

## A Patient With Allergic Bronchopulmonary Mycosis Caused by *Aspergillus fumigatus* and *Candida albicans*

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### ABSTRAK

*Mikosis Bronkopulmonar Alergi (MBA) merupakan respons imunologi tubuh yang berlebihan terhadap kolonisasi jamur di saluran napas bawah. Penyakit ini dapat disebabkan oleh berbagai jenis jamur; namun Aspergillus fumigatus merupakan penyebab yang paling sering dijumpai. Meskipun demikian, jenis jamur selain Aspergillus fumigatus dan organisme jamur lainnya seperti Candida albicans ternyata juga turut menyebabkan MBA. Aspergillus fumigatus dan Candida albicans dapat dijumpai di dalam dan di luar ruangan dan menyebabkan sensitisasi dan stimulasi patologi penyakit dan manifestasi klinisnya. Sejumlah prosedur diagnostik dapat digunakan untuk mendukung penegakan diagnosis MBA yang disebabkan oleh Aspergillus fumigatus dan Candida albicans.*

*Artikel ini membahas satu kasus mikosis bronkopulmoner yang disebabkan oleh Aspergillus fumigatus dan Candida albicans pada pria berusia 48 tahun. Pasien diobati dengan antijamur, kortikosteroid dan antibiotik untuk infeksi bacterial sekunder. Kondisi pasien membaik tanpa mengalami efek samping yang berarti.*

**Kata kunci:** mikosis bronkopulmonar alergi, *Aspergillus fumigatus*, *Candida albicans*.

### ABSTRACT

*Allergic Bronchopulmonary Mycosis (ABPM) is an exaggerated immunologic response to fungal colonization in the lower airways. It may cause by many kinds of fungal, but Aspergillus fumigatus is the most common cause of ABPM, although other Aspergillus and other fungal organisms, like Candida albicans, have been implicated. Aspergillus fumigatus and Candida albicans may be found as outdoor and indoor fungi, and cause the sensitization, elicitation of the disease pathology, and its clinical manifestations. Several diagnostic procedures may be implicated to support the diagnosis of ABPM caused by Aspergillus fumigatus and Candida albicans.*

*A case of allergic bronchopulmonary mycosis caused by Aspergillus fumigatus and Candida albicans in a 48 year old man was discussed. The patient was treated with antifungal, corticosteroids, and antibiotic for the secondary bacterial infection. The patient's condition is improved without any significant side effects.*

**Key words:** allergic bronchopulmonary mycosis, *Aspergillus fumigatus*, *Candida albicans*.

## INTRODUCTION

Allergic bronchopulmonary mycosis is a condition characterized by an exaggerated response of the immune system to fungus, most commonly *Aspergillus fumigatus*, and other fungal organisms, like *Candida albicans*.<sup>1,2</sup> Infection by *Aspergillus fumigatus* and *Candida albicans* are classified into opportunistic fungal infection, commonly happened in immunocompromised patients.<sup>3</sup> The one caused by *Aspergillus fumigatus* is called by Allergic Bronchopulmonary Aspergillosis (ABPA), and the one caused by *Candida albicans* is called by Allergic Bronchopulmonary Candidiasis (ABPC), but some authors prefer the term allergic bronchopulmonary Mycosis, considering that, in addition to *Aspergillus fumigatus*, other fungi, such as *Candida albicans*, can also colonize in the bronchi.<sup>4</sup>

Infections by *Aspergillus fumigatus* and *Candida albicans* are classified into opportunistic fungal infections that happened to immunocompromised persons. Sandhu RS, et al<sup>5</sup>, in 1979 reported 20 cases of ABPA and 13 cases of ABPC respectively with one case both of them. Donnelly SC, et al<sup>6</sup>, in Ireland during 1985-1988, reported 14 cases of ABPM and ABPC constitutes a higher proportion than previously considered.

*Aspergillus fumigatus* is a saprophytic fungus and its natural ecological is the soil, wherein it survives and grows on organic debris. It is one of the most ubiquitous of those with airborne conidia that released into the atmosphere in diameter small enough (2 to 3  $\mu\text{m}$ ) to reach lung alveoli, and it needs an extreme exposures of conidia to create lung disorders up to  $5 \times 10^3/\text{m}^3$ .<sup>7</sup> *Candida albicans* is a commensal microorganism, especially on the skin, oral cavity, feces, and vagina. In immunocompromised persons, *Candida albicans* will spread to many organs. In the lung, candidiasis almost all happens hematogenously.<sup>8-9</sup>

Several diagnostic procedures have been implicated to support the ABPM. They are: chest X-ray, direct microscopic examination and culture of samples from the body, antigen detection, and serologic examinations especially antibodies against the fungal organisms.<sup>2</sup>

The treatment of ABPM aims to treat acute exacerbations of the disease and to limit progressivity of the disease. It includes antifungal

agents and also corticosteroids.<sup>10</sup>

Reported below is a case of 48 year old man with ABPM caused by *Aspergillus fumigatus* and *Candida albicans*, with the main complaint difficulty of breathing.

## CASE ILLUSTRATION

A 48 year old man came from Ternate, North Mollucas, to our clinic with main complaint difficulty of breathing since 3 month ago, accompanied by coughing with lots of brown yellowish sputum. He had a routine control for this complaint by medical doctors at Ternate who told him that he had pulmonary infection and gave him medications with antibiotics. The complaint was getting worse in a month before, accompanied by 1 episode of fever. He never had any specific therapy for lung tuberculosis before and he only took routine medication for his hypertension. He was only one who felt this complaint in his family.

He worked as teacher at an elementary school and lived in a small house in a crowded area. His house had many broken ceilings and moist walls since water came into his house everytime the rain was falling down.

On the clinic, the patient was fully conscious, blood pressure 160/90 mmHg, pulse rate 106 x/minute regularly, respiratory rate 28 x/minute, regular and symmetrically, the body temperature 36.6°C, and the body weight 65 kg. The chest examination revealed ronchi and wheezing on auscultation especially at the middle region. The other parts of the body were in normal limit.

The early laboratory examination in Manado, demonstrated his hemoglobin 12.6 g/dL, WBC 12,900/ $\mu\text{L}$ , platelet count 238,000/ $\mu\text{L}$ , MCV 82 fL, MCH 29 pg, MCHC 33.3%, fasting blood sugar 80 mg%, AST 23 U/L, ALT 21 U/L, blood ureum 20 mg%, serum creatinine 0.7 mg%, Widal test positive (titer anti O 1/160 and anti H 1/320), and urinalysis was in normal limit. Electrocardiogram (ECG) was found normal. In the chest X-ray, there were dilatated central bronchi, infiltrates with massive bilateral consolidation, suggested a pulmonary tuberculosis with pulmonary mycosis as the differential diagnosis (**Figure 1A**).

Based on all clinical data above, the patient was suspected to have bronchial asthma with secondary bacterial infection with pulmonary tuberculosis and pulmonary mycosis as

differential diagnosis, typhoid fever, and stage II hypertension. The patient was treated with levofloxacin 500 mg once daily for the secondary infection in the lungs and typhoid fever, ambroxol tablet three times daily and acetensa tablet 100 mg once daily. The eosinophyl count and serum total IgE, sputum microscopic examination and cultures-sensitivity for acid fasting bacteria (three times), other bacterias, and fungal were planned.

On the 10th day of the treatment, the patient returned to the clinic. He felt a slight reduction in the difficulty of breathing with cough and white sputum. The patient was fully conscious, blood pressure 130/80 mmHg, pulse rate 90 x/minute regularly, respiratory rate 24 x/minute, regular and symmetrically, the body temperature 36.6°C. The chest examination still revealed ronchi and wheezing on auscultation especially at the middle region. Additional examination results were: Peak Expiratory Flow (PEF) was 0.290 L (predicted 0.350-0.550 L), absolute eosinophil count  $0.61 \times 10^3/\mu\text{L}$  (normal  $0.045\text{--}0.44 \times 10^3/\mu\text{L}$ ), total serum IgE 223 IU/mL (normal 0-100 IU/mL), the microscopic examination was positive for *Staphylococcus* spp. and fungal hyphae, the culture-sensitivity examination was positive for *Aspergillus fumigatus*, *Candida albicans*, and *Staphylococcus aureus* that still sensitive to levofloxacin (**Figure 2**). Skin sensitivity test was positive for immediate and late phase reactions to aspergillus and candida antigens. The patient was diagnosed to have allergic bronchopulmonary mycosis caused by *Aspergillus fumigatus* and *Candida albicans* with *Staphylococcus aureus* as secondary bacterial infection, typhoid fever, and drug controlled hypertension. The patient received treatments with levofloxacin tablet 500 mg once daily for one week more, methylprednisolone tablet 4 mg three times daily for 2 weeks continued by alternate day, Fluconazole tablet 150 mg once weekly, inhalation of budesonide 80 mcg together with formoterol fumarate 4.5

mcg two puffs three times daily, ambroxol tablet 30 mg three times daily, and acetensa tablet 100 mg once daily for three weeks. A chest X-ray for comparison to the first one was planned.

Three weeks after the last visit, the patient visited the clinic again and bring the new chest X-ray for comparison. He felt much better than before, the difficulty of breathing was reduced only when he took the methylprednisolone tablet and the cough was sometime still remain accompanied by a little white sputum. The physical examination on the chest still revealed a little ronchi on both side especially at the middle region. The PEF was 0.370 L (predicted 0,350-0,550 L). On the chest X-ray, comparing to the first one, we found progressivity of the infiltrates (**Figure 1B**). The treatment with levofloxacin and Fluconazole as antifungal agent was discontinued and changed with Itraconazole tablet 200 mg once daily for two weeks. The other treatments were continued and the comparing chest X-ray was planned after 4 weeks of treatments. The patient was told to make some restoration on his house, especially the broken ceilings and the moist walls.

Four weeks after the last visit, the patient visited the clinic again and bring the new chest X-ray for comparison. He only took methylprednisolone tablet if he felt the difficulty of breathing. He felt much better than before, the difficulty of breathing was minimal, but he had cough accompanied by a yellow sputum. The physical examination on the chest still revealed a little ronchi on both side especially at the middle region. On the chest X-ray, comparing to the first one, we found restoration on both side of lungs, especially at the superior lobes (**Figure 1C**). A bacterial culture and drug resistant test from sputum was done, and the result is *Pseudomonas aeruginosa* which was still sensitive to amikacin, amoxicillin, cefoperazone, chloramphenicol, gentamycin, kanamycin, ofloxacin, tetracycline, cephalixin, and azythromycin. ceftriaxone.

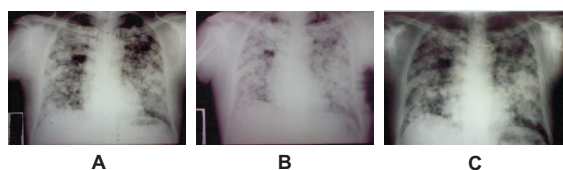


**Figure 1.** The patient's chest X-ray. A). Before treatment; B). After 3 weeks of treatment with fluconazole; C). After 4 weeks of treatment with itraconazole

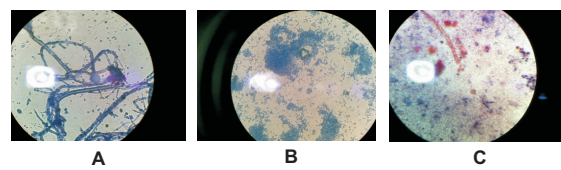


**Figure 2.** The microscopic examination from sputum culture. A). *Aspergillus* spp.; B). *Candida albicans*; C). *Staphylococcus aureus*

The treatment with Itraconazole was continued and we gave amikacin injection 500 mg intramuscular for 5 consecutive days for the bacterial infection. On the 5th day, the patient felt much better and the treatment with Itraconazole was continued together with levofloxacin tablet 500 mg for 10 days, and the comparing chest X-ray was planned after 4 weeks of treatments.

## DISCUSSION

Allergic Brochopulmonary Mycosis is a lung disease caused by immunologic responses to multiple antigens from fungal colonize the bronchi such as *Aspergillus fumigatus*, *Candida albicans*, and other kind of fungus, and they can produce a similar immune response in immunocompromised persons with genotype of HLA-DR2 and or HLA-DR5. Most fungal's reproduction is asexual way by forming conidia (asexual spores). The conidia is inhaled into the lungs (alveolus), then it will grow and forming the accumulated hyphae.<sup>1-4</sup>

The fungal cell wall consists of various antigenic molecules. *Aspergillus fumigatus* has many antigenic molecules at its cell wall, but the stronger antigenic properties are Asp f 1, Asp f 2, Asp f 4, and Asp f 6, meanwhile *Candida albicans* has mannans as antigenic molecule and complement receptors.<sup>11</sup> The body's immune system, both innate and adaptive immune systems, will react to these antigens. In the innate immune system, defensins have antifungal as well antibacterial, and collectin surfactant proteins A and D can bind, aggregate, and opsonize fungi for phagocytosis, by neutrophils

and macrophages through degranulation and release of toxic materials onto large indigestible hyphae or ingestion of yeast or conidia.<sup>12,13</sup> Toll-Like Receptor (TLR2 and TLR4/CD14) family also plays important role along with mannose receptor. *Candida albicans* mannan via TLR4 will induce proinflammatory chemokine responses, where as the ligation of candidal phospholipomannan and glucans with TLR2/dectin-1 generates a strong IL-10 response, which may inhibit immune response.<sup>13-15</sup> In adaptive immunity against fungal infection, T cells and macrophage activation play protective role and lead to high titer of fungal specific IgE, IgG, IgM, IgA, and C3 (type I, III, and IV hypersensitivity) (Figure 3).<sup>16-18</sup>

Almost all patient with ABPM caused by *Aspergillus fumigatus* and *Candida albicans* have clinical asthma, even cough variant asthma or exercise-induced asthma, usually present with episodic wheezing, expectoration of sputum containing brown plugs, pleuritic chest pain, reduction in lung function, and fever.<sup>19</sup> The patient in this case had difficulty of breathing since 3 month ago, accompanied by coughing with lots of brown yellowish sputum, reduction in lung function (reduced value of PEF) and an episode of fever.

Additional examinations that may be done to support ABPM caused by *Aspergillus fumigatus* and *Candida albicans* as the diagnosis are: the lung function measurement, chest x-ray, direct microscopic examination and culture of samples from the body, antigen  $\beta$ -glucan from the funggal cell wall in the serum or using Polymerase Chain

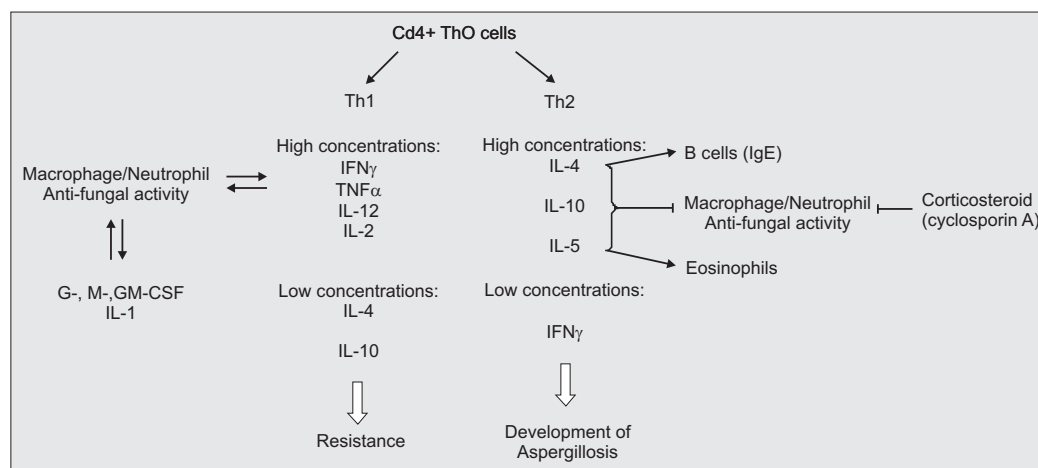


**Figure 3.** Adaptive immune response to *Aspergillus* infection

Reaction (PCR) technology, specific IgE and IgG level as serologic examinations, and skin sensitivity test using *Aspergillus* and *Candida* antigens.<sup>19</sup> In the chest x-ray, we may find perihilar infiltrates, air-fluid levels from dilated central bronchi filled with fluid and debris, massive consolidation that may be unilateral or bilateral, roentgenographic infiltrates, “toothpaste” shadows result from mucoid impactions in damaged bronchi, “gloved-finger” shadows from distally occluded bronchi filled with secretions, and “tram-line”, which are two parallel hairline shadows extending out from the hilum.<sup>2</sup> The patient in this case had better PEF value after took corticosteroid, dilated central bronchi, infiltrates with massive bilateral consolidation on the chest X-ray and new one after took three weeks of treatment was worse comparing to the first one, elevation on IgE level reflecting type I hypersensitivity to the fungal infection, positive microscopic examination for *Staphylococcus* spp. and fungal hyphae, positive culture-sensitivity examination for *Aspergillus fumigatus*, *Candida albicans*, and *Staphylococcus aureus* that still sensitive to levofloxacin, positive skin sensitivity test for immediate and late phase reactions to *aspergillus* and *Candida* antigens, and leucocytosis probably caused by *Staphylococcus aureus* as secondary bacterial infection. The type IV hypersensitivity could not be proved since we did not do the intra-cutaneous test with *Aspergillus* and *Candida* allergen, which might show the delayed reaction after 48-72 hours. We did not do other kind of examinations because we had facility limitations.

Since there was no published criteria for ABPM, in this case we had used diagnostic criteria similar to that of ABPA and ABPC: asthma, chest roentgenographic infiltrates, immediate cutaneous reactivity to the fungus, elevated total serum IgE concentration, elevated serum IgE-Af and/or IgG-Af antibodies, serum precipitating antibodies to Af, proximal bronchiectasis, and peripheral blood eosinophilia. If six of these seven criteria are present, the diagnosis is almost certain.<sup>4</sup> In ABPA, based on clinical and radiological criteria, there are five stages have been identified: acute, remission, exacerbation, corticosteroid-dependent asthma, and end or fibrotic stage (**Table 1**).<sup>2,19</sup> The patient in this case had the asthma, chest roentgenographic infiltrates, elevated total serum IgE concentration,

immediate and late phase of cutaneous reactivity to *Aspergillus* and *Candida*, and peripheral blood eosinophilia. According to the ABPA stage, this patient was classified into stage IV, since the difficulty of breathing only reduced when he took corticosteroid (methylprednisolone).

**Table 1.** Stages of ABPA

| Stage | Description                     | Radiographic infiltrates                                            | Total serum IgE    |
|-------|---------------------------------|---------------------------------------------------------------------|--------------------|
| I     | acute                           | Upper lobes or middle lobe                                          | Sharply elevated   |
| II    | Remission                       | No infiltrate and patient off prednisone for >6 mo                  | Elevated of normal |
| III   | Exacerbation                    | Upper lobes or middle lobe                                          | Sharply elevated   |
| IV    | Corticosteroid-dependent asthma | Often without infiltrates, but intermittent infiltrates might occur | Elevated or normal |
| V     | End stage                       | Fibrotic, bullous, or cavitary lesions                              | Might be normal    |

The goals of the treatment of ABPM caused by *Aspergillus fumigatus* and *Candida albicans* are to treat acute exacerbations of the disease and to limit progressivity of the disease. Based on the experience in adults asthma, the mainstay of therapy ABPM as well as ABPA is corticosteroids; the role of antifungal agents remain unclear.<sup>19</sup> Oral corticosteroids targeting the hypersensitivity, suppress the inflammatory response provoked by the fungal rather than eradicating the organism. The treatment with corticosteroids leads to the relief of bronchospasm, the resolution of radiographic infiltrates, and the reduction in serum total IgE and peripheral eosinophilia. Two weeks of daily therapy of oral corticosteroids, followed by gradual tapering, has been recommended.<sup>20</sup> Inhaled corticosteroids should be used in an effort to control asthma but one should not depend on them to prevent exacerbations.<sup>4</sup> Several studies have been done on the utility of the antifungal agents. The fungal cell wall consists of two important parts in the interaction with antifungal agents: chitin which is interacted with echinocandins and ergosterol which is interacted with amphotericin B and

azole based.<sup>10</sup> Itraconazole as antifungal agent also has antiinflammatory effects or delaying effect on corticosteroid elimination, and already reported reductions in daily corticosteroid use and clearance of *A. fumigatus*.<sup>4</sup>

The patient in this case received treatments with levofloxacin tablet 500 mg once daily for pulmonary secondary bacterial infection and typhoid fever, methylprednisolone tablet 4 mg three times daily for 2 weeks continued by alternate day, Fluconazole tablet 150 mg once weekly, inhalation of budesonide 80 mcg together with formoterol fumarate 4.5 mcg two puffs three times daily, ambroxol tablet 30 mg three times daily, and acetensa tablet 100 mg once daily for three weeks. Since there was a progressivity of infiltrates on the chest X-ray comparing to the first one. The antifungal agent was changed into Itraconazole tablet 200 mg once daily, since the there was progressivity on the patient's last chest X-ray and the patient had to take corticosteroid to relief the symptoms. Four weeks of treatment with Itraconazole, there was a restoration on the chest X-ray especially at the superior lobes of both lungs. The treatment with Itraconazole was planned for 2 until 5 months.

The early diagnosis and treatment are important. The importance of a patient achieving remission is that it prevents the progression to more severe stages of the disease. Symptomatic patients need treatment because of the risk of pulmonary fibrosis and central bronchiectasis, and patients should encouraged not to be overly pessimistic.<sup>21</sup> According to some authors, serologic ABPA can represent an initial stage of the disease. Therefore, it should be diagnosed and treated early, even before it develops central bronchiectasis, in order to reduce the chance of anatomical and functional pulmonary damage. Mortality in stage V can reach 100%. When the FEV1 was 0,8 L or less after aggressive initial corticosteroid administration, the outcome was poor.<sup>4</sup> The patient in this case was in stage<sup>4</sup>, since he felt better only when he took corticosteroid (methylprednisolone). The prognosis is dubia, since the patient was depending on corticosteroid to relief the symptoms and get the PEF in predicted value.

## CONCLUSION

A case of allergic bronchopulmonary mycosis caused by *Aspergillus fumigatus* and *Candida*

*albicans* in 48 year old man has been discussed. The patient received treatments with levofloxacin tablet 500 mg once daily for secondary bacterial infection and typhoid fever, methylprednisolone tablet 4 mg three times daily for 2 weeks continued by alternate day, Fluconazole tablet 150 mg once weekly and changed to Itraconazole tablet 200 mg once daily for 2 until 5 months, inhalation of budesonide 80 mcg together with formoterol fumarate 4.5 mcg two puffs three times. The patient in this case was in stage IV, and as long as he had an appropriate treatment, he could enter the remission stage without any chance to have progression of his disease.

## REFERENCES

1. Zeidler M, Kleerup EC, Roth MD. Immunologic disease of the lung. In: Adelman DC, Casale TB, Corren J, eds. Manual of allergy and immunology. 4th ed. Philadelphia: Lippincott; 2002. p. 138-64.
2. Greenberger PA. Allergic bronchopulmonary aspergillosis. In: Grammer LC, Greenberger PA, eds. Patterson's allergic diseases. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2009. p. 439-56.
3. Edman JC. Mikologi kedokteran. In: Brooks GF, Butel JS, Orston LN, Jawetz, Melnick & Adelberg, eds. Mikrobiologi kedokteran. 20th ed. Jakarta: EGC penerbit buku kedokteran; 1996. p. 608-42.
4. Gondor M, Michael MG, Finder JD. Non-aspergillus allergic bronchopulmonary in a pediatric patient with cystic fibrosis. *Pediatrics*. 1998;102:1480-2.
5. Sandhu RS, Metha SK, Khan ZU, et al. Role of aspergillus and candida species in AMPM: a comparative study. *Scan J Respir Dis*. 1979;60(5): 235-42.
6. Donnelly SC, McLaughlin H, Bredin CP. Period prevalence of allergic bronchopulmonary mycosis in a regional hospital outpatient population in Ireland 1985-88. *Ir J Med Sci*. 1991;160(9):288-90.
7. Kolstad HA, Brauer C, Iversen M, et al. Do indoor molds in nonindustrial environments threaten workers' health? A review of epidemiologic evidence. *Epidemiol Rev*. 2002;24:203-17.
8. Nieminen SM, Karki R, Auriola S, et al. *Appl Environ Microbiol*. 2002;68(10):4871-5.
9. Nasronudin. AIDS dengan manifestasi infeksi jamur. In: Barakbah J, Soewandjo E, Suharto, et al, eds. HIV & AIDS pendekatan biologi molekuler, klinis, dan sosial. 2nd ed. Surabaya: Airlangga university press; 2007. p. 203-15.
10. Zmeili OS, Soubani AO. Pulmonary aspergillosis: a clinical update. *Q J Med*. 2007;100:317-34.
11. Banerjee B, Greenberger PA, Fink JN, et al. Immunological characterization of Asp f 2, a major allergen from *aspergillus fumigatus* associated with allergic bronchopulmonary aspergillosis. *Infect Immun*. 1998;66:5175-82.
12. Brancoff GJ. Immunity to bacteria and fungi. In: Male D, Brostoff J, Roth DB, et al, eds. Immunology. 7th ed. Philadelphia: Mosby elsevier; 2006. p. 257-76.

13. Segal BH. Aspergillosis. *N Engl J Med*. 2009;360(18):1870-84.
14. Hohl TM, Feldmesser M. *Aspergillus fumigatus*: principles of pathogenesis and host defense. *Eukaryot Cell*. 2007;6(11):1953-63.
15. Kurup VP, Kumar A. Immunodiagnosis of aspergillosis. *Clin Micro Rev*. 1991;4:439-56.
16. Latge JP. *Aspergillus fumigatus* and aspergillosis. *Clin Micro Rev*. 1999;12:310-43.
17. Martinez JP, Gil ML, Ribot JLL, et al. Serologic response to cell wall mannoproteins and proteins of *Candida albicans*. *Clin Micro Rev*. 1998;11:121-41.
18. Jones JM. Laboratory diagnosis of invasive candidiasis. *Clin Micro Rev*. 1990;3:32-45.
19. Greenberger PA. Allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol*. 2002;110(5):685-92.
20. Denning DW, O'driscoll BR, Hogaboam CM, et al. The link between fungi and severe asthma: a summary of the evidence. *Eur Respir J*. 2006;27:615-26.
21. Kalil ME, Fernandez ALG, da Silva Ac, et al. Allergic bronchopulmonary aspergillosis presenting a glove-finger shadow in radiographic images. *J Bras Pneumol*. 2006;32(5):472-5.