Hypersensitivity pneumonitis induced by a smut fungus *Ustilago esculenta*

Kazuko Yoshida, Moritaka Suga, Hisato Yamasaki, Kenji Nakamura, Toyozo Sato, Makoto Kakishima, James A Dosman, Masayuki Ando

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

(Thorax 1996;51:650-651)

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

*Ustilago* is the most prevalent smut fungus in grain. It is listed as an aeroallergen associated with bronchial asthma, but not with hypersensitivity pneumonitis. 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. Of the 150 ml saline injected, 100 ml of bronchoalveolar fluid was recovered. The total cell yield was 78.4 x 10⁶ (87.1 x 10⁶/ml), and the differential cell count was 54.7% lymphocytes, 41.5% pulmonary alveolar macrophages, 3.5% polymorphonuclear leucocytes, 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 woods 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. 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. Antigen was extracted from the teliospores of *U. esculenta* with sodium bicarbonate buffered saline by a modified version of Santilli's method. 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 coworkers and expressed as a stimulating index: the mean cpm of wells containing 1 x 10⁶ 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...
Hypersensitivity pneumonia induced by Ustilago esculenta

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.10 *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 also 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.1-7 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.7

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.1-3 Our observation of the dust from Saskatchewan grain elevators revealed that it still contained highly immunoreactive smut spores (unpublished data).

The writers wish to thank Dr Yasuhiko Nakagawa for notice of the patient, Dr Toshihito Kawaiwa, Director General of the Japan Plant Protection Association for the advice about smut fungi, Dr Miho Moriyama and Mr Manning Luo for their assistance, and the members of Centre for Agricultural Medicine for their cooperation.


Published reports of smut-related allergic respiratory diseases

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>No of patients</th>
<th>Symptoms</th>
<th>Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1937</td>
<td>USA</td>
<td>1</td>
<td>Asthma</td>
<td><em>U. zeae</em> (= <em>maydis</em>), <em>Tilletia levis</em> (= <em>fortis</em>) etc.</td>
</tr>
<tr>
<td>1939</td>
<td>USA</td>
<td>13</td>
<td>5 asthma, 6 hayfever, 2 hayfever with asthma</td>
<td><em>T. levis</em>, <em>U. zeae</em>, <em>A. oryzae</em>, <em>T. levis</em>, <em>T. verrucaria</em></td>
</tr>
<tr>
<td>1940</td>
<td>USA</td>
<td>103</td>
<td>17 asthma, 2 nasal allergy</td>
<td><em>T. levis</em>, <em>U. zeae</em> etc</td>
</tr>
<tr>
<td>1940</td>
<td>USA</td>
<td>34</td>
<td>Asthma, and/or hayfever</td>
<td><em>Sphaeroteca sp.</em></td>
</tr>
<tr>
<td>1940</td>
<td>USA</td>
<td>19</td>
<td>17 asthma, 2 nasal allergy</td>
<td><em>T. levis</em>, <em>U. zeae</em> etc</td>
</tr>
<tr>
<td>1941</td>
<td>Spain</td>
<td>2</td>
<td>Asthma</td>
<td><em>T. carrier</em>, <em>T. foetida</em></td>
</tr>
<tr>
<td>1952</td>
<td>Brazil</td>
<td>1</td>
<td>Asthma</td>
<td><em>T. levis</em></td>
</tr>
<tr>
<td>1957</td>
<td>France</td>
<td>5</td>
<td>Asthma</td>
<td><em>U. esculenta</em></td>
</tr>
<tr>
<td>1965</td>
<td>India</td>
<td>7</td>
<td>Respiratory troubles</td>
<td><em>U. esculenta</em></td>
</tr>
<tr>
<td>1968</td>
<td>Japan</td>
<td>1</td>
<td>Asthma</td>
<td><em>U. esculenta</em></td>
</tr>
<tr>
<td>1979</td>
<td>Japan</td>
<td>2</td>
<td>Hypersensitivity pneumonitis</td>
<td>N.I.</td>
</tr>
</tbody>
</table>

WBC (u/l) 6890

CRP (mg/dl) 0.25

PO₂ (kPa) 12.7

VC (l) 3.15

Results of inhalation challenge test with *U. esculenta* performed on the patient using 1 mg of buffer extract antigen inhaled through an ultrasonic nebuliser. The same provocation test did not show any effect on a healthy control subject.

NI = not identified. The antigen was not identified but the authors suspected *U. esculenta* to be the causative antigen in these cases.

Details of the references are available from the authors on request.

next 48 hours. The patient showed immediate and Arthus-type reactions to the antigen but two healthy control subjects did not show any reaction.

INHALATION CHALLENGE TEST

Ten ml of the extracted antigen (0.1 mg/ml) were inhaled through an ultrasonic nebuliser (Omuron, Japan). Symptoms, signs, and laboratory findings were recorded during the next 48 hours. Symptoms and signs were reproduced five hours later with maximum effect nine hours later. Laboratory findings also worsened as shown in the figure. A healthy control subject who had an identical test did not show any abnormality.

The patient’s symptoms have not recurred since moving to alternative employment.
Hypersensitivity pneumonitis induced by a smut fungus Ustilago esculenta.

K Yoshida, M Suga, H Yamasaki, K Nakamura, T Sato, M Kakishima, J A Dosman and M Ando

Thorax 1996 51: 650-657
doi: 10.1136/thx.51.6.650

Updated information and services can be found at:
http://thorax.bmj.com/content/51/6/650

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/