Introduction

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* complex is the leading cause of death and diseases from a single infectious agent and continues to be a major global public health problem [1]. However, with early diagnosis and commencement of an appropriate treatment regimen, an estimated 58 (53–64) million lives globally have been saved from TB between 2000 and 2018 [1,2].

Are these lives saved forever?

In the last few decades, there has been a renewed interest in the study of the long-term outcomes of patients previously treated for TB [3,4]. In a recent meta-analysis, persons previously treated for TB were found to be 2 to 5 times more likely to die compared to the general population or matched controls [5]. The excess mortality among these individuals has been attributed to the increased risk of recurrent TB, as well as related communicable and noncommunicable diseases [3,5–7].

Pulmonary TB (PTB), the most common form of TB, causes extensive structural lung changes in more than two-thirds of the patients that persists after treatment despite microbiological cure of the active disease [8–10]. These residual changes can be categorized into parenchymal, airway disease, pleural/chest wall, vascular, and mediastinal pathologies, collectively referred to as post-TB lung disease (PTBLD) [3,8]. Infectious complications, including chronic pulmonary aspergillosis (CPA), is common in PTBLD [3,4].

How common is CPA after treated PTB?

CPA is a progressive respiratory syndrome that largely occur in immunocompetent or subtly immunocompromised individuals with underlying structural lung diseases, most commonly treated TB [11]. Residual cavities remain in between 20% to 40% of lungs of patients following treatment for PTB [12,13]. Cavitation and ectatic lesions in PTBLD allows saprophytic colonisation and growth of *Aspergillus* species following inhalation of infectious spores from the environment. This leads to expansion of the existing or creation of new cavities with associated parenchymal and pleural damage [11]. A complex mixture of *Aspergillus* hyphae, tissue debris, inflammatory cells, and mucus known as a fungal ball (aspergilloma) may form in these cavities [11].

The significance of treated PTB in the pathogenesis of CPA was established by a large cohort study across over 50 clinics in Great Britain in the mid- to late 1960s [14]. In this landmark study, 544 patients who had a persistent cavity of at least 2.5 cm in diameter and negative *M. tuberculosis* bacilli in their sputum for at least a year were studied. About 25% of the patients had positive *Aspergillus* precipitins (i.e., precipitating immunoglobulin M [IgM] and immunoglobulin G
[IgG] antibodies) in their serum, 14% had aspergillomas, and 10% had precipitins without evidence of an aspergilloma. Three years later, 34% had positive Aspergillus precipitins, 22% had aspergillomas, and 14% had precipitins alone. In more recent studies among patients previously or currently being treated for TB, up to 39% of whom had residual cavities, the prevalence of CPA ranged between 6.3% and 13.7% [13,15,16]. Among patients with CPA, treated PTB is the primary underlying respiratory condition in 17%–93% of the cases [12,17].

In high-burden TB countries, the proportion of CPA with TB as underlying condition is higher than low–TB-burden countries [12,17,18]. However, the precise burden of post-TB CPA remains unknown. Based on a deterministic model, the global burden of post-TB CPA was estimated at 1.2 million cases annually [19]. In this model, the prevalence rate ranged from <1 case per 100,000 population in the United States (low TB burden) compared to 42.9 per 100,000 in Nigeria (high TB burden) [19]. A similar mathematical modelling was performed to estimate the burden of CPA-complicating TB in India [20]. In this study, the annual incidence of CPA was estimated at between 27,000 and 170,000 cases given the very high TB incidence rate of 2.1 million cases [20].

It is important to note that most patients with CPA have multiple underlying lung conditions [12]. Other important non-TB underlying conditions include chronic obstructive pulmonary disease (COPD), fibrocystic sarcoidosis, pneumothorax, and other [12,21].

Why is CPA misdiagnosed as PTB?

CPA presents with chronic productive cough, systemic symptoms (weight loss, fatigue, fevers, etc.), haemoptysis, and chest pain [22]. These symptoms are clinically indistinguishable from those of PTB. Furthermore, progressive cavitation, fibrosis, and pleural thickening seen in confirmed CPA are similar to radiological features observed in PTB, PTBD, and in relapse of PTB [3,8,14]. PTB constitutes over 85% of the global TB burden; however, only 65% of these patients are bacteriologically confirmed cases [23]. The non-bacteriologically confirmed cases likely are a mixture of patients, including those with false-negative PTB and those with PTBD, including CPA. In a single study among Nigerians, 13 of the 17 patients with CPA were being treated for “smear-negative PTB” [15]. In addition, the lack of awareness and low index of suspicion for CPA among clinicians, as well as the non-availability of essential diagnostics for CPA, are associated with misdiagnosis of CPA [24]. Other differential diagnoses such as chronic cavitary pulmonary histoplasmosis [25], coccidioidomycosis, paracoccidioidomycosis in endemic areas, non-tuberculous mycobacterial (NTM) infection, and other cavitary lung diseases should be considered and evaluated if indicated.

How is CPA differentiated from PTB and PTBD?

Given the striking similarities in the clinical and radiological manifestations of these diseases, more specific microbiological and serological tests are required to make a definitive diagnosis [22,26]. Aspergillus-specific IgG is particularly sensitive and is positive in over 90% of patients with CPA [11,27–29]. The diagnosis of CPA requires a combination of characteristics: one or more cavities with or without a fungal ball present or nodules on thoracic imaging, direct evidence of Aspergillus infection (microscopy or culture from biopsy) or an immunological response to Aspergillus spp., and exclusion of alternative diagnoses, all present for at least 3 months [22,26]. Isolation of Aspergillus spp. is time consuming, has low sensitivity, and may represent colonization or contamination. Therefore, Aspergillus serology is the cornerstone for CPA diagnosis. Introduction of a cheap and rapid point-of-care Aspergillus IgG/IgM lateral flow assay with a sensitivity and specificity of 91.6% (86%–95.4%) and 98.0% (94.2%–99.6%), respectively, has made the diagnosis of CPA possible even in resource-constrained settings [24,27]. PTB can usually be excluded through routine sputum microscopy or culture or by use
of the rapid molecular assay (GeneXpert) [30,31]. However, NTM infection cannot be diagnosed with *M. tuberculosis* GeneXpert. NTM is a cause of smear-positive/*M. tuberculosis* GeneXpert-negative mycobacterial infection with a very high risk of concurrent or precedent CPA development [32]. CPA patients with NTM have a particularly poorer prognosis [32]. There is currently no guidance on the identification and management of PTBLD [3]. PTBLD is a subject of further research, and management is based on expert opinion.

**Can PTB and CPA coexist?**

Both CPA and PTB are caused by the opportunistic respiratory pathogens, *Aspergillus* spp. and *M. tuberculosis*, respectively [1,11]. However, co-isolation is uncommon, and colonisation is suggested in most cases [33]. A systematic review and meta-analysis of cross-sectional studies from Asia and Africa showed an *Aspergillus* co-infection rate of 15.4% (95% CI: 11.4–20.5) among patients with PTB [34]. In one study, co-isolation of *Aspergillus* in respiratory samples of patients with confirmed *M. tuberculosis* was achieved in 50 out of 140 (35.7%) patients, of whom 92% had underlying lung conditions, 35 (70%) had positive *Aspergillus* IgG, and 3 (6%) were confirmed to have CPA [33]. Among HIV-TB co-infected Ugandans, 9% of the patients had a positive *Aspergillus* IgG at the end of their TB treatment [35]. However, full diagnostic work-up for CPA was not performed. CPA-PTB-*Klebsiella pneumoniae* triple co-infection has also been described in a patient with poorly controlled diabetes mellitus [36]. Two clinical studies demonstrated a CPA prevalence of 13.7% (of 124 HIV-negative TB patients) [13] and 8.7% (of 208 153-HIV positive TB patients) patients in the last month of their TB treatment [15]. Concurrent treatment of CPA and TB is very challenging due to the significant drug-drug interactions between anti-TB agents and the triazoles. Rifampicin markedly reduces exposures to itraconazole to sub-therapeutic levels, and hence co-administration should be avoided.

**How is post-TB CPA treated?**

The management of post-TB CPA is the same as that for any underlying lung disease such as COPD or sarcoidosis and depends on the radiological phenotype of CPA [22]. An incidental finding of an asymptomatic *Aspergillus* nodule may not necessitate therapy; a simple aspergilloma occurring in a well-circumscribed cavity without extensive destruction of surrounding lung tissue is best managed surgically. Meanwhile chronic cavitary pulmonary aspergillosis (CCPA) and chronic fibrosing pulmonary aspergillosis (CFPA)—characterised by multiple enlargement of existent or creation of new cavities and extensive destructive fibrotic pleuroparenchymal changes—respectively are the most common forms of aspergillosis and always require antifungal management [22,37]. Long-term oral antifungals with itraconazole at a dose of 400 mg/day or voriconazole at a dose of 400 mg/day administered for at least 6 months is the recommended first-line therapy for CPA associated with improvement in quality of life, relief of symptoms, and retardation of disease progression [38,39]. Newer generation triazoles with better pharmacodynamics and pharmacokinetic profiles, namely, posaconazole and isavuconazole, are alternative azoles for the salvage therapy for patients who are intolerant or have *Aspergillus* spp. isolates resistant to the first-line agents [40–42]. Azole resistance is an increasingly important challenge in the management of patients with CPA. Resistance can develop in-host during treatment (patient route) or alternatively through exposure to azole fungicides in the environment (environmental route) [43]. In cases of complete intolerance or pan-azole resistance, short courses of intravenous amphotericin B or an echinocandin has been used to treat CPA with an overall response rate of about 61% (95% CI: 52%–70%) [44].
Antifungal treatment improves survival. However, survival rates vary significantly among published studies. Reported survival rates are 58%–93% at 1 year of follow-up, 17.5%–85% at 5 years of follow-up, and 30%–50% at 10 years of follow-up [45–49]. In a selected group of patients with CPA, weekly subcutaneous injections of interferon gamma (IFNγ) has been shown to improve disease control (reduced frequency of exacerbation and hospitalisation) and also helps with bacterial clearance [50]. Several factors have been reported to affect mortality, including by underlying pulmonary disease, advanced age, NTM infection, quality of life scores, and serum albumin levels [49].

In addition to conventional antifungal treatment, pulmonary rehabilitation has been shown to improve symptoms and quality of life of patients with PTBLD, including those with post-TB CPA [3]. At the moment, it is unclear whether all post-TB patients should be screened for CPA or whether genetic risk profiling may be of help. Management occurs in the context of a multidisciplinary setting, including chest physicians, radiologists, infectious diseases physicians, chest physiotherapist, occupational therapist, pharmacists, and nurses.

Conclusion

The relationship between CPA and TB is well established. CPA complicates previously treated TB due to the residual structural lesions. About one-third of patients previously treated for PTB will have residual lung cavities. Specific serological and microbiological tests are mandatory to differentiate CPA from active PTB disease, recurrent PTB, and PTBLD.

References

1. WHO. Tuberculosis Fact Sheet. In: World Health Organisation, Geneva, Switzerland. 2020.
2. Kyu HH, Maddison ER, Henry NJ, Ledesma JR, Wiens KE, Reiner R, et al. Global, regional, and national burden of tuberculosis, 1990–2016: Results from the Global Burden of Diseases, Injuries, and Risk Factors 2016 Study. Lancet Infect Dis. 2018; 18: 1329–1349. https://doi.org/10.1016/S1473-3099(18)30623-X PMID: 30507459
3. van Kampen SC, Wanner A, Edwards M, Harries AD, Kirenga BJ, Chakaya J, et al. International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review. BMJ Glob Heal. 2018; 3: e000745. https://doi.org/10.1136/bmjgh-2018-000745 PMID: 30057796
4. Hsu D, Irfan M, Jabeen K, Iqbal N, Hasan R, Migliori GB, et al. Post-tuberculosis treatment infectious complications. Int J Infect Dis. 2020; 92: S41–S45. https://doi.org/10.1016/j.ijid.2020.02.032 PMID: 32114203
5. Romanowski K, Baumann B, Basham CA, Ahmad Khan F, Fox GJ, Johnston JC. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis. 2019; 19: 1129–1137. https://doi.org/10.1016/S1473-3099(19)30309-3 PMID: 31324519
6. Irfan M. Post-tuberculosis pulmonary function and noninfectious pulmonary disorders. Int J Mycobacteriology. 2016; 5: S57. https://doi.org/10.1016/j.ijmyco.2016.08.015 PMID: 28043612
7. Qualfe M, Houben RMGJ, Allwood B, Cohen T, Coussens AK, Harries AD, et al. Post-tuberculosis mortality and morbidity: valuing the hidden epidemic. Lancet Respir Med. Elsevier Ltd; 2020; 8: 332–333. https://doi.org/10.1016/S2213-2600(20)30039-4
8. Khan R, Malik NI, Razaque A. Imaging of pulmonary post-tuberculosis sequelae. Pakistan J Med Sci. 2020; 36: S75–S82. https://doi.org/10.12669/pjms.36.ICON-Supp.1722 PMID: 31933611
9. Meghji J, Simpson H, Squire SB, Mortimer K. A systematic review of the prevalence and pattern of imaging defined post-TB lung disease. PLoS ONE. 2016; 11: 1–17. https://doi.org/10.1371/journal.pone.0161176 PMID: 27518438
10. Nima G, Dogra V, Jha S, Menon B. Evaluation of the radiological sequelae after treatment completion in new cases of pulmonary, pleural, and mediastinal tuberculosis. Lung India. 2015; 32: 241. https://doi.org/10.4103/0970-2113.156233 PMID: 25983409
11. Denning DW, Riniotis K, Dobrashian R, Sambatakou H. Chronic Cavitary and Fibrosing Pulmonary and Pleural Aspergillosis: Case Series, Proposed Nomenclature Change, and Review. Clin Infect Dis. 2003; 37: S265–S280. https://doi.org/10.1086/376526 PMID: 12975754
12. Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. Eur Respir J. 2011; 37: 865–872. https://doi.org/10.1183/09031936.00054810 PMID: 20595150

13. Hedayati MT, Azimi Y, Droudinia A, Mousavi B, Khalilian A, Hedayati N, et al. Prevalence of chronic pulmonary aspergillosis in patients with tuberculosis from Iran. Eur J Clin Microbiol Infect Dis. 2015; 34: 1759–65. https://doi.org/10.1007/s10096-015-2409-7 PMID: 26003310

14. Thoracic British and Association Tuberculosis. Aspergilloma and residual tuberculosis cavities—the results of a resurvey. Tuberucle. 1970; 227–245. PMID: 5495645

15. Oladele RO, Iruhe NK, Foden P, Akanmu AS, Gbaja-Biamila T, Nwosu A, et al. Chronic pulmonary aspergillosis as a cause of smear-negative TB and/or TB treatment failure in Nigerians. Int J Tuberc Lung Dis. 2017; 21: 1056–1061. https://doi.org/10.1058/jiltld.17.0060 PMID: 28826456

16. Page ID, Byanyima R, Hosmans E, Onyachi N, Opira C, Richardson M, et al. Chronic pulmonary aspergillosis commonly complicates treated pulmonary tuberculosis with residual cavitation. Eur Respir J. 2019; 53. https://doi.org/10.1183/13993003.01184–2018

17. Nam HS, Jeon K, Um SW, Suh GY, Kim H, et al. Clinical characteristics and treatment outcomes of chronic necrotizing pulmonary aspergillosis: a review of 43 cases. Int J Infect Dis. 2010; 14: e479–82. https://doi.org/10.1016/j.ijid.2009.07.011 PMID: 19910234

18. Agarwal R, Vishwanath G, Aggarwal AN, Garg M, Gupta D, Chakrabarti A. Itraconazole in chronic cavitary pulmonary aspergillosis: A randomised controlled trial and systematic review of literature. Mycoses. 2013; 56: 559–570. https://doi.org/10.1111/myc.12075 PMID: 23496375

19. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. Bull World Health Organ. 2011; 89: 864–872. https://doi.org/10.2471/BLT.11.089441 PMID: 22271943

20. Agarwal R, Denning DW, Chakrabarti A. Estimation of the burden of chronic and allergic pulmonary Aspergillosis in India. PLoS ONE. 2014; 9: e114745. https://doi.org/10.1371/journal.pone.0114745 PMID: 25478929

21. Bongomin F, Asio LG, Baluku JB, Kwizera R, Denning DW. Chronic Pulmonary Aspergillosis: Notes for a Clinician in a Resource-Limited Setting Where There Is No Mycolgist. J Fungi. 2020; 6: 75. https://doi.org/10.3390/jof6020075 PMID: 32498415

22. Denning DW, Cadranel J, Beigelman-Aubry C, Ader F, Chakrabarti A, Blot S, et al. Chronic pulmonary aspergillosis: Rationale and clinical guidelines for diagnosis and management. Eur Respir J. 2016; 47: 45–68. https://doi.org/10.1183/13993003.00583-2015 PMID: 26699723

23. World Health Organization. World Health Organization. Global tuberculosis report. 2018. In: WHO [Internet], 2018 [cited 2019 Apr 18]. Available from: http://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1.

24. Kwizera R, Katende A, Teu A, Apolot D, Worodria W, Kirenga BJ, et al. Algorithm-aided diagnosis of chronic pulmonary aspergillosis in low- and middle-income countries by use of a lateral flow device. Eur J Clin Microbiol Infect Dis. 2020; 39. https://doi.org/10.1007/s10096-019-03782-x PMID: 31811506

25. Baker J, Kosmidis C, Rozaliyani A, Wahyuningsih R, Denning DW. Chronic Pulmonary Histoplasmosis—A Scoping Literature Review. Open Forum Infect Dis. 2020; 7. https://doi.org/10.1093/ofid/ofaa119 e479–82. https://doi.org/10.1016/j.ijid.2009.07.011 PMID: 29920796

26. Takazono T, Izumikawa K. Recent Advances in Diagnosing Chronic Pulmonary Aspergillosis. Front Microbiol. 2018; 9: 1810. https://doi.org/10.3389/fmicb.2018.01810 PMID: 30174658

27. Stucky Hunter E, Richardson MD, Denning DW. Evaluation of LDBio Aspergillus ICT Lateral Flow Assay for IgG and IgM Antibody Detection in Chronic Pulmonary Aspergillosis. J Clin Microbiol. 2019; 57. https://doi.org/10.1128/JCM.00538-19 PMID: 31217272

28. Sehgal IS, Choudhary H, Dhoooria S, Aggarwal AN, Garg M, Chakrabarti A, et al. Diagnostic cut-off of Aspergillus fumigatus -specific IgG in the diagnosis of chronic pulmonary aspergillosis. Mycoses. 2018; 61: 770–776. https://doi.org/10.1111/myc.12815 PMID: 29920796

29. Volpe Chaves CE, do Valle Leone de Oliveira SM, Venturini J, Grande AJ, Sylvester TF, Poncio Mendes R, et al. Accuracy of serological tests for diagnosis of chronic pulmonary aspergillosis: A systematic review and meta-analysis. Agarwal R, editor. PLoS ONE. 2020; 15: e0222738. https://doi.org/10.1371/journal.pone.0222738 PMID: 32182249

30. Floyd K, Glaziou P, Zumla A, Raviglione M. The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. The Lancet Respiratory Medicine. 2018. pp. 299–314. https://doi.org/10.1016/S2213-2600(18)30057-2 PMID: 29595511

31. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane database Syst Rev. 2014; CD009593. https://doi.org/10.1002/14651858.CD009593.pub3 PMID: 24448973
32. Naito M, Kurahara Y, Yoshida S, Ikagami N, Kobayashi T, Minomo S, et al. Prognosis of chronic pulmonary aspergillosis in patients with pulmonary non-tuberculous mycobacterial disease. Respir Investig. 2018; 56: 326–331. https://doi.org/10.1016/j.resinv.2018.04.002 PMID: 29764749

33. Delièvre S, Angebault C, Fihman V, Foulet F, Lepeule R, Maitre B, et al. Concomitant Presence of Aspergillus Species and Mycobacterium Species in the Respiratory Tract of Patients: Underestimated Co-occurrence? Front Microbiol. 2020; 10. https://doi.org/10.3389/fmicb.2019.02980 PMID: 31998267

34. Hosseini M, Shakerimoghadam A, Ghazalibina M, Khaledi A. Aspergillus coinfection among patients with pulmonary tuberculosis in Asia and Africa countries: A systematic review and meta-analysis of cross-sectional studies. Microb Pathog. 2020; 141: 104018. https://doi.org/10.1016/j.micpath.2020.104018 PMID: 32006367

35. Kwizera R, Parkes-Ratanshi R, Page ID, Sekaggya-Wiltshire C, Musaazi J, Fehr J, et al. Elevated Aspergillus-specific antibody levels among HIV infected Ugandans with pulmonary tuberculosis. BMC Pulm Med. 2017; 17: 149. https://doi.org/10.1186/s12890-017-0500-9 PMID: 29162063

36. Ekwueme C, Otu AA, Chinenye S, Unachuku C, Oputa RN, Korubo I, et al. Haemoptysis in a female with diabetes mellitus: A unique presentation of chronic pulmonary aspergillosis, pulmonary tuberculosis, and Klebsiella pneumoniae co-infection. Clin Case Reports. 2016; 4: 432–436. https://doi.org/10.1002/ccr3.542 PMID: 27099746

37. Patterson TF, II RT, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016; 63: 1–60. https://doi.org/10.1093/cid/ciw209

38. Al-Shair K, Atherton GT, Harris C, Ratcliffe L, Newton PJ, Denning DW. Long-term antifungal treatment improves health status in patients with chronic pulmonary aspergillosis: A longitudinal analysis. Clin Infect Dis. 2013; 57: 828–835. https://doi.org/10.1093/cid/cit411 PMID: 23788240

39. Bongomin F, Harris C, Hayes G, Kosmidis C, Denning DW. Twelve-month clinical outcomes of 206 patients with chronic pulmonary aspergillosis. Chotirmall SH, editor. PLoS ONE. 2018; 13: e0193732. https://doi.org/10.1371/journal.pone.0193732 PMID: 29634721

40. Rodriguez-Gonczer I, Harris C, Kosmidis C, Muldoon EG, Newton PJ, Denning DW. Assessment of posaconazole salvage therapy in chronic pulmonary aspergillosis using predefined response criteria. Int J Antimicrob Agents. 2018; 52: 258–264. https://doi.org/10.1016/j.ijantimicag.2018.06.001 PMID: 29905667

41. Bongomin F, Maguire N, Moore CB, Felton T, Rautemaa-Richardson R. Isavuconazole and voriconazole for the treatment of chronic pulmonary aspergillosis: A retrospective comparison of rates of adverse events. Mycoses. 2019; 62: 217–222. https://doi.org/10.1111/myc.12885 PMID: 30570179

42. Sehgal IS, Dhooria S, Muthu V, Prasad KT, Agarwal R. An overview of the available treatments for chronic cavitary pulmonary aspergillosis. Expert Rev Respir Med. 2020; 14: 1–13. https://doi.org/10.1080/17476348.2020.1750956 PMID: 32249630

43. Verweij PE, Ananda-Rajah M, Andes D, Arentrup MC, Brüggemann RJ, Chowdhary A, et al. International expert opinion on the management of infection caused by azole-resistant Aspergillus fumigatus. Drug Resist Updat. 2015; 21–22: 30–40. https://doi.org/10.1016/j.drup.2015.08.001 PMID: 26282594

44. Bongomin F, Asio EG, Olum R, Denning DW. Intravenous Therapy for Chronic Pulmonary Aspergillosis: A Systematic Review and Meta-analysis. Mycoses. 2020; 106: 724–729. https://doi.org/10.1111/myc.13131 PMID: 32542771

45. Tomlinson JR, Sahn SA. Aspergilloma in sarcoid and tuberculosis. Chest. 1987; 92: 505–8. https://doi.org/10.1378/chest.92.3.505 PMID: 3822028

46. Jhun BW, Jeon K, Eom JS, Lee JH, Suh GY, Kwon OJ, et al. Clinical characteristics and treatment outcomes of chronic pulmonary aspergillosis. Med Mycol. 2013; 51: 811–7. https://doi.org/10.1111/myc.12014 PMID: 23059854

47. Ohba H, Miwa S, Shirai M, Kanai M, Elfuku T, Suda T, et al. Clinical characteristics and prognosis of chronic pulmonary aspergillosis. Respir Med. 2012; 106: 724–729. https://doi.org/10.1016/j.rmed.2012.01.014 PMID: 22349065

48. Jiewkes J, Kay PH, Paneth M, Citron K. Pulmonary aspergillosis: analysis of cavitating invasive pulmonary aspergillosis in immunocompromised patients. Ann Thorac Surg. 1983; 53: 621–4.

49. Lowes D, Al-Shair K, Newton PJ, Morris J, Harris C, Rautemaa-Richardson R, et al. Predictors of mortality in chronic pulmonary aspergillosis. Eur Respir J. 2017; 49. https://doi.org/10.1183/13993003.01062–2016

50. Monk EJ, Harris C, Döfflinger R, Hayes G, Denning DW, Kosmidis C. Interferon gamma replacement as salvage therapy in chronic pulmonary aspergillosis: effects on frequency of acute exacerbation and all-cause hospital admission. Thorax. 2020;2018; thoraxjnl-2019–213606. https://doi.org/10.1136/thoraxjnl-2019-213606 PMID: 32229542