OCCURRENCES OF CRYPTIC *ASPERGILLUS* SPECIES AND *TALAROMYCES SPP* IN SEVERE CHRONIC PULMONARY ASPERGILLOSIS PATIENTS FROM INDONESIA: A CASE SERIES

Anna Rozaliyani[1,2],* Findra Setianingrum [1,2], Asriyani Abdullah[1,3], Sresta Azahra[1,3], Ayu Eka Fatril[1], Harmi Rosianawati[4], Erlina Burhan[2,4], Diah Handayani [2,4], Mulyati Tugiran [1,2], Robiatul Adawiyah [1,2], Ridhawati Syam [1,2], Retno Wahyuningsih [2,5] ,Heri Wibowo [1,2], Chris Kosmidis [6] and David W Denning [6]

[1]Department of Parasitology, Faculty of Medicine, Universitas Indonesia;[2]Indonesia Pulmonary Mycoses Centre;[3]Magister Program of Biomedical Sciences, Faculty of Medicine, Universitas Indonesia;[4]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia;[5]Persahabatan National Respiratory Referral Hospital;[6]Department of Parasitology, Faculty of Medicine, Universitas Kristen Indonesia;[7]Manchester Academic Health Science Centre, Division of Infection, Immunity and Respiratory Medicine, Faculty of Biology, School of Biological Sciences, Medicine and Health, University of Manchester

INTRODUCTION

Aspergillus and *Talaromyces* are two closely related genera with diverse important species potentially causing disease in human. *Aspergillus fumigatus* is the most common species known as the etiological cause of chronic pulmonary aspergillosis. Indonesia is included as the endemic area of *Talaromyces spp*. However, studies on the clinical spectrum and molecular profiles of cryptic species of *Aspergillus* and *Talaromyces spp* are limited.

OBJECTIVE

This study's aim was to describe the clinical and radiological features, and molecular profiles of fungi isolated from severe chronic pulmonary aspergillosis (CPA) patients.

RESULTS

- In total, four cases of *Talaromyces spp* were identified, three of them mixed with cryptic *Aspergillus* species. Patient's age ranged from 42 to 75 years; all males were included. All patients were admitted to hospital with severe symptoms. Three patients had acute or massive haemoptysis and one patient had dyspnea with oxygen desaturation.
- History of previous tuberculosis was present in all patients. One patient with history of multi drug resistant TB was admitted to the emergency room with severe anemia (Hb: 5g/dL). This patient showed positive culture from sputum (*Aspergillus fumigatus*, *A. tubingensis*, and *Talaromyces spp*).
- Another patient had an aspergilloma proven by chest CT (figure 1 &2) and presented with acute haemoptysis and positive fungal culture (*A. aculeatus* and *Talaromyces spp*). Radiological deterioration was observed in this patient with massive pleural effusion. The morphology identification had previously identified the cryptic species as *A. niger.*
- The *Aspergillus* IgG antibody was positive in three patients (75%) including one patient with only *Talaromyces spp* detected in the culture. Other chronic diseases in the patients were uncontrolled diabetes, chronic obstructive pulmonary disease, and hypertension

Table 1. Clinical profile patients with CPA

No	Age/Sex	Duration TB to CPA (month)	Name of symptoms	Radiology findings	Fungal Identificaions	Other Diseases
1	42/M	12	cough, massive haemoptysis	Cavity, nodul, fibrosis	*A. fumigatus, A. tubingensis, Talaromyces spp.*	Anemia, uncontrolled diabetes mellitus
2	75/M	96	dyspnea, productive cough	Cavity, pericavitary fibrosis, pleural thickening, bronchiectasis, nodule, fibrosis, infiltrates	A. *aculeatus, Talaromyces spp*.	COPD, hypertension
3	55/M	18	cough, fatigue	Multiple cavities, aspergilloma, consolidation, fibrosis, infiltrates	*A. aculeatus, Talaromyces spp*.	Anemia, uncontrolled diabetes mellitus
4	56/M	6	cough, haemoptysis, fatigue	Cavity, infiltrates	T*alaromyces spp.*	None

METHODS

We reviewed the culture collection of CPA patients with positive *Talaromyces spp* cultures from Parasitology Department, Universitas Indonesia from 2018-2020. Demographic, clinical features and radiological data were assessed from medical records. The species identity of isolates was determined by combined analysis of morphology of the colonies (*Talaromyces spp*), and the sequencing of ITS and beta-tubulin genes (*Aspergillus spp*). The *Aspergillus* IgG were measured using point-of-care test (immunochromatography, LDBio, France).

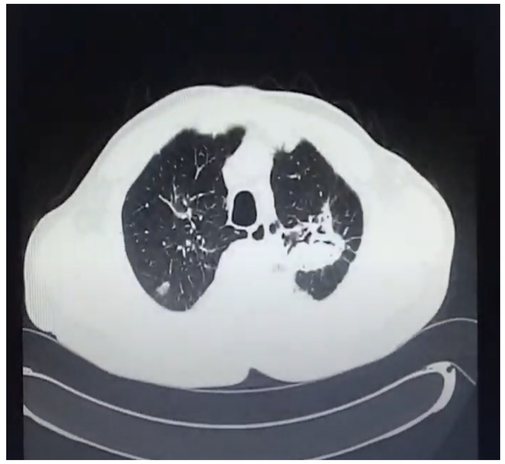

Figure 1. The CT scan of patient no.3 showed multiple cavities, an aspergilloma, consolidation and infiltrates.

CONCLUSION

This study demonstrates the clinical importance of cryptic and endemic fungi in CPA cases. Molecular identification offers precise identification of fungi to species level. Further study is required to assess the susceptibility profile of cryptic *Aspergillus* and the significance of *Talaromyces spp* towards better diagnosis and management of lung mycoses cases in Indonesia