Cryptococcus neoformans pneumonia occurs frequently in immunocompromised patients. The organism is a non-mycelial budding yeast found in the soil and in pigeons droppings. It is rare in immunocompetent patients. The aim of this study was to analyze computed tomography (CT) findings of pulmonary cryptococcosis in both immunocompromised and immunocompetent subjects. Twelve patients of proved pulmonary cryptococcosis were reviewed. Their CT findings were pulmonary nodules (n=10), masses (n=5), micronodule (n=1), consolidation (n=1) with subpleural location (n=11), and lower lobe predilection (n=8). The margin of the nodules were ill-defined (n=7), spiculated (n=7) and lobulated (n=4). Some of them had air-bronchogram (n=6), halo sign (n=6) and cavitation (n=3).

The clinical picture of pulmonary cryptococcosis is non-specific. Therefore familiarity with the CT findings can make the diagnosis of pulmonary cryptococcosis earlier and easier.

Key words: Cryptococcosis; Computed tomography (CT); Lung

Cryptococcosis is caused by Cryptococcus neoformans, which is yeast form unimorphic fungus that exists in worldwide especially in contaminated soil by pigeon droppings. The organisms are usually round to oval in shape and from 2 to 20 um in diameter. The route of infection is through inhalation of contaminated soil or pigeon droppings. In immunocompetent patients, it happens rarely and can resolve spontaneously. In immunocompromised patients, it can infect the lung and via hematogeneous spreading to skin, bone, and central nervous system [1, 2].

There are three radiographic patterns of pulmonary cryptococcosis including one or more spherical nodules or masses, one or more areas of patchy consolidation, multiple small nodules or irregular shadows. Hilar and mediastinal lymphadenopathy, pleural effusion are uncommon [3, 4].

Familiar with the pictures of pulmonary cryptococcosis is important, because pulmonary cryptococcosis can resolve spontaneously in most patients. However, it can progress to severe disease in immunocompromised patients. Early and aggressive treatment after diagnosis is warrant. The purpose of the article is to review the computed tomography findings of pulmonary cryptococcosis.

MATERIALS AND METHODS

Twelve patients were diagnosed as pulmonary cryptococcosis at our hospital since April 1998 to April 2005. The twelve patients included nine men and three women. The age was ranged from 28 to 76 years old (mean age : 55). The chief complaints of these patients were cough (n=7), chest tightness (n=2), lower grade fever (n=1), body-weight loss (n=4) and hemoptysis (n=2). Two of them revealed abnormal chest radiograph during health examination and one was found to have abnormal chest radiograph at emergency room due to traffic accident. One patient was immunocompromised due to human immunodeficiency virus (HIV)
infection. Two patients had underlying connective tissue disease as rheumatoid arthritis and Sjogren syndrome. The others were immunocompetent. The criteria for diagnosis of pulmonary cryptococcosis were smears or culture of sputum or bronchial washing or cerebrospinal fluid (CSF), transthoracic biopsy, serum or CSF antigen [2].

Our patients were proved by serum antigen and bronchoalveolar lavage with culture (n = 1), serum antigen combined with blood and CSF culture (n = 1), high serum antigen titer (over 4096)(n = 1), transthoracic biopsy (n = 4), video-assisted thoracotomy (n = 3), thoracotomy with resection (n = 1), and pneumonectomy (n = 1). The one with pneumonectomy was due to coincident adenocarcinoma of lung. All of our patients got well except for two. One patient with rheumatoid arthritis who developed meningitis and died later. Another one with HIV infection was referred to other hospital.

CT scans were obtained by a CT scanner (Hispeed CTi scanner, GE Medical Systems, Milwaukee, Wis) with contiguous levels from lung apices to bases. Helical mode was performed with 10mm collimation, 1second scan time, 200-260mA and 120KVp in 10 patients. Thin section high resolution CT scan was performed with 1mm collimation, 10mm interval, 1second scan time, at 200mA and 140KVp in 1 patient. Low dose CT scan was done with 10mm collimation, 10 mm interval, 1second scan time, at 50mA and 120KVp in 1 patient. Intravenous contrast medium was injected in 9 patients. Total examination time was 15-25 minutes. The time between chest radiograph and CT scans of these patients were not longer than 21 days.

CT scans were reviewed on print film (n = 9) or Picture Archiving and Communication System (PACS) viewer (n = 3). The lung parenchyma window/level setting were -600HU/1,800HU for helical CT, -700HU/1,500HU for thin section high resolution CT, -600HU/1,800HU for low dose CT. For the purpose of CT imaging analysis, nodule was defined as focal nodular opacity, with diameter between 0.7 to 3cm. Mass was defined as focal opacity larger than 3cm. Micronodule was used for multiple nodules less than 7mm [5]. “Halo sign” was used as a halo of ground-glass opacity surrounding a nodule or a mass.

The differences of the CT findings between immunocompetent and immunocompromised patients were analyzed. The chi square was used to obtain the p values, and p<0.05 was defined as statistically significant.

RESULTS

The findings of CT included consolidation (n=1), nodule (n=10), mass (n=5), and micronodule (n=1), as listed in Table 1. They included nodule (n=2), mass (n=1), micronodule (n=1) in immunocompromised group of our patients. Eleven of them were subpleural location and one of them was random distribution. Three of them were bilateral location and nine were unilateral location. They were lower lobe distribution in eight patients, upper lobe in one case, both upper and lower lobes distribution in three patients. The numbers of the nodules were one nodule in five patients, two nodules in two patients, three nodules in one patient, five nodules in one patient, and more than five nodules in three patients. Two patients of immunocompromised group had more than five nodules. The margin of the nodules were ill-defined (n = 7) (Fig. 1), spiculated (n = 7) or lobulated (n = 4). Both nodules and masses were presented in five patients. They were in the same lobe in three patients. The numbers of the masses were one in all five patients. Air-bronchogram was revealed in six patients including one consolidation (Fig. 2), two nodules, and three masses. It presented in two patient of immunocompromised group. Halo sign were detected in four patients of nodules, one patient of nodules and masses (Fig. 3), and one patient of consolidation. It was found in one patient of immunocompromised group. There were three patients with cavity formation including one

<table>
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<th>Table 1. Comparison of the CT findings of 12 patients:</th>
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<td>Group1 (n = 9)</td>
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<td>Pattern</td>
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* group 1: immunocompetent patients
  group 2: immunocompromised patients
patient of micronodule (Fig. 4) in immunocompromised group, one patient of nodule and one patient of mass in immunocompetent group. No pleural effusion was detected. There was only one patient with enlarged mediastinal lymph nodes in immunocompetent group. The CT presentation of three immunocompromised patients were micronodule with cavitation, more than five ill-defined and spiculated nodules with halo sign, five nodules and one mass with ill-defined and spiculated margin respectively. The comparison of the CT findings between immunocompetent and immunocompromised patients were summarized in table 1. No significant statistical difference was observed in the CT findings of two groups.

**DISCUSSION**

The characteristic features of Cryptococcus neoformans are variation of size and shape of the yeast cells, single and narrow-based budding and mucia-
It distributes worldwide especially in pigeon-droppings contaminate soils. After inhaling to pulmonary system, it can transmit via blood stream to many organs including brain and meninges [1]. Cryptococcosis may present different microscopic appearance related to the host’s immune status. In immunocompetent patients, granulomatous inflammatory reaction with composition of histiocytes, multinucleate giant cells and mononuclear cells (Fig. 5) is found. In immunocompromised patients, the organisms transit through the alveolar septae with none to minimal granulomatous inflammatory reaction [6].

It usually happens in adult male. Although the organisms exist in pigeon drops, repeat exposure to pigeon does not mean more chance to get infection. Most of the pulmonary cryptococcosis is asymptomatic and subclinical. The symptomatic cases are frequently due to immune problems. There are some predisposing
factors for symptomatic cryptococcosis including acquired immune deficiency syndrome, reticuloendothelial disease, organ transplantation, and corticosteroid treatment. It rarely occurs in immunocompetent subject. The symptoms of the clinical cases include cough, chest pain, sputum production, body weight loss, fever, hemoptysis, dyspnea and night sweats. Headache presents in immunocompromised cases with dissemination to central nervous system. The mostly frequent clinical presentations are cough, chest pain, sputum production or asymptomatic [7].

The radiologic findings of pulmonary cryptococcosis are three patterns including one or more spherical nodules or mass, one or more areas of patchy consolidation, multiple small nodules or irregular shadows. Hilar and mediastinal lymphadenopathy, pulmonary cavitation and pleural effusion are uncommon and mostly occur in immunocompromised patients [3, 4].

The CT findings of pulmonary cryptococcosis are limited in articles. Nodules of various number were the common imaging findings. It presented in 10 (83%) of our study in comparison 91% in Zinck et al [8], 90% in Lindell et al [9]. Multiple nodules (77%) were more common than single nodule (23%) in Lindell et al [9], as in our study (70%; 30%). The margin of the nodules could be ill-defined, spiculated or lobulated. None of the nodules of our patients showed smooth margin, in comparison with the 77% in the study of Lindell et al [9]. Five cases of masses and one case of consolidation were found. Low incidence of nodules and high incidence of consolidation in immunocompromised patient were noted in Lacomis et al [10]. Micronodule were presenting in one patient of immunocompromised group. Air-bronchogram presented in six, halo sign in six, cavity formation in three of all patients were seen. “Halo sign” means granulomatous inflammation adjacent to the nodule [7]. It was found in 6 (50%) of our patients, which is slightly higher than the 40% in the study of Zinck et al [8]. Eleven of them were subpleural location. Unilateral location (75%) was more than bilateral location. Lower lobe distribution (66%) higher than others. No lobar predilection was found in the studies of Zinck et al and Lacomis et al [8,10]. Middle and upper lung predominance was noted in the study of Lindell et al [9]. No case of pleural effusion in all patients and only one patient of enlarged mediastinal lymphadenopathy were found in immunocompetent group. Low incidence of consolidation, lymphadenopathy, pleural effusion and cavitation were noted in the study of Lindell et al [9], which were accordant to our study. No significant difference in imaging findings between immunocompetent and immunocompromised groups of our study, which is more similar to the result of Lindell et al [9], but not that of Lacomis et al [10]. It might be due to that the percentage of immunocompetent group is much larger than immunocompromised group in our study.

The diagnosis of pulmonary cryptococcosis is difficult because the organisms frequently colonized in the upper airway and both the symptoms and radiological manifestation are non-specific [6]. The diagnosis of pulmonary cryptococcosis can be made by smear or culture of sputum or bronchial washing or CSF, transthoracic biopsy, serum or CSF antigen [2]. Serum antigen is usually normal except for patient with disseminated disease [4].

Most patients of pulmonary cryptococcosis can resolve Spontaneously and no treatment is indicated. In immunocompromised patient, treatment with oral fluconazole for 6-8 weeks is warrant [110].

There are some limitation in our study. The patient group is too small to make a significant result. It is hard to define the difference between the CT pictures of immunocompromised and immunocompetent groups. Not all of our patients were proved by pathologic specimen. Three of them were diagnosis as pulmonary cryptococcosis by serum antigen or bronchoalveolar lavage culture or CSF culture or blood culture. Since this was a retrospective study, the protocols of the CT scans were not uniform and not all of our cases underwent contrast enhancement.

In conclusion, the clinical picture of pulmonary cryptococcosis is non-specific. Therefore familiarity with the CT findings can help make the diagnosis of pulmonary cryptococcosis earlier and easier. .

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肺部隱球菌肺炎之電腦斷層影像表徵：
十二個病例研究報告

李紋瑜1,4 吳錦桐2,4 鄭慶明1,4 徐志育2,4 劉榮森3,4 王永成1,4 吳昭瑩1
張筱筠1,4 黃永堅1 楊展明1,4 孔慶惠1,4

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肺部隱球菌肺炎好發於免疫不足之病人，這是一種沒有菌絲的芽體真菌生長於土壤及鴨子
翼便中，其罕見於免疫完備的病人。本文之目的在於分析肺部隱球菌肺炎於免疫不足及免疫完備
的病人之電腦斷層影像。

閱檢 12 個已證明為肺部隱球菌症之病例，其電腦斷層發現為一個或多個結節（個數為十），
一個或多個塊（個數為五），無數個小結節（個數為一）或肺實質化（個數為一），好發於近肋
膜處（個數為十一）及下肺葉。（個數為八）。結節其邊緣為不明顯（個數為七），針刺狀（個
數為七）及小葉狀（個數為四）。其中有一些有空氣氣管圍（個數為六），毛玻璃狀（個數為六）
及空腔（個數為三）。

由於肺部隱球菌肺炎的無特殊臨床表徵，所以熟悉電腦斷層之表現，可以使肺部隱球菌肺炎
之診斷更加容易，更加有效率。

關鍵詞：隱球症；電腦斷層；肺