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DOI: 10.2478/rjom-2018-0004

Case Reports

Extrinsic allergic alveolitis induced by spores of Penicillium in a salami factory worker

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Abstract

We report a case of subacute extrinsic allergic alveolitis due to occupational exposure to Penicillium spores in a 43-years old female working in a salami factory that developed a dry cough that gradually evolved to productive cough, shortness of breath, fatigue and body weight loss. Over time she complained of several episodes of flu-like symptoms that worsen around the periods in which she removed the excess mould from the surface of the salami a work. On admission, physical examination revealed crackles in both lungs on chest auscultation, pulmonary function tests showed a restrictive pattern with reduced diffusion capacity of carbon monoxide and imagistic tests identified centrilobular nodules of ground-glass opacity in both lung fields, particularly in the upper lobes. BAL showed lymphocytosis associated with neutrophilia, a pattern consistent with EAA. She was put on systemic corticosteroids and ceased exposure. The patient was compliant and after one year her medication was gradually withdrawn and in the absence of exposure, symptoms and pulmonary function normalized. The reported case had a favorable outcome due to relatively early detection and absence of exposure. Currently, the identification and removal of the causative agent remains the cornerstone of prevention, evolution and prognosis.

Keywords: *extrinsic allergic alveolitis, occupational disease, Penicillium nalgiovensis, salami worker's lung*

Introduction

Extrinsic allergic alveolitis (EAA), also known as hypersensitivity pneumonitis is a complex entity characterized by lung inflammation due to repeated inhalation and sensitization to numerous organic and inorganic particles that affect the distal airways and alter gas exchange [1]. EAA varies in clinical presentation, evolution and prognostic and for this reasons, it continues to be a diagnostic challenge for any clinician. A good understanding of its etiology is required to establish effective treatment. Currently, the identification and removal of the causative agent remains the cornerstone of prevention, evolution and prognosis. It was established that EAA prognosis may be improved if the antigen is early identified [2] and cessation of exposure occurs before fibrotic changes appear [3]. For this reason, determining the cause may increase the possibility of an early diagnosis and a favorable evolution of the disease. We report a case of subacute AAE due to occupational exposure to mould spores in a salami factory.

Case report

A 43-year-old female was admitted to our clinic with eight months' history of dry cough that gradually evolved to productive cough, shortness of breath, fatigue and a four kg body weight loss over the previous months. The cough and dyspnoea persisted despite repeated treatment with antihistamines and antibiotics prescribed by her general physician at local outpatient clinic. She was a non-smoker, from an urban setting with no atopic background or history of respiratory problems. Her personal and family history was unremarkable and denied taking any medication on admission. She had no previous exposure to animals, birds or mouldy environment at home. She worked in the food industry for 26 years at the same workplace, where she was involved in the production of dry salami. The patient's workplace activities involved hanging the salami sticks, spraying them with the mould solution and removing the excess mold from the products. She did these tasks five days a week for eight hours a day and did not use any respiratory protection. The task of brushing the mould was done periodically, whenever the products were ready for this phase of the process.

Notably, in the last 3 years she had flu-like symptoms that worsen around the days she carried out the task of brushing the mould from the salami surface.

When presenting to our clinic, physical examination revealed no fever, BMI=24.3 kg/m2, normal respiratory rate, pulse oximetry 96% on room air, thoracic kyphosis, fine crackles in the lung apex and decrease of vesicular murmur on chest auscultation. Blood tests revealed a non-specific inflammatory syndrome, with no other abnormalities. Pulmonary function tests showed a mild restrictive pattern with VC= 2.27% (71% reference) and reduced diffusion capacity of carbon monoxide (65% reference). The chest X-ray revealed bilateral reticulonodular opacities (figure 1). The chest computed tomography scan showed centrilobular nodules of ground-glass opacity in both lung fields, particularly in the upper lobes (figure 2), which was consistent with EAA. Bronchoscopy with bronchoalveolar lavage (BAL) was performed. Exploration of the tracheobronchial tree using the fiberoptic bronchoscope revealed a normal larynx, no active lesions. Bronchoalveolar lavage was performed in the middle lobar region and showed macrophages 36.2%, lymphocytes 56.6% of which the ratio of CD4 and CD8 was <1, neutrophils 3.8%, eosinophils 1.8%, mast cells 2.4%, plasmocytes 1.2% and granulocytes 3.6%. Post-bronchoscopy sputum smear had no evidence of bacillus resistant acid or other pathogens. Bronchial aspiration identified mucus, altered bronchial epithelial, frequent lymphocytes and neutrophils. Cellular and immunocytologic characteristics of BAL fluid advocated for EAA.

In this case, the diagnosis of EAA was based on occupational history (exposure to Penicillium spores), physical examination, imaging tests and bronchoalveolar lavage. We started treatment with 32 mg oral methylprednisolone daily and advised her to avoid exposure to the antigen and change her occupation. The patient complied with the recommendation. Her follow-up visits post-diagnosis were conducted at one month, six months and every one year and included respiratory function tests and imaging tests. After one month, although not entirely resolved, her symptoms have significantly improved with medication and transfer factor for carbon monoxide showed an increase to 70% predicted. At her 1 year follow-up, her symptoms had resolved, CT scan showed an improvement (figure 3) of centrilobular ground-glass nodules pattern and her medication was gradually reduced in dosage before stopping with the medication completely. The patient's symptoms and pulmonary function normalized over time. Now, after 7 years post-diagnosis, she resumed her professional activity in another workplace with no exposure to respiratory allergens or irritants.

Discussion

The clinical history and pathology of this patient supports the subacute EAA diagnosis that is usually difficult to identify because it is most often based on a non-specific clinical picture requiring evidence of interstitial imaging signs, the presence of lymphocytic alveolitis in BAL fluid or a granulomatous reaction found on pulmonary biopsy [4]. Similar cases due to occupational exposure to mould spores in salami factories have also been reported in the literature [5-9].

Salami is a type of cured sausage made from minced beef of pork, mixed with spices, fermented and dried properly. The manufacturing process of salami consists of four main stages: preparation, curing, fermentation and drying. The preparation involves the mincing and mixing of the raw meat with other ingredients such as salt, sugar, spices and yeast. Then, the resulting mixture is filled into natural or collagen casings and hung up in order to cure. The maturation includes the last three stages and it is the process in which biochemical transformations occur conditioned by certain parameters of humidity, temperature and air circulation and may last 3 to 6 months. At the

beginning of this period, the products are treated with a mold culture of Penicillium nalgiovensis and a mixture of different types of Penicillium that promotes the drying process, flavor and prevents spoilage. This procedure is done using a solution containing the mould that is sprayed on the surface of the salami.

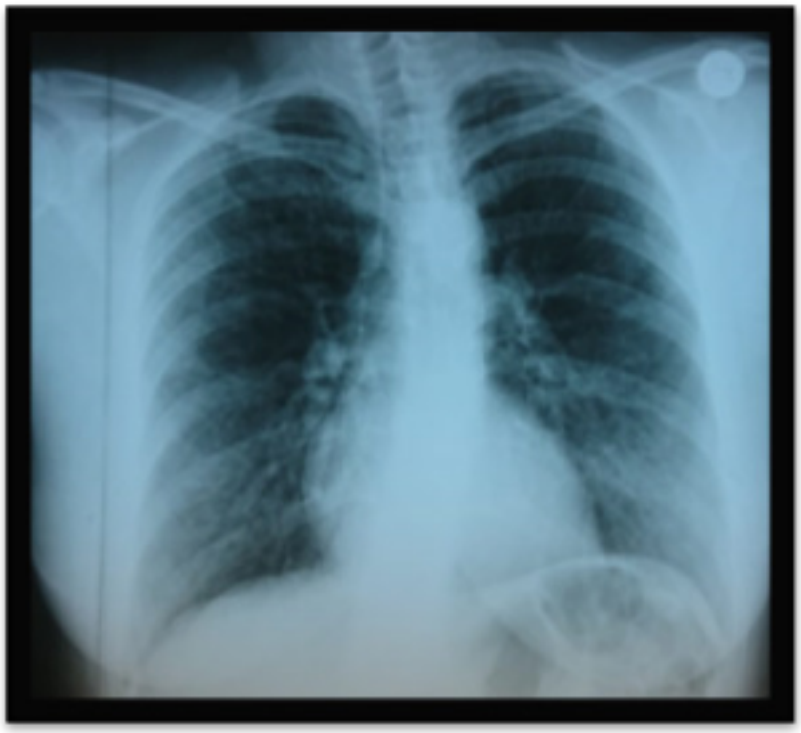

Figure 1.

Chest X-ray on admission: bilateral reticulonodular opacities.

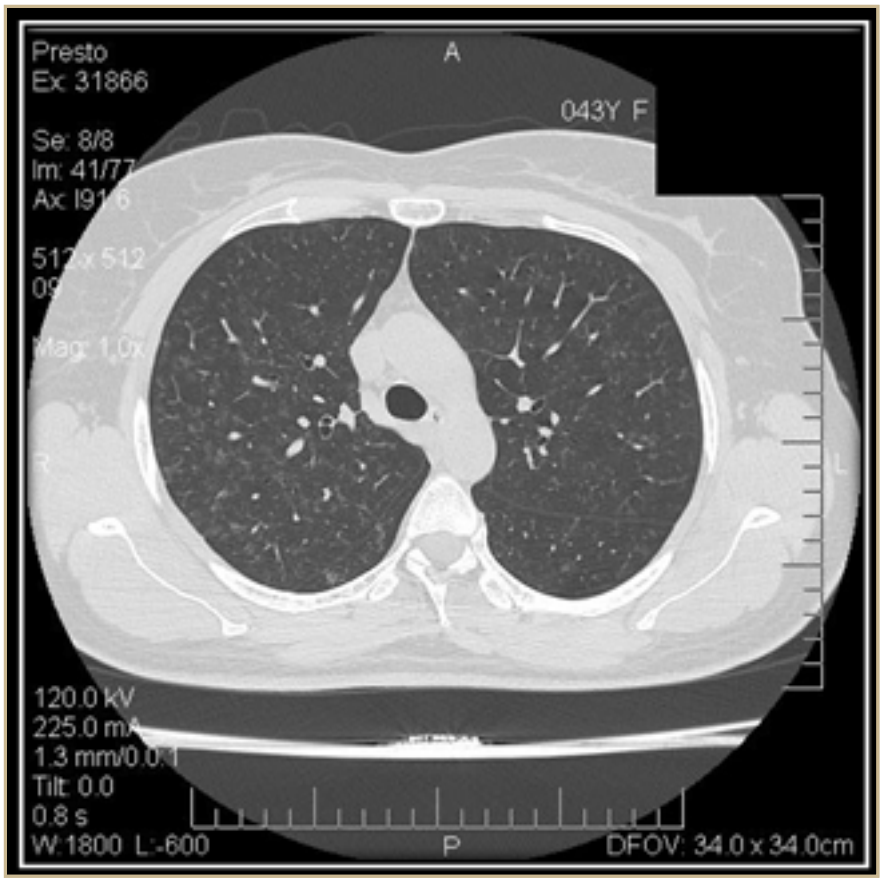

Figure 2.

CT scan on admission: centrilobular nodules of ground-glass opacity in both lungs, particularly in the upper lobes.

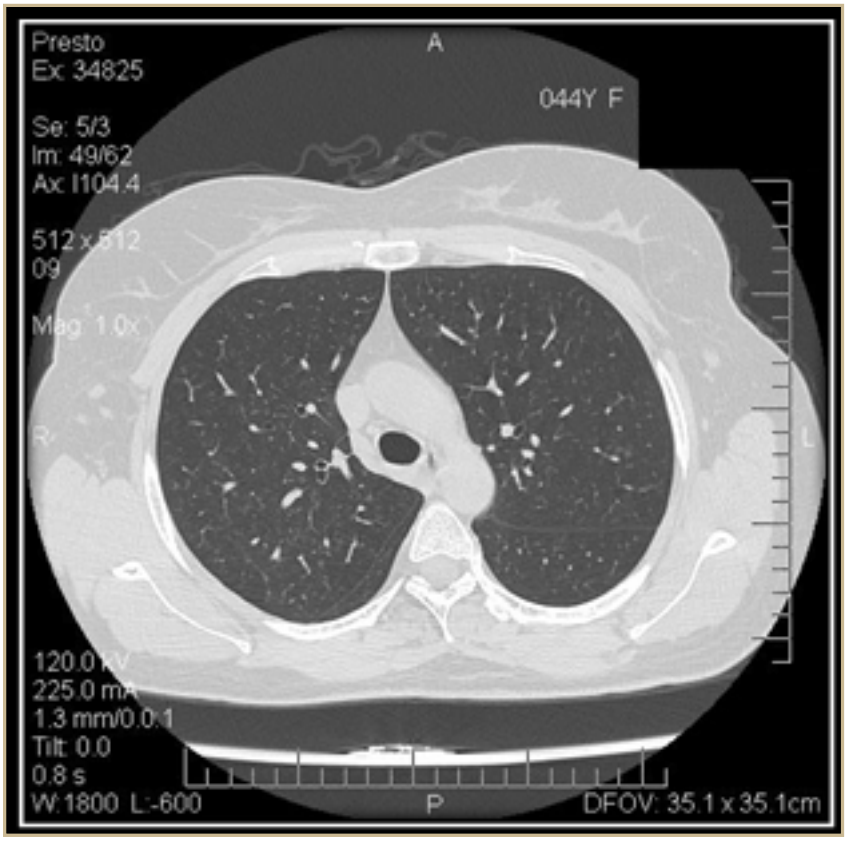

Figure 3.

CT scan: improvement of centrilobular ground-glass nodules pattern at 6 month follow-up.

This procedure is done using a solution containing the mould that is sprayed on the surface of the salami. After a month, when the products are entirely covered with mold, it is removed manually by brushing the surface with a wire tool. The products are then left to dry further in a controlled environment.

The exposure to these bioaerosols may also cause bronchial asthma [10], contact dermatitis [11,12] and contact urticaria [13]. Other sources of exposure have be found in other natural or anthropogenic activities, especially from agriculture, textile industries, biotechnology, research laboratories, medical units, waste disposals other food processing industries. EAA is frequently unrecognized and misdiagnosed as respiratory infection, asthma, COPD or idiopathic pulmonary fibrosis [14] due to the small number of cases reported in general population and variety of clinical presentation and course. This was also the case of the reported patient, who was initially treated with antibiotics and antihistamines for several months before the causative agent was suspected.

Depending on the duration, intensity, frequency and sensitization of exposure, EAA may present as acute, subacute (intermittent) or chronic form. Although there are cases where symptoms occur only a few weeks after exposure, most cases of EAA develop after months or years. The acute form occurs in hours or days after exposure and involves an intermittent or short-term exposure. In this case, symptoms include fever, cough, dyspnoea, asthenia and may persist as long as there is exposure to the causative agent or may improve upon cessation of exposure. At continuous low grade or intermittent exposure, symptoms gradually evolve to productive cough, dyspnea, anorexia and weight loss (subacute form) [1,14]. Unrecognizing these episodes enables the disease to evolve to the chronic form that is associated with unfavorable prognosis [15]. In our case, the patient had a prolonged, but intermittent exposure to the antigens because the brushing task was not always performed daily, but only when the technological process required it. This means a long latency period of years between the first moment of exposure and the onset of symptoms; it seems that the acute episodes have been misinterpreted as recurrent respiratory infections. In EAA, imagistic findings reveal ground-glass infiltrates and nodular opacities in acute/subacute phase and fibrosis and honeycombing pattern in the chronic form [16]. Lung function tests show a restrictive ventilatory pattern and impaired gas exchange, especially in the advanced forms of EAA [17]. These findings were seen in our patient as well. In EAA, BAL fluid may show the presence of a large number of lymphocytes, more

than 25% suggesting a granulomatous pathology such as EAA or sarcoidosis. A lymphocyte count greater than 50% associated with neutrophilia greater than 3% is highly suggestive of EAA [17]. In the present report, we could differentiate EAA from sarcoidosis based on BAL fluid findings and normal levels of angiotensin converting enzyme. After requiring systemic corticosteroid therapy for several months, the patient had a favorable outcome due to relatively early detection and absence of exposure. increased risk of developing asthma as well [18].

Conclusions

EAA is preponderantly an occupational disease [17], therefore occupational physicians must know the sources of exposure from the workplace and make the necessary recommendations for prevention and control. Also, reporting and registering occupational EAA is essential in order to understand the size of the problem caused by this disease, to facilitate preventive policy in order to plan intervention programs, resource allocation and to help workers benefit from compensation and treatment. EAA is a cause of work disability and decreased productivity with economic and social impact, both for the worker and society. As such, we need to recognize the risk, identify the risk factors using a thorough investigation, recommend and implement appropriate preventive measures.

An integrated approach is needed, involving a multidisciplinary collaboration among the specialties dealing with this pathology, with the aim of early detection and improvement of patients' quality of life.

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