspergillus fumigatus* – were isolated at the similarly configured workplace of the aforementioned female patient presenting with this clinical picture [1]. IgG antibodies in patient serum were only against the *Penicillium* species and *Fusarium solani*, not against the other pathogens detected. Merget and coworkers also found antibodies against *Aspergillus fumigatus*. By means of inhibition tests, the authors were able to show immunological cross-reactivity between *Aspergillus fumigatus* and the *Penicillium* species, as already observed by earlier investigators [7]. Thus, only the fungal species *Penicillium* and *Fusarium* were relevant.

Cladosporium antibodies were not determined in that particular investigation. In our opinion, this requires reconsideration. Firstly, the mold *Cladosporium* is widely found both in- and outdoors. Furthermore, we determined an extremely high antibody titer in our patient (**Tab. 1**). Finally, in their study, Watanuki et al. [8] found an increased prevalence of IgG antibody to *Cladosporium* in interstitial lung disease. Therefore, greater attention than hitherto should be paid to this inhalation challenge-proven antigen in allergic alveolitis.

In our patient, it was only possible to establish that he had inhaled large volumes of mold-containing dust, without the molds being further differentiated. It is likely that our patient was also exposed to *Penicillium* and *Fusarium*, since he exhibited antibodies to these species. In addition, he reacted to *Cladosporium herbarum* – the mold known for its occurrence outdoors in large amounts. We are unable to judge whether our patient's test reaction to *Aspergillus fumigatus* was due to inhalative contact with this pathogen or whether the reaction was caused by cross-reacting *Penicillium* antibodies. As with our patient, the female patient initially described also showed no IgG antibodies to *Saccharopolyspora rectivirgula*, nor did she exhibit a reaction to *Thermoactinomyces vulgaris* [1].

Thus, according to the current state of knowledge, the antigens *Penicillium chrysogenum* and *Fusarium solani* or *Fusarium proliferans* are primarily of relevance. The role of antibodies detected to *Aspergillus fumigatus* and *Cladosporium herbarum* remains unclear in this clinical picture. However, the reduction in antibody levels for *Aspergillus fumigatus* and *Cladosporium herbarum* between 25.09.2013 and 15.05.2014 (see **Tab. 1**) points to reduced mold exposure in this time period. The patient had already ceased work during that particular period.

The high endotoxin levels in the workplace suggested the presence of organic dust toxic syndrome (ODTS) besides EAA. However, in contrast to EAA, ODTS does not result in long-term radiological lung changes and causes no diffusion impairment, as was the case here [6, 9].

Ultimately, EAA left lasting effects on the patient presented here. Indeed, the lesions visible on X-ray have not resolved to date. Furthermore, the patient still exhibits significant, persistent diffusion impairment and right strain load in the form of tricuspid valve insufficiency and elevated pulmonary pressure. Thus, our patient represents a case following a severe, fibrotic course, in contrast to the female patient initially described, whose symptoms resolved completely [1]. Having said that, our patient had been subject to exposure for a period of over 20 years, whereas the first patient had been performing her work activities for less than 1 year [1].

EAA in our patient was unequivocally attributed to occupational contact with inhaled antigens, thereby qualifying it in Germany as the occupational disease „extrinsic allergic alveolitis“ according to occupational disease number 4201, which is associated with a reduced capacity to work [2, 10].

Antigen avoidance is the most important therapeutic measure [6, 11]. With regard to the ubiqui-

tous molds *Penicillium*, *Fusarium*, and *Cladosporium*, it is important to be bear in mind that not only disease-causing exposure in the workplace needs to be avoided; rather, exposure through molds found in pot plants, aquariums, bird dust, compost, and similar sources of spread need to be minimized as far as possible. Whether a patient is effectively avoiding antigens, and hence the cause of disease, can be deduced from declining antibody concentrations. We were able to show this for our patient with regard to *Aspergillus* and *Cladosporium* (**Tab. 1**). We have therefore made our recommendation to the employer's liability insurance association that the patient has to be monitored regularly for these antigens.

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Conflict of interests

The authors state that there are no conflicts of interest.

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References

1. Merget R, Sander I, Rozynek P, Raulf-Heimsoth M, Bruenig T. Occupational hypersensitivity pneumonitis due to molds in an onion and potato sorter. *Am J Ind Med* 2008;51:117-19
2. Sennekamp J, Lehmann E, Joest M. Berufsbedingte exogen-allergische Alveolitis. *ASU Arbeitsmed Sozialmed Umweltmed* 2015;50:38-52
3. Schulte W, Sennekamp J. Allergische Alveolitis durch *Bacillus subtilis* in einem biologischen Reinigungsmittel – Diagnostik und Krankheitsverlauf. *Allergologie* 2010;33:570-2
4. Sennekamp J, Müller-Wening D, Amthor M et al. [Arbeitsgemeinschaft exogen-allergische Alveolitis]. Empfehlungen zur Diagnostik der exogen-allergischen Alveolitis. *Pneumologie* 2007;61:52-6
5. Morell F, Currull V, Orriols R, De Garcia J. Skin tests in bird breeder's disease. *Thorax* 1986;41:538-41
6. Sennekamp J. Extrinsic allergic alveolitis – hypersensitivity pneumonitis. Monographie. München – Orlando: Dustri 2004
7. Brouwer J. Cross-reactivity between *Aspergillus fumigatus* and *Penicillium*. *Int Arch Allergy Immunol* 1996;110:166-73
8. Watanuki Z, Okada S, Chiba S et al. Increased prevalence of high anti-*Cladosporium* antibody titers in interstitial lung diseases. *Tohoku J Exp Med* 2012;226:287-91

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9. Sennekamp J. ODTS – Toxische Alveolitis organischer Stäube. In: Letzel S, Nowak D, eds. Handbuch der Arbeitsmedizin. Landsberg:Ecomed 2008;D I-3.3.2: 1-18
 10. Baur X. Exogen-allergische Alveolitis als Berufskrankheit. Zbl Arbeitsmed 1996;46:438-42
 11. Koschel D. Prävention der exogen-allergischen Alveolitis. Atemwegs Lungenkrkh 2008;34:182-86