Chronic Hypersensitivity Pneumonitis Induced by Shiitake Mushroom Spores Associated with Lung Cancer

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Abstract

A 61-year-old man was admitted to our hospital with a 6-month history of productive cough. He, along with his wife, had been involved with Shiitake mushroom cultures for a period of 12 years. On admission, chest radiography showed bilateral fine-nodular shadow and CT scans showed reticulonodular opacities and a ground-glass appearance predominantly in the subpleural area in both lungs, and a mass in the left S6. Resected pathological specimens obtained by left lower lobectomy revealed lung adenosquamous carcinoma (stage IB), interstitial changes accompanied with lymphocyte proliferation and fibrosis, and granuloma with giant cells. Serum precipitins for Shiitake mushroom antigens were positive. The productive cough improved after the hospital admission and occurred again when he returned to work with the Shiitake mushroom production. Therefore, chronic hypersensitivity pneumonitis (HP) caused by Shiitake mushroom spores was diagnosed. Moreover, his wife was found to have HP caused by mushrooms at this time. There are only two previous reports of chronic HP caused by Shiitake mushroom in Japan, and this is the first case of chronic HP associated with lung cancer.

Case Report

A 61-year-old non-smoking man who had suffered from a 6-month history of persistent productive cough was admitted to the hospital in December 1995. He had been engaged in Shiitake mushroom production in a large vinyl tent for 12 years together with his wife and for 4 years with his son. He was 164 cm tall and weighed 72 kg. On initial physical evaluation, bilateral fine crackles were audible in the base of both lungs at the back. No clubbing of fingers was noted. Laboratory findings were within normal limits except for positive C-reactive protein and elevated white blood cell counts. The measurement of arterial blood gas levels while breathing room air indicated a PaO2 of 61 Torr; serum cytokeratin 19 fragment (CYFRA) level was 4.5 ng/ml (cut off level, 2.8 ng/ml), and serum level of surfactant protein D was 118 ng/ml (cut off level, 110 ng/ml). The results of pulmonary function tests showed a reduction of vital capacity (VC) (73.4% of predicted) and a decrease in the diffusing capacity of the lung for carbon monoxide (DLCO; 78.7% of predicted). Chest roentgenogram revealed a fine-nodular shadow (Fig. 1) and CT scans showed reticulonodular opacities, a ground-glass appearance predominantly in the subpleural areas, and a mass about 3 cm in diameter in the left S6 (Fig. 2). Fiberoptic bronchoscopy was done and the cytologic specimen obtained by curretting revealed adenocarcinoma. He was found to have primary lung cancer of clinical T2N0M0, stage IB. Left lower lobectomy and mediastinal lymph node dissection were performed. The resected pathological specimen demonstrated lung adenosquamous carcinoma without lymph node metastasis, and furthermore interstitial fibrosis, alveolitis with lymphocytic infiltration, and granuloma with giant

Key words: mushroom worker’s lung, extrinsic allergic alveolitis, fibrosis, malignant tumor

Introduction

Hypersensitivity pneumonitis (HP) is an allergic immunoreaction induced pulmonary disease caused by inhalation of a variety of environmental agents (1). Recently, HP caused by inhalation of mushroom spores has been reported to be increasing (2–4). HP is divided into acute, subacute, and chronic forms on the basis of clinical features. The chronic type HP is further divided into two groups; repeated acute onset group and insidious onset group. The clinical features, radiological findings, pulmonary functions, and prognosis of the insidious onset type are very similar to those of idiopathic pulmonary fibrosis (IPF) (5). On the other hand, there has been no case report of insidious onset type HP following primary lung cancer. We describe a rare case of chronic HP induced by the Shiitake mushroom spores associated with lung cancer.

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Received for publication February 21, 2001; Accepted for publication July 2, 2001
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Internal Medicine Vol. 40, No. 11 (November 2001)
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Figure 1. Chest roentgenogram on admission shows a fine reticulonodular shadow.

Figure 2. Chest CT scans on admission show reticulonodular opacities, ground-glass appearance predominantly in subpleural areas, and a mass in the left S6 (arrow).

cells were disclosed (Figs. 3 and 4). Serum precipitins for the Shiitake mushroom spore antigens were positive, however, not for Microsporum faeni, Thermactinomyces vulgaris, Aspergillus fumigatus, or Aspergillus niger. The Shiitake antigens used were made originally. Spores of Shiitake mushroom were collected from the mushroom itself at the patient’s workplace under sterile conditions and were cultured in Sabouraud’s glucose broth, followed by protein extraction with 50%, 60% and 70% ammonium sulfate. The sample was centrifuged at 3,000 rotations/min for 15 minutes, and the pellet was dialyzed with distilled water. The stimulation index of lymphocyte proliferation in response to Shiitake mushroom antigens using peripheral blood was positive of 9.4 (positive >1.8). The productive cough improved after this admission and occurred again when he was discharged from the hospital and returned to work with Shiitake mushroom cultures. From these results, he was diagnosed as having chronic HP caused by the mushroom associated with subsequent lung cancer.

In December 1995, his 62-year-old non-smoking wife who was working in the same workplace, also visited our hospital because of a 9-month history of persistent low grade fever and productive cough. Her serum precipitins to Shiitake mushroom spores and lymphocyte proliferation test to the spore antigens using peripheral blood were positive. She was also diagnosed as HP induced by the Shiitake mushroom spores. And their 30-year-old smoking son who was working in the same circumstance, complained of a cough, also in December 1995. Serum precipitins to the Shiitake mushroom spores were positive, but
there were no abnormal findings radiologically. After these episodes, the family stopped working in the Shiitake mushroom factory and their HP symptoms gradually subsided following oral prednisolone therapy.

Discussion

We diagnosed this patient as having chronic HP caused by Shiitake mushroom spores according to the following criteria: 1) over 6 months duration of productive cough; 2) reticulonodular opacities and ground-glass appearance on CT scans that suggested interstitial change; 3) reduction in VC, DLco and arterial PaO2; 4) pathological evidence of lymphocytic alveolitis with fibrosis and granuloma with giant cells; 5) the presence of serum precipitins to Shiitake mushroom spores and lack of precipitins to Micropolyspora faeni, Thermoactinomyces vulgaris, Aspergillus fumigatus, or Aspergillus niger; 6) a positive result of lymphocyte proliferation in response to Shiitake mushroom antigens. There have been some cases in which mushrooms spores, for example Shimeji mushroom, Nameko mushroom, Oyster mushroom, Bunashimeji mushroom, and Shiitake mushroom, have been suggested to cause hypersensitivity pneumonitis among mushroom workers (2–4). In Japan, the edible Shiitake mushroom has been grown indoors for many years (2). Oak wood logs are used instead of usual compost or wood chips. The Shiitake mushrooms are grown on the surface of oak wood logs, in small closed buildings, kept at a suitable temperature and humidity. When the mushrooms are fully grown, the cultivating rooms are filled with the mushroom spores. The size of these oval spores is 4 to 8 μm. The spores of Nameko and Bunashimeji mushroom are 4 to 6 μm in size; the spores of Shiitake itself are small enough to be a potential cause of hypersensitivity pneumonitis (6–8).

Yoshizawa and coworkers reported that among 36 patients with chronic HP in Japan, 10 patients were summer-type, 7 patients were bird fancier’s lung (9), and chronic HP caused by mushroom spores is rare. There have been only two reported cases of chronic HP caused by Shiitake mushroom (10, 11). In these two cases, the period from beginning cultivation of Shiitake mushroom in a vinyl tent to onset of symptoms were 20 and 27 years, respectively. In the present case, it was 12 years. It seems to take a long time to develop to chronic HP in Shiitake mushroom workers. The chronic form of HP can be divided into 2 types: the insidious onset type and repeated acute episodes type (9). Because there has been no repeated acute episodes, the present case was classified as insidious onset type. Clinical features of chronic HP including imaging and pathological findings are similar to idiopathic pulmonary fibrosis (IPF) or cryptogenic fibrosing alveolitis (5). Therefore, it is possible that many cases of chronic HP, especially insidious onset type, have been mistakenly diagnosed as IPF or cryptogenic fibrosing alveolitis.

However, to our knowledge, there has been no reported case of chronic HP associated with lung cancer. When chronic HP has progressed to the advanced stage, interstitial inflammation, fibrosis, and altered alveolar architecture with regeneration and remodeling are characteristic in pathological findings. Pardo and colleagues demonstrated that in subacute/chronic hypersensitivity pneumonitis there is an increase of lung neutrophils, which contained gelatinase B and interstitial collagenase, and that increased neutrophil infiltration shows some correlation with development of lung fibrosis (12). Therefore, these inflammatory processes which result in the remodeling of the lung, might play an important role in the development of lung cancer. In this study, a relationship between chronic HP and lung cancer was not precisely clarified, however, it will be necessary to carefully observe patients with chronic HP for the development of lung cancer. Further additional research into
the mechanism of the development of lung cancer subsequent to chronic HP is needed.

Acknowledgements: The authors thank Isao Takeya, Tomakomai Prefecture Hospital for making shiitake mushroom antigens and detecting serum precipitins.

References