Comparative analysis of patients with chronic pulmonary aspergillosis and invasive pulmonary aspergillosis: a ten-year retrospective study

Jasper Fuk-Woo Chan[1,2,3,4,*], Susanna Kar-Pui Lau[1,2,3,4], Sally Cheuk-Ying Wong[2], Kelvin Kai-Wang To[1,2,3,4], Ivan Fan-Ngai Hung[3,5], Vincent Chi-Chung Cheng[2], Kwok-Yung Yuen[1,2,3,4], and Patrick Chiu-Yat Woo[1,2,,3,4]

[1]State Key Laboratory of Emerging Infectious Diseases, [2]Department of Microbiology, [3]Research Centre of Infection and Immunology, [4]Carol Yu Centre for Infection, [5]Department of Medicine, The University of Hong Kong, Queen Mary Hospital, HKSAR, China. (*Correspondence: Jasper F. W. Chan. Email: jfwchan@hku.hk. Tel: (852) 22554892. Fax: (852) 28551241.)

Objectives: Chronic pulmonary aspergillosis (CPA) is considered as a "semi-invasive" form of pulmonary aspergillosis that occurs in patients with chronic lung disease or mild immunosuppression. A major limitation of published studies on CPA is the lack of direct and systematic comparison of the characteristics of CPA with those of invasive pulmonary aspergillosis (IPA) in patients from the same population over a unified study period. Thus, their comparative epidemiological, clinical, radiological, mycological, and prognostic characteristics remain incompletely understood. Misdiagnosis of IPA as CPA may occur in patients without classical risk factors, especially critically ill patients in the intensive care unit and patients with chronic obstructive pulmonary disease. We therefore conducted this 10-year retrospective cohort study to compare the characteristics of CPA with those of IPA in hospitalised patients at a tertiary referral center in Hong Kong.

Methods: The case records of hospitalised patients diagnosed with CPA and IPA (using previously described diagnostic criteria) at Queen Mary Hospital, Hong Kong, between 1 July 2003 and 30 June 2013 were reviewed. For IPA, only patients with proven, probable, or probable IPA without prespecified radiologic findings were included. Their characteristics and outcome were recorded into a predefined database and compared.

Results: A total of 29 and 51 patients with CPA and IPA respectively were included. The CPA group was significantly older than the IPA group (p<0.001). Significantly more patients in the CPA group had past pulmonary tuberculosis, chronic lung diseases, silicosis, and/or bronchiectasis (p<0.001-0.008). The presenting symptoms differed significantly, with the CPA group having weight loss and predominantly respiratory symptoms including cough, sputum, and haemoptysis, while the IPA group often had fever with minimal respiratory symptoms and weight loss (p<0.001-0.004). The CPA group had higher lymphocyte count, haemoglobin level, platelet count, and globulin level, and lower total bilirubin, sodium, and urea levels (p<0.001-0.034).

Fig 1. Kaplan-Meier survival curves for CPA and IPA through one year after admission

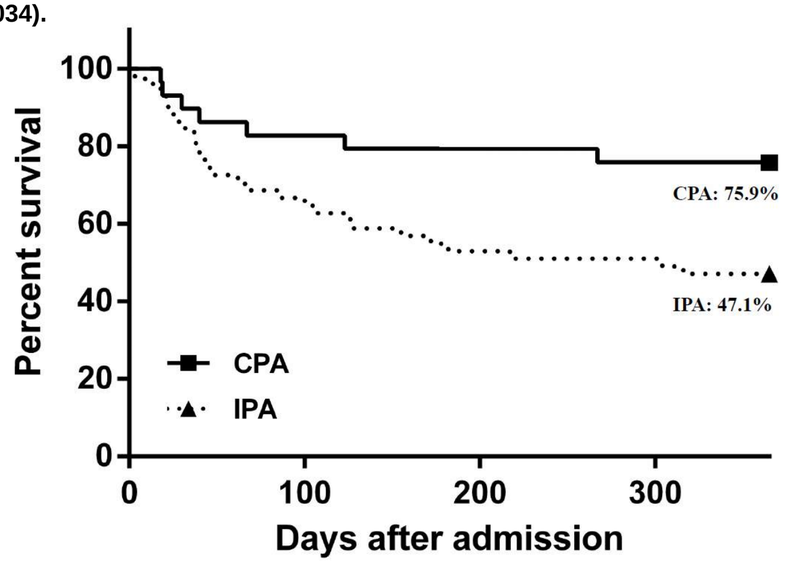

Table 1. Significant differences between patients with CPA & IPA

Variable	CPA (n = 29)	IPA (n = 51)	*P* (CPA vs IPA)
Age, years	64 (7-83)	51 (7-82)	<0.001
Underlying medical conditions:			
Previous pulmonary tuberculosis	20 (69.0)	5 (9.8)	<0.001
Chronic lung disease	23 (79.3)	14 (27.5)	<0.001
COPD	12 (41.4)	1 (2.0)	<0.001
Silicosis	6 (20.7)	1 (2.0)	0.008
Corticosteroid or immunosuppressants	1 (3.4)	36 (70.6)	<0.001
Chemotherapy	0 (0.0)	14 (27.5)	0.001
Haematological malignancy	0 (0.0)	27 (52.9)	<0.001
HSCT	0 (0.0)	20 (39.2)	<0.001
SOT	0 (0.0)	13 (25.5)	0.003
Presenting symptoms:			
Fever	8 (27.6)	39 (76.5)	<0.001
Cough	21 (72.4)	21 (41.2)	0.010
Sputum	18 (62.1)	11 (21.6)	0.001
Haemoptysis	12 (41.4)	6 (11.8)	0.004
Weight loss	7 (24.1)	0 (0.0)	<0.001
Duration of hospitalisation, days	19.0 (1.0-150.0)	38.0 (1.0-177.0)	0.031
Antifungal treatment:			
Use of antifungal drugs	29 (100.0)	41 (80.4)	0.011
Laboratory parameter			
Lymphocyte count, × 10^9 cells/L	1.3 (0.3-3.1)	0.4 (0.0-14.9)	<0.001
Haemoglobin, g/dL	11.4 (8.6-16.0)	10.2 (7.0-14.8)	0.001
Platelet count, × 10^9 cells/L	292.0 (37.0-731.0)	115.0 (4.0-598.0)	<0.001
Sodium, mmol/L	135.0 (126.0-150.0)	139.0 (128.0-153.0)	0.001
Globulin, g/L	43.0 (27.0-73.0)	30.0 (12.0-78.0)	<0.001
Total bilirubin, μmol/L	7.0 (3.0-33.0)	14.0 (2.0-103.0)	<0.001
CXR:			
Cavitary lesion(s)	19 (65.5)	8 (15.7)	<0.001
Consolidation or collapse	10 (34.5)	31 (60.8)	.036
Fibrosis	13 (44.8)	7 (13.7)	<0.001
Thoracic CT scan:			
Cavitary lesion(s), halo or air-crescent sign	26 (100.0)	12 (37.5)	<0.001
Fibrosis	14 (53.8)	6 (18.8)	<0.001
Mycological investigations:			
Serum anti-*Aspergillus* antibody	11 (45.8)	3 (7.1)	<0.001

Results: Cavitary lesion and consolidation/collapse were the most common findings in both CXR and thoracic CT scan in the CPA and IPA groups respectively. Only around one-third of the IPA group had the classical findings of cavitary lesion, halo and/or air-crescent signs. Fibrosis was more commonly found in the CPA group in both CXR and thoracic CT scan (p<0.001). The seropositive rate of anti-*Aspergillus* antibody was significantly higher in the CPA group (p<0.001). Nearly one-tenth of the culture-positive CPA patients had >1 species isolated from respiratory tract specimens. More patients in the CPA group received antifungal treatment (p=0.011). The duration of hospitalisation was significantly shorter in the CPA group (p=0.031). Significantly more patients in the IPA group died at one year after admission (p=0.019).

Conclusion: The comparative characteristics of patients with CPA and IPA were identified. The outcome of patients with CPA supported the notion that it was a "semi-invasive" form of pulmonary aspergillosis.