Hypersensitivity pneumonitis induced by Shiitake mushroom spores

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Hypersensitivity pneumonitis (HP) is a pulmonary granulomatosis involving an immunoullergic mechanism caused by chronic inhalation of antigens, most frequently organic substances, as well as chemicals. We report the first European case of hypersensitivity pneumonitis due to the inhalation of Shiitake mushroom spores. A 37-year-old French Caucasian man with a one-month history of persistent dry cough, shortness of breath and loss of weight was admitted to our hospital on December 2010. Anamnesis showed he was involved in mushroom production beginning in the summer of 2010. His temperature on admission was 36.6°C and he had a normal blood pressure (135/90 mmHg). Bilateral fine crackles were audible in the base of both lungs. Pulmonary function tests showed a mild restrictive pattern with decreased DLco and a PaO₂ of 65 mmHg. Chest CT scan revealed reticulonodular shadows, slight ground glass opacities, linear atelectasis, and subpleural opacities in both lung fields. Bronchoscopy was normal but cytological examination of BAL revealed a predominant lymphocytosis (55%). Serum precipitins to the Shiitake mushroom spores were positive (3 precipitins arcs with high intensity) and as a result we advised the patient to cease his mushroom production activities. The diagnosis of hypersensitivity pneumonitis due to inhalation of Shiitake mushroom spores was established as a result of the improvement of all of his clinical symptoms, i.e., cough, weight loss, bilateral fine crackles, mild restrictive pattern of pulmonary function, and reticulo-nodular shadows on chest CT, once exposure was eliminated. Recent interest in exotic mushrooms varieties, e.g., Shiitake, in developed countries because of their possible medicinal properties might increase the potential risk of HP among mushrooms workers. Therefore, healthcare professionals have to take this new potential respiratory disease into account.

Keywords mushroom, Shiitake, hypersensitivity pneumonitis, serodiagnosis

Introduction

Hypersensitivity pneumonitis (HP) is a pulmonary granulomatosis with an immunoullergic mechanism caused by chronic inhalation of antigens, more often of organic substances but occasionally due to chemicals. Acute and subacute HPs represent the most active forms of the disease, but it may become chronic. New antigens are
Case report

A 37-year-old French Caucasian man with a one-month history of persistent dry cough, shortness of breath and loss of weight was admitted to our hospital in December 2010. In addition to his primary occupation as a market gardener, he had been engaged, for the first time, in the production of mushrooms since the late summer of 2010. Since the harvest of the crops of Shiitake and Pleurotus spp. in November 2010, he reported shortness of breath, illness, and later on, a dry cough with fever. In spite of a small improvement after a general practitioner’s treatment (amoxicillin, 2 g/day), he complained of recurring chest pain and worsened dyspnea. On admission, his height was 183 cm and he weighted 79 kg, but he had lost 3 kg since his mushroom harvest. He noted, as part of his history, that he had smoked 11 packs of cigarettes/year. His temperature was 36.6°C, blood pressure of 135/90 mmHg, a pulse rate at 95 beats per minute, and a respiration rate of 20 cycles per min. Bilateral fine crackles were audible in the base of both lungs. Measurement of arterial blood gas levels while breathing room air indicated a PaO₂ of 65 mmHg, a PaCO₂ of 34 mmHg, and a pH of 7.46. Complete blood cell count revealed an elevated white cell count of 12.6x10⁹ (reference ranges from 3.5–10.5x10⁹), without hyper-eosinophilia and anemia. C-reactive protein was slightly positive and activated white cell count of 12.6x10⁹ (reference ranges 10³–10⁵/ml) with predominant lymphocytosis (55%), 24% macrophages, 20.5% polynuclear neutrophils, and 0.5% eosinophils polynuclear. The CD4/CD8 ratio of lymphocyte surface markers in the BAL fluid was 0.5 and microbiologic studies of the BAL were negative.

Precipitins against Shiitake mushrooms were detected (three precipitins arcs with high intensity), associated with precipitins against Alternaria spp. and Pleurotus spp. (one precipitin arc) (Fig. 2). Patient serological reactions were analyzed using the agar gel double-diffusion method (Ouchterlony method), and sterile in-house extracts. Briefly, Shiitake mushrooms, grown by the patient, were homogenized with glass beads to obtain powder, then mixed with 100 ml of distilled water under agitation for 48 h, followed by millipore filtration. The supernatant was dialyzed against deionized water and lyophilized Alternaria spp. and Pleurotus spp. stock antigens from the laboratory’s stock collection. The three antigens were dissolved in distilled water (200 mg/ml), allowed to stand at room temperature four 1 h, and placed in three cathodal wells in 25 μl quantities per antigen, while the patient’s serum (500 μl) was added to the anodal well (Fig. 2).

The patient was initially empirically treated with ciprofloxacin, 1 g/day for 7 days and since clinical, radiological, biological and functional parameters were found to be within normal ranges, he was discharged after 8 days. As advised, the patient stopped his mushroom production, and resumed more traditional cultivation of vegetables (carrots, potatoes and French beans). Although a new CT obtained two weeks after discharge showed no improvement of chest opacities, the patient described a dramatic improvement of respiratory symptoms. Six months later, all opacities have disappeared according to the control CT scan (Fig. 1). The pulmonary function tests, as well as biological parameters were normal and the patient has gained about 10 kg in weight (Table 1).

Discussion

Shiitake mushroom cultivation is one of the oldest in the history of human mushroom farming, such as in China and Japan where they have been grown since prehistoric times. The oldest record regarding the cultivation of Shiitake mushrooms dates back to AD 199 at the time of Emperor

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Chūai in Japan. Its name is related to the tree where it usually grows, i.e., *Castanopsis cuspidata*, which is named ‘shii’ in Japanese. Its commercial production in Western countries began in the 1980s (first in the USA, then in Europe, and more recently in Brazil and Russia). Shiitake has become the second most widely cultivated mushroom in the world with 140 kilo tons in 2002 [2].

However, to our knowledge, there has been only one suspected case of mushroom worker’s lung due to Shiitake in Europe [3]. The diagnosis of HP caused by inhalation of the mushroom spores was established in our case on the basis of all of the following criteria; respiratory compatible symptoms (dry cough, dyspnea, bilateral fine crackles, weight loss), antigenic exposure (anamnesis, serum precipitins to Shiitake), presence of an alveolar lymphocytosis in the BAL fluid, hypoxemia, slightly reduction of DLCO, radiologic elements (ground glass opacities, subpleural opacities, linear atelectasis, reticulonodular shadow). These criteria are considered to be significant for establishing the diagnosis of HP [4–7] and clinical improvement was achieved by removing the patient from exposure to the mushrooms [6].

The first cases of ‘mushroom-related respiratory disease’ were recorded in 1959 in the USA and a 20% incidence of HP among mushroom farm workers was reported in 1992 [8]. A three-year follow-up study of mushroom workers reported that; (i) more than 70% of the affected individuals had a chronic cough and other respiratory symptoms, (ii) more than 90% had positive rate of serum precipitins to the spore in the third year of study, (iii) 30% had to leave their jobs because of their symptoms, and (iv) 5% developed HP [9,10].

According to the literature, HP caused by Shiitake spores is not frequently described, but it is probably under-reported. About 20 cases of HP involving spores of different mushroom species have appeared in the literature, with 6 cases reportedly induced by Shiitake (*Lentinus edodes*) spores [6,7,11–14]. After reviewing these published cases, the interval between spore exposure and the beginning of symptoms seems to have been particularly brief in our patient (about 4 months) [6,7,11–14]. Cough and fever were described as occurring within three months, while the reported periods of sensitization range from 1 month to 13 years [10,15]. Despite a lack of information regarding HP natural history due to insufficient number of longitudinal studies [16], exposure to high level of causative antigen might explain acute or subacute clinical presentation [12]. Review of the CT scan revealed ground-glass opacities usually found with HP, but subpleural opacities are uncommon. These opacities are usually described as centrolobular nodules and represent focal irregular areas of organizing pneumoniae [17]. The clinical improvement of our patient after several months following his cessation of mushrooms cultivation (and consequently the end of antigen exposure) is another significant clinical element of HP diagnosis.
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Since organic dust toxic syndrome (ODTS) it is a form of inhalation fever quite similar to the less common acute HP, it would have been a reasonable diagnosis given the clinical history in the present case [18]. However, the temporal relationship between the development of symptoms, the radiological signs, and the existence of improvement upon cessation of mushroom exposure are more indicative of HP.

In conclusion, Shiitake spores are now recognized as an aetiological agent of mushroom workers’ lung [1,19]. Recent interest about handling exotic mushrooms varieties such as Shiitake in developed countries might increase the potential risk of HP among mushrooms workers. Healthcare professionals have therefore to take this new potential respiratory disease into account.

Acknowledgements

The authors thank Dr Cyrielle Jardin for English editing.

References


Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

This paper was first published online on Early Online on 6 February 2012.

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