

## Imported Mycoses in Japan

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The authors surveyed the present situation for imported (introduced) mycoses from papers published in Japan by the end of December, 2001. The results revealed 31 cases of coccidioidomycosis, 33 of histoplasmosis, 17 of paracoccidioidomycosis and one of penicilliosis marneffeii. In coccidioidomycosis the ages ranged from 12 to 55, for 27 males and 4 females of which 2 were fatal. For histoplasmosis, the ages ranged from 17 to 74 of which 24 cases were male and 8 female. All of the patients with paracoccidioidomycosis were infected in Latin American countries. They consisted of 15 males and 2 females, and the ages ranged from 24 to 68. A single case of penicilliosis marneffeii (38 years old, male) was reported very recently. The case was complicated by AIDS and became critical. Blastomycosis has not yet been reported. This survey indicates that the number of the imported mycoses in Japan is increasing. It is necessary for the persons concerned to counter measures to cope with this situation.

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### 1. Introduction

With the large increase in Japanese internationalization, a great number of Japanese have gone abroad for tourism, work or study purposes. Unfortunately, some of them have suffered from serious endemics peculiar to each country visited, and have then returned to Japan<sup>1</sup>. As a result, Japanese physicians have had the opportunity to examine imported mycoses such as coccidioidomycosis, histoplasmosis, paracoccidioidomycosis, penicilliosis marneffeii and blastomycosis<sup>2</sup>. The causative agents of these imported mycoses are classified into 'Class 3

(very dangerous fungi)'. Physicians and researchers must work with these fungi carefully using an isolated biohazards laboratory<sup>3,4</sup>.

Recently, 2 or 3 patients with serious cases of imported mycoses are reported every year in Japan. However, the Welfare Ministry of Japan has still not taken a serious interest in the imported mycoses (recently the Ministry designated coccidioidomycosis as one of the dangerous mycosis). One of the reasons is that fungal infectious processes are definitely different from those of other microbial infections. In the imported mycoses, the infection from person to person or animal to person does not occur. Filamentous fungi infect persons due to a unique system. They produce conidia which are scattered into a laboratory from a culture medium due to air flow and as a result, laboratory personnel inhale the conidia and contract the disease. Among the various causative agents, *Coccidioides immitis* is the most dangerous fungus. Recently, the num-

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ber of patients with imported mycoses is gradually increasing. Nevertheless, detailed statistics have not been published and it is, therefore, very important to carry out an epidemiological survey of the imported mycoses and to clarify the present situation to prevent an outbreak of these dangerous mycoses.

## 2. Journals referred to

This time the authors surveyed reports on the imported mycoses published in Japan until December 31, 1998. More than half of the reports were abstract and were not full. In addition, plural reports were published about the same patients.

## 3. Results and discussions

### 1) *Coccidioidomycosis*<sup>5-7</sup>

*Coccidioidomycosis* is an endemic located in the United States (California, Arizona, Nevada, New Mexico, Utah, Texas), Mexico, Central American countries, Paraguay, Venezuela and Argentina. San Joaquin valley in California is especially notorious for the highest incidence and prevalence of the disease. In this area the disease is named as 'valley fever', 'desert rheumatism', 'San Joaquin fever', 'bump' or 'coccidioidal granuloma'. The causative agent of the disease is *C. immitis* which inhabits the soil of semiarid areas and produces arthroconidia. These conidia are scattered into the air by strong winds or by public engineering works. The local inhabitants inhale the scattered arthroconidia and contract pneumonia. At approximately 0.5% rate, the disease disseminates from the lung to the whole body and half of these patients die. According to Ajello *et al.*<sup>1</sup>, in the United States approximately 100,000 cases occurs every year and approximately 70 of these patients die.

Since Sakakibara and Mizuno reported the first case in 1937, 31 cases have been counted by the

end of December, 2001. Since 1984, the number of patients has increased. The proposed reason is that during the 1980's, Japanese highly developed industrialization took place and in proportion to this many Japanese have now visited the South-Western United States.

Male patients predominate and their ages ranged from 12 to 55. Most of the patients contracted the disease in California, Arizona and Mexico. A demobilized soldier from the Solomon Islands suffered from *coccidioidomycosis* on returning to Japan and died. It is unclear whether or not *C. immitis* inhabits the soil of the Solomon Islands. It is possible that as returning, he was taken a prisoner by war and might have encountered materials brought by the US army. Interestingly, there were 2 cases who may have contracted disseminated *coccidioidomycosis* from cotton wool imported from the United States. They had not travelled abroad and were employees of spinning companies.

### 2) *Histoplasmosis*<sup>9</sup>

*Histoplasmosis* occurs by inhaling airborne infectious spores of *Histoplasma capsulatum*. The disease includes 3 names according to differences of the causative agents. They are *histoplasmosis capsulati* caused by *Histoplasmosis capsulatum* variety *capsulatum*, *histoplasmosis duboisii* by *H. capsulatum* var. *duboisii* and *histoplasmosis farciminosi* by *H. faciminosum*. *Histoplasmosis capsulati* has been reported from temperate and tropical regions all over the world. On the other hand, *histoplasmosis duboisii* is confined basically to the African continent, so referred to as African *histoplasmosis*. However, mycologically *H. capsulatum* var. *capsulatum* is not differentiated from *H. capsulatum* var. *duboisii*. The parasitic form of *H. capsulatum* var. *duboisii* and tissue reaction to the fungus are different from those of the former in the following two features. The yeast cells of *H. capsulatum* var. *duboisii* in pathological lesions are

larger (8~15 µm in diameter) than those of the former and many giant cells appear in the granulomatous lesions of histoplasmosis duboisii. Histoplasmosis farciminosi is an equine disease which is chronic in horses, sheep, goat, donkey, dog etc.

By the end of December 2001, 33 patients with histoplasmosis have been reported in Japan. The ages ranged from 17 to 74. Interestingly, 8 cases were infected in Amazon region of Brazil at the same time. They were all TV crew members and went into a cave where a large number of bats lived. Other places for the infection were as follows; Mexico, USA, Bolivia, Malaysia, India, Peru, Argentina, and the remainings had no history of foreign journeys related to the disease. A very interesting case was reported by Hotchi *et al.* The patient was transplanted with a kidney from a colored man from Texas (USA), who had contracted histoplasmosis. As a result the disease disseminated his whole body and he died. Until 1993 there were controversy on whether or not *H. capsulatum* is present in Japan. Since the report of Nagai *et al.*, it became clear that the fungus also exists in this country. This patients was treated with steroid ointment for a long time for a diagnosis of papuloerythroderma and contracted the primary cutaneous histoplasmosis. Maekawa *et al.* carried out an epidemiological study of histoplasmosis in Okayama, in 1959 using histoplasmin.

All the patients with disseminated histoplasmosis died. One of them underwent gastrectomy which might have been a trigger for the fatal dissemination. The others all had various underlying diseases such as tuberculosis, disseminated carcinoma, aplastic anemia or AIDS.

### 3) Paracoccidioidomycosis<sup>10</sup>

Paracoccidioidomycosis is basically a pulmonary mycotic disease. Characteristically mucocutaneous-lymphangitic lesions are frequently observed. This type of disease occurs in the oral mucosa, the gums,

the nasal and anal mucosa. The causative agent is *Paracoccidioides brasiliensis*. Its endemic areas are Central America and the South American continent but not Chile, Guyana and Surinam. Brazil, Colombia and Venezuela are the nations showing the highest incidence.

As of the end of December, 2001, 17 cases have been reported and their ages ranged from 24 to 68. Fifteen cases were infected in Brazil, one contracted the disease in Bolivia and the remaining one in Paraguay. All patients except for one were immigrants to South American countries, and one case was a housewife who had gone to Brazil together with her family. Interestingly male patients predominate in paracoccidioidomycosis. According to Sano *et al.*<sup>11</sup>, a sex hormone(estrogen) may inhibit the growth of *P. brasiliensis*.

### 4) Penicilliosis marneffe<sup>12</sup>

This disease is endemic in the mountain areas located in the southern and northern parts of the Republic of China and Vietnam. Most of the indigerous bamboo rats are infected with the fungus *Penicillium marneffe*. As the cases of histoplasmosis, patients show a decreasing activity of cell-mediated immunity and the disease progresses and becomes serious. The parasitic from and tissue reactions are very similar to those of histoplasmosis. At present many patients with the disease have been reported in Thailand because of the existence of many AIDS patients. In 1998, the first case of peicilliosis marneffe<sup>12</sup> was reported at the annual meeting of the Japanese Society for medical Mycology. He was 38 years old and suffered from AIDS. He had visited several countries including Thailand, Pakistan and Africa etc. He had suffered from AIDS and was diagnosed for penicilliosis marneffe<sup>12</sup> following autopsy. It is supposed that the number of patients with penicilliosis marneffe<sup>12</sup> will increase in the near future in Japan.

### 5) Blastomycosis

Blastomycosis is basically restricted to the North American continent. The causative agent is *Blastomyces dermatitidis*. Recently some cases have been reported from African countries and Israel. Fortunately, there have been no reports in Japan.

### 4. Conclusion

Epidemiological survey on the imported mycoses in Japan were conducted to clarify the present situation for these diseases. As a result, coccidioidomycosis was 31 cases, histoplasmosis 33, paracoccidioidomycosis 17 and penicilliosis marneffe<sup>1</sup>.

### REFERENCES

1. Fujio J, Nishimura K, Miyaji M. Epidemiological Survey of the Imported Mycoses in Japan. *Jpn J Med Mycol* 1999; 40: 103-109
2. Miyaji M. The imported mycoses. *Pathology and Clinical Medicine* 1991; 9: 1301-1307
3. Iwata K. *Microbiological Biohazards: General Considerations and Control*, Tokyo: Soft Science, Inc., 1980
4. Miyaji M. The imported mycoses and biohazards. *Jpn J Med Mycol* 1993; 34: 113-120
5. Drutz DJ, Catanzaro A. Coccidioidomycosis Part I. *Rev Res Dis* 1993; 117: 558-585
6. Drutz DJ, Catanzaro A. Coccidioidomycosis Part II. *Rev Res Dis* 1993; 117: 727-771
7. Miyaji M. Coccidioidomycosis-the most dangerous imported mycosis. *Nihon Iji Shinpou* 1992; 3573: 26-31
8. Chandler FW, Kaplan W, Ajello L. Coccidioidomycosis. A Colour and Textbook of the Histopathology of Mycotic Diseases. London: Wolfe Medical Publication Ltd., 1980: 50-53
9. Ajello L. Histoplasmosis - a dual entity; histoplasmosis capsulati and histoplasmosis duboisii. *L'Igiene Moerna* 1983; 79: 3-30
10. Chandler FW, Kaplan W, Ajello L. Paracoccidioidomycosis. A Colour and Textbook of the Histopathology of Mycotic Diseases. London: Wolfe Medical Publication Ltd., 1980: 88-91
11. Sano A, Miyaji M, Nishimura K. Studies on the relationship between the estrous cycle of BALB/c mice and their resistance to *Paracoccidioides brasiliensis* infection. *Mycopathologia* 1992; 119: 141-145
12. Deng Z, Connor DH. Progressive disseminated penicilliosis caused by *Penicillium marneffe*. Report of eight cases and differentiation of the causative organism from *Histoplasma capsulatum*. *Am J Clin Pathol* 1985; 84: 323-327