大韓微生物學會誌 : 第18卷 第1號 1983
J. Kor. Soc. Microbiol., Vol. 18, No. 1, 1983

Report of Four Cases of Pulmonary Pseudallescheriasis from Korea

Sang Jae Kim, Young Pyo Hong, Sin Ok Kim and Young Ja Yoon

Korean Institute of Tuberculosis, Korean National Tuberculosis Association, Youngdeungpo P.O. Box 120, Seoul-150, Korea

=국문초록=

肺 *Pseudallerscheria* 症 4例

대한결핵협회 결핵연구원

김상재 · 홍영표 · 김신옥 · 윤영자

저자 등은 결핵으로 인해 생긴 공동을 가진 4명의 남자 환자에 있어서 성공적인 결핵화학요법으로 결핵은 치유되어 객담검사에서 결핵균은 더이상 검출되지 않았으나, 계속되는 각혈로 진균검사를 실시한 결과 *Pseudallerscheria boydii*(불완전세대 *Scedosporium apiospermum*)에 의한 진균종(眞菌腫)임이 밝혀졌다. 여러 차례의 객담검사로부터 6개월 또는 2년 이상 계속 동일한 균종이 불리 배양되었고 그리고 그들의 혈청은 *P. boydii* 배양여액 항원과 immunodiffusion test를 실시한 결과 precipitin bands를 형성하였다. 4환자의 흉부 X-선 사진상에는 뚜렷한 진균종음영을 볼 수 없었다. 2명의 환자 객담에서는 *P. boydii*와 더불어 *Candida albicans*와 *Aspergillus fumigatus*가 계속해서 분리 배양되었고 그리고 그들의 혈청에서 그러한 진균들의 항원에 대한 침강항체를 검출할 수 있었다. 3명의 환자는 폐기능이 진균종 제거수술을 허용하지 않았고 1명의 환자는 수술을 거부하였다.

INTRODUCTION

Pseudallescheria boydii(imperfect form, *Scedosporium apiospermum*) (18, 21) is widely distributed in the human habitat, having been isolated from the soil and water samples in many countries(1, 2, 7, 11, 16, 21). Such ubiquity in the nature facilitates the fungus to a frequent involvement in a variety of diseases in men and animals. The fungus has been recognized as an important etiologic agent of eumycetomas, pulmonary mycoses, meningitis, and rarely of otomycosis, prostatis, and keratitis(3-5, 8-14, 17, 19-22). There has been no report of the isolation of *P. boydii* neither from environments nor from clinical sources in Korea previously.

We have repeatedly isolated *P. boydii* or *S. apiospermum* from sputum specimens of patients with healed pulmonary tuberculosis whose sera produced precipitin bands with antigen from *P. boydii* on immunodiffusion tests. The following is a descripition of what appears to be the first pulmonary pseudallescheriasis from Korea.

CASE PRESENTATION

Case No. 1

A 34 year-old office clerk residing in Seoul visited the chest clinic of Korean Institute of

Tuberculosis(KIT) for the first time in 1978 with complaints of dyspnea, cough and hemoptysis. He suffered from pulmonary tuberculosis for long time with a history of unsuccessful chemotherapy mainly due to irregular drug ingestion and poor regimens since his pulmonary tuberculosis was diagnosed at a physical examination for conscription in 1970. He took para-aminosalicylic acid for about 50 days and stopped therapy until he visited the health center in 1973 because symptom worsened further. He was irregularly treated with isoniazid, para-aminosalicylic acid and streptomycin for 2 years. In the spring of 1975, his clinical symptom aggravated again and so another round of combined chemotherapy with ethambutol, isoniazid and streptomycin, was introduced but no clinical improvement was noticed. When he appeared in the KIT clinic, October 1977, for the first time, numerous tubercle bacilli(*Mycobacterium tuberculosis*)were demonstrated in sputum specimens by both smear and culture. Bacilli were resistant to isoniazid, para-aminosalicylic acid, but remained sensitive to other antituberculous drugs tested, laboratory findings before treatment revealed that SGOT and SGPT were 13 and 7 units; uric acid, 6.4 mg/*dl*; BUN, 7.5 mg/*dl*; creatinine, 6.5 mg/*dl*. Cytological and chemical findings of urine tests were within normal range. Chest roentgenograms showed a huge cavity(approximately 7×8 cm) in left upper lobe and another approximately 1.8×3 cm cavity in right middle field. Infiltration was also seen in right upper and left midzone as seen in figure 1. The patient underwent intensive combined chemotherapy of rifampicin 450 mg, pyrazinamide 1,500 mg, and prothionamide 500 mg. but unfortunately severe toxicity was noticed one month later, showing hapatomegaly, jaundice, and arthritis. SGOT and SGPT increased up to 680 and 220 units and bilirubin 11.6 mg/*dl*(direct 2.2 mg, indirect 5.4 mg). After stopping therapy for one month, he continued chemotherapy with rifampicin-prothionamide-cycloserine(500 mg) but SGOT and SGPT rose again. The regimen had been changed again to rifampicin-cycloserine-kanamycin after brief interruption of therapy and thereafter no more episode of toxicity encountered. Sputum converted to negative for tubercle bacilli after four month therapy and his latest chest roentgenogram (after 5-year treatment) revealed apparent shrinkage of cavity in left upper lobe with over-all improvement in both lung fields(Figure 1).

On February 1980, he complained of intermittent hemoptysis and chronic cough in spite of continuous sputum negativity for acid fast bacilli. Cultural examination of sputum specimens for fungus produced numerous colonies of *P. boydii*. The same fungus was repeatedly isolated from sputum specimens collected on April, May and September 1980 and March 1983. Serum specimen produced more than 3 precipitin bands with home-made antigen prepared from 8 week-old culture filtrate of *P. boydii*(15) on immunodiffusion test and this precipitating antibody persisted in serum collected on March 1983. Serum also reacted to similarly prepared antigen of *Candida albicans*, but not to antigens of *A. fumigatus*, *A. niger*, *A. nidulans*, and *Rhizopus arrhizus*. *C. albicans* was also repeatedly isolated from sputum specimens and precipitation antibody to this fungus persisted.

Conoly of *P. boydii* on Sabouraud's agar was brown when young, but, with time elapsing, became smoky gray mainly due to increased fluffy aerial hyphae and sporulation. Reverse of conoly remained dark brown color. Oval or elliptical conidia(aleuriospores) with truncated base were produced singly at the

tip of hyphae or of short lateral branches as seen in figure 3 and their size was approximately 4-8 x 7-8 μ. Two week-old culture produced many of dark brown colored, globose cleistothecia with 90 to 250 μ in diameter, in which 4-7 x 7-8 μ elliptical ascospores were produced. Occasional hemoptysis continued, but unfortunately surgical excision of affected area was not indicated.

Case No. 2

A 34 year-old pharmacist(male) suffered from pulmonary tuberculosis for long time. He had been treated with a combined chemother-a py of isoniazid, para-aminosalicylic, acid and streptomycin for 2 years from September 1967 when his pulmonary tuberculosis was found for the first time. In 1974, he, allegedly, had an occasional hemoptysis for which another round of chemotherapy with isoniazid, ethambutol and rifampicin was introduced for one and half years. From May 1977, he was treated with the same regimen for 10 months in another hospital and thereafter acid fast bacilli were no longer demonstrated on smear and culture examinations. He, allegedly, had a massive hemoptysis(approximately 100 ml) on April 1981 and he visited in a university hospital where no acid fast bacilli and *Paragonimus westermani* ova were found on repeated sputum examinations.

This patient appeared in the KIT clinic, June 1981, with chief complaint of occasional hemoptysis. Chest roentgenograms taken on June 1981 showed irregular multiple micronodular and nodular mottlings and linear shadows in right subclavicular region. Acid fast bacilli were not demonstrated on sputum smear and culture, but numerous colonies of *P. boydii* were isolated form sputum specimens collected on July 1 and 15 1981 and precipitating antibody to only *P. boydii* antigen were detected on immunodiffusion test. Morphological feature of the fungus was same as in Case No. 1. The same fungs was repeatedly isolated from sputum specimen collected on february 1983, and precipitating antibody to this fungus also persisted.

He refused surgical removal of the affected areas.

Case No. 3

A 42 year-old merchant had been unsuccessfully treated for pulmonary tuberculosis from 1959 with isoniazid and para-aminosalicylic acid. Two years treatment with isoniazid and ethambutol from August 1973 in a hospital improved clinical symptom for a while. In 1980, symptom aggravated again and so he was put on a combined chemotherapy of para-aminosalicylic acid, rifampicin and kanamycin. In spring of 1981, regimen was changed to isoniazid, ethambutol, rifampicin and capreomycin and continued till February 1982 when he visited in the KIT clinic with complaints of exertional dyspnea, coughing, sputum and occasional hemoptysis. Chest roentgenograms showed cystic changes and cavities with fluid level in left whole lung field and in right upper zone as seen in figure 1. Remaining right lung field was hyperluscent. Monthly sputum smear and culture examinations from February 1982 to January 1983 showed negative results for acid fast bacilli, suggesting that his pulmonary tuberculosis had been treated successfully. No clinically significant fungus was isolated from sputum specimen collected on June 1982, but his serum reacted with antigens of *A. fumigatus* and *P. boydii*(figure 2). Repeated sputum culture on January 1983 produced 6—9 colonies of *P. boydii* and a few of *A. fumigatus* and serum specimen also reacted with both fungal antigens.

Occasional hemoptysis persisted but unfortunately surgery was not indicated.

Case No. 4

A 34 year-old office clerk visited in the KIT clinic, December 1981, with chief complaint of hemoptysis(approximately 300 ml).

His pulmonary tuberculosis was allegedly found in 1973 and treated with isoniazid, ethambutol and rifampicin for 5 years. Chest roentgenograms showed a 3×4.5 cm cavity in left apex and multiple micronodular and linear shadows in both upper lung fields as seen in figure 1. Sputum specimen collected on December 1981 produced negative result for acid fast bacilli on smear and culture, however, culture for fungus yielded numerous colonies of *S. apiospermum*. The fungs did not produce ascospores and morphological features were same as imperfect state of *P. boydii* as seen in figure 4.

Serum specimen strongly reacted with antigen derived from clinical isolate of his own sputum, but not with antigen of reference *P. boydii* strain, which we used to routine immunodiffusion tests. Numerous colonies of the same fungus was repeatedly isolated from sputum specimen of January 1983 and precipitating antibody to this fungus also persisted, but no acid fast bacilli were demonstrated on sputum smear and culture, suggesting that current occasional hemoptysis might occurred due to *S. apiospermum* infection.

Unfortunately surgical removal of the affected area was not indicated.

DISCUSSIONS

It has been published elsewhere that aspergilloma mainly due to *A. fumigatus* is most common fungal complication in an open-negative cavity preformed by pulmonary tuberculosis(6, 15). England survey showed that 15% of pulmonary tuberculosis patients having open-negative cavity had aspergilloma(6). In Korean patients, fungal infection was noticed in nearly 30% of cases who complained of occasional hemoptysis and/or chronic productive cough after their pulmonary tuberuclosis was successfully treated(15). Reports of *P. boydii* infection were recorded in many countries, indicating the world-wide distribution of fungs. Subcutaneous infection with *P. boydii* was one of the common eumycetomas(1, 9), however pulmonary complication was not rare in patients with pulmonary tuberculosis(4, 8, 10, 11, 13, 14, 20, 21), in atopic individuals(3, 5), and in immunocompromised hosts(12, 17, 19). Fatal disseminated mycosis due to *P. boydii* could occur in the latter patient group(12, 17, 19).

Definitive diagnosis of pulmonary *P. boydii* infection could be made by demonstrating the fungus in affected tissue, however, serolcgical and cultural findings should be very useful diagnostic adjunct if the fungus infected secondarily in healed or concurrent tuberculous lung lesions of patients without apparent immunosuppression(4, 13). In spite of that chest roentgenograms of the cases presented in this paper did not show a distinct mycetomal shadow, all four patients were apparently infected with *P. boydii* or imperfect state, *S. apiospermum* because they expectorated the same fungus repeatedly for over 6 months in one case and for over 2 years in other three cases and precipitating antibody to this fungus also persisted in their sera. As all four patients suffered from pulmonary tuberculosis for long time, the fungus might colonized in healed tuberculosis lesions and hence it caused occasional hemoptysis or chronic productive cough.

Besides *P. boydii* second fungi might have been involved in case No. 1 and 3. Second

fungi of case No. 1 was *C. albicans* and of case No. 3, *A. fumigatus* and sera from these patients also reacted with antigen of the corresponding fungus.

It has been noticed that there were two distinct types of colony morphology in clinical isolates of *P. boydii*(10). Clinical specimen from all but one patient also yielded two types of colony on culture examination. Case No. 4, however, expectorated only one type of colony which was fluffy, sporulated poorly, and did not produced ascospores, and patient's serum reacted only with antigen prepared from clinical isolate of his own sputum specimen. Although serum specimen from case No. 3 reacted very weakly with this *S. apiospermum* antigen, sera from the other two patients did not react at all, suggesting that *P. boydii* and it's imperfect variant did not share close antigenic relation. Isolation of *P. boydii* both from environments and clinical sources has never been reported in Korea, therefore this presentation is a first description of pulmonary pseudallescheriasis in Korea.

Chemotherapy is not usually effective in pulmonary mycetoma produced in preformed cavitary lesions by tuberculosis (6, 11, 12). Surgical excision was indicated in only one case but he refused it.

SUMMARY

Four cases of pulmonary pseudallescheriasis in patients with healed pulmonary tuberculosis are described. All four patients had a long history of antituberculous chemotherapy for pulmonary tuberculosis, but continuous sputum negativity for acid fast bacilli indicated apparent recovery from tuberculosis. They, however, complained continued intermittent hemoptysis and chronic cough. Although their chest roentgenograms did not show a clearcut mycetomal shadows in preformed cavitary lung lesions, *Pseudallescheria boydii* or *Scedosporium apiospermum* was repeatedly isolated from serial sputum specimens collected at different days for a period of over half an year or two years and their serial serum specimens produced precipitin bands with home-made antigen from 8-week old culture filtrate of *P. boydii*. Second fungus was isolated from sputum specimens of two patients and one was *Candida albicans* and the other was *Aspergillus fumigatus*. Sera from both patients reacted with antigens of those second fungi.

Unfortunately pulmonary function of three patients did not allow surgical excision of the infected area and one patient refused surgery.

REFERENCES

1) Ajello, L.: *The isolation of* Allescheria boydii *Shear, an etiologic agent of mycetomas, from soil. Amer. J. Trop. Mea. Hyg., 1 : 277, 1952.*
2) Alteras, I. & Evolceanu, R.: *First isolation of* Allescheria boydii *from Romanian Soil. Sabouraudia, 7 : 135, 1969.*
3) Ariewitsch, A.M., Stepaniszewa, S.G. & Tiufilna, O.W.: *Ein fall des durch* Monosporium apiospermum *herorgerufenen lungenmyzetoms. Mycopathologia, 37 : 171, 1968.*
4) Arnett, J.C. & Hatch, H.B.: *Pulmonary allescheriasis. Arch. Int. Med. 135 : 1250, 1975.*
5) Bakerspigel, A., Wood, T. & Burke, S.: *Pulmonary allescheriasis: report of a case from Ontario, Canada. Amer. J. Clin. Pathol. 68 : 299, 1977.*
6) British Tuberculosis Association.: *Aspergilloma and residual tuberculous cavities-the results of a resurvey. Tubercle, 51 : 277, 1970.*
7) Cooke, W.B.: *Check list of fungi isolated from polluted water and sewage. Sydowia Suppl, 1 : 146, 1957.*
8) Creitz, J. & Harris, H.W.: *Isolation of* Allescheria boydii *from sputum. Amer. Rev. Tuber.*

71 : 126, 1955.

9) Dowding, E.S.: Monosporium apiospermum *a fungus causing madura foot in Canada. Can. Med. Assoc. J. 33 : 28, 1935.*

10) El-Ani, A.S.: Allescheria boydii*: wild type and a variant from human pulmonary allescheriasis. Mycologia, 66 : 661, 1974.*

11) Emmons, C.W., Binford, C.M., Utz, J.P. & Kwon-Chung, K.J.: *Medical mycology, Lea & Febiger, 1977.*

12) Fetter, B.F., Klintworth, G.K. & Hendry, W. S.: *Mycoses of the central nervous system. Williams & Wilkins, Co., Baltimore, pp. 172—177, 1967.*

13) Hainer, J.W., Ostrow, J.A. & Mackenzie, D. W.R.: *Pulmonary monosporiosis: report of case with precipitating antibody. Chest, 66 : 601, 1974.*

14) Jung, J.Y., Salas, R., Almond, C.H., Saab, S. & Reyna, R.: *The role of surgery in the management of pulmonary monosporiosis. A collective review. J. Thora. Cardio. Surg., 73 : 139, 1977.*

15) Kim, S.J., Hong, Y.P. & Kim. S.C.: *Pulmonary fungal infection in patients with healed tuberculosis or other underlying diseases. Kor. J. Microbiol. 19 : 142, 1981.*

16) Kirk, P.W.: *A comparison of saline tolerance and sporulation in marine and clincial isolates of* Allescheria boydii *Shear. Mycopath. Mycol. Appl. 33 : 65, 1967.*

17) Lutwick, L., Galgiani, J.N., Johnson, R.H. & Stevens, D.A.: *Visceral fungal infections due to* Petriellidium boydii(Allescheria boydii). In vitro *drug sensitivity studies. Amer. J. Med. 61 : 632, 1976.*

18) Mcginnis, M.R., Padhye, A.A. & Ajello, : Pseudallescheria *Negroni et Fischer, 1943 and its later synonym* Petriellidium *Mallock, 1970. Mycotaxon, 14 : 94, 1982.*

19) Meadow, W., Tipple, M. & Rippon, J.: *Endophthalmitis caused by* Petriellidium boydii *first report of pediatric case. Amer. J. Dis. Child. 135 : 378, 1981.*

20) Reddy. P.C., Christianson, C.S. & Gorelick, D.F.: *Pulmonary monosporiosis: an uncommon pulmonary mycotic infection. Thorax, 24 : 722, 1969.*

21) Rippon, J.W.: *Medical mycology, 2nd ed. W.B. Saunders, Co., Philadelphia, pp. 595—614, 1982.*

22) Tong, J.L., Valentine, E.H., Durrance, J.R., Wilson, G.M. & Fischer, D.A.: *Pulmonary infection with* Allescheria boydii. *Amer. Rev. Tuber. 78 : 604, 1958.*

Legends for Figures

Fig. 1. Chest roentgenograms. Left roentgenogram of case No. 1 was taken before antituberculous treatment and right radiograph after 5 year-treatment. Chest roentgenograms of case No. 3 and 4 were taken on first visit to the chest clinic of Korean Institute of Tuberculosis.

Fig. 2. Immunodiffusion slides. Patient's serum in top wells were reacted with 5 or 7 fungal antigens of different species(2mg/ml) in 1% noble agar for 3 days and then the slides were washed with 5% sodium citrate. Antigens: 1: mycelial extract of *Aspergillus fumigatus*(15), 2—7 : concentrated 8 week-old culture filtrate antigens(precipitated at 50% saturation of ammonium sulfate) of *Candida albicans, Pseudallescheria boydii, Asp. flavus, Asp. nidulans, Rhizopus arrhizus,* and *Scedosporium apiospermum*(15). *S. apiospermum* was isolated from sputum specimen of case No. 4 and all other strains were from reference stock cultures of this institute.

Fig. 3. Morphological features of clinical isolates of *Pseudallescheria boydii* from case No. 1, 2 and 3. ① Ten day-old colony on sabouraud's agar. ② Cleistothecia(X 50). ③ Ascospores and a cleistothecium (X 200). ④ Young cleistothecia(X 400). ⑤ and ⑦ Terminal single aleuriospores(condia) and released aleuriospores(X 400). ⑥ Arthrospore-like sporulation(X 400).

Fig. 4. Morphological features of clinical isolate of *Scedosporium apiospermum*(imperfect state of *Pseudallescheria boydii*). ① and ② Elliptical or oblong aleuriospores(conidia) and their single terminal sporulation(X 400). ② Ten day-old colony on sabouraud's agar.

≫ 논문 사진 부도 ≪

≫ 논문 사진 부도 ≪

≫ 논문 사진 부도 ≪

≫ 논문 사진 부도 ≪