Hypersensitivity pneumonitis induced by a smut fungus *Ustilago esculenta*

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Abstract

A case of hypersensitivity pneumonitis caused by a smut fungus *Ustilago esculenta* is presented.

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Keywords: hypersensitivity pneumonitis, smut, *Ustilago esculenta*.

*Ustilago* is the most prevalent smut fungus in grain.1-3 It is listed as an aeroallergen associated with bronchial asthma, but not with hypersensitivity pneumonitis.4-7 This is the first reported case of hypersensitivity pneumonitis to be caused by *Ustilago esculenta*. We present this case in order to raise the possibility of *Ustilago* induced hypersensitivity pneumonitis among grain workers and farmers.

Case report

A 40 year old woman engaged in Japanese traditional handicrafts developed increasing dyspnoea, cough, and fever. She recovered completely after two weeks away from work but developed the same symptoms again at midnight on the day she returned to work.

The results of physical examination, routine laboratory studies, and pulmonary function tests were normal. A chest radiograph and high resolution computed tomographic scan showed diffuse bilateral fine nodular shadows without hilar adenopathy. Cultures for microorganisms including mycobacteria from sputum, bronchoalveolar lavage fluid, and gastric juice showed normal flora or were negative. The bronchoalveolar lavage was performed a week after the last exposure by methods described previously.7 Of the 150 ml saline injected, 100 ml of bronchoalveolar fluid was recovered. The total cell yield was 78.4 x 10^6 (87.1 x 10^5 ml), and the differential cell count was 54.7% lymphocytes, 41.5% pulmonary alveolar macrophages, 3.5% polymorphonuclear leukocytes, and 0.3% eosinophils with a CD4/CD8 ratio of 1.61. A transbronchial lung biopsy specimen revealed granulomatous alveolitis.

The causative antigen suspected was smut spores in her work place. She sprinkled these spores on lacquered wares and blew the excess off, producing a rusty colour. Macroscopically, the spores were brown and powdery, and microscopically they were single, globular or ellipsoid, measuring 5-0-10.2 x 4.2-6.5 μm. The smut teliospores were identified by morphometric examination as *Ustilago esculenta*.

Several procedures were conducted to prove that the spores of *U. esculenta* were the causative antigen.

**INDIRECT FLUORESCENT ANTIBODY (IFA) TEST**

The method of Vogel, slightly modified, was performed as previously reported.8 Spores of *U. esculenta* and dust from the work place of the patient were tested with the patient's serum and with control serum samples. The spores were only reactive to the patient's serum among the dusts tested and showed an IFA titre of 1:512, while control serum samples showed less than 1:8.

**GEL DOUBLE DIFFUSION TEST**

The method of Gerber and Jones, slightly modified, was performed as previously reported.9 Antigen was extracted from the teliospores of *U. esculenta* with sodium bicarbonate buffered saline by a modified version of Santilli's method.6 The serum of the patient showed dense precipitins against the extracted antigen (10 mg dry weight/ml) and a faint precipitin against only *Aspergillus niger* from among common hypersensitivity pneumonitis related and *Aspergillus* related antigens (Hollister-Steir, Spokane, Washington).

**LYMPHOCYTE PROLIFERATIVE RESPONSE TEST FOR PERIPHERAL BLOOD CELLS**

Cellular incorporation of [3H]thymidine was determined by the method of Moore and co-workers10 and expressed as a stimulating index: the mean cpm of wells containing 1 x 10^7 lymphocytes (viability 98%) and antigen or mitogen divided by the mean cpm of wells without stimulant. Lymphoproliferative responses to the extracted antigen were observed in a dose dependent manner. The maximum net stimulation and stimulation index value were 5443 cpm and 23.8, respectively, at 0.8 μg/ml concentration. No significant response was observed in control cells.

**SKIN TEST**

Skin reaction to the extracted antigen was made by intradermal injection with 0.02 ml of a solution (0-1 mg/ml) and was read during the
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Discussion

We have shown the smut fungus *U. esculenta* to be an aetiological antigen of hypersensitivity pneumonitis. The patient reacted to the antigen and did not show any precipitins to common hypersensitivity pneumonitis related antigens tested. These results agree with findings utilising an animal model where spores of basidiomycetes (including smuts) possessed antigens which were not cross reactive with those of certain fungi imperfecti.  

*U. esculenta* is distributed widely throughout Asia, and is parasitic on Manchurian wild rice (*Zizania latifolia*). In Japan the pure spores have been used as paint in the traditional lacquer industry. Hypersensitivity pneumonitis in millers who process wild rice that is infected by *U. esculenta* has not been reported but the antigen was not defined as an inhalation challenge was carried out using the whole flour (table).

Smuts were listed as provocative antigens in bronchial asthma. Recently, Marx reported that the frequency of a positive skin test or RAST to grain smut was significantly higher (11-2%) among farming cases than controls (0%) in Wisconsin.  

At present, smuts are not as common in advanced countries as they used to be because of the development of fungicides and smut-resistant grains. However, *Ustilago* is still predominant in grain dust or among atmospheric spores. Our observations on the dust from Saskatchewan grain elevators revealed that it still contained highly immunoreactive smut spores (unpublished data).

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