

## Successful treatment of chronic pulmonary aspergillosis in a patient with early pulmonary tuberculosis and COVID-19: a case report

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### ABSTRACT

**Introduction:** Chronic pulmonary aspergillosis (CPA) often develops in residual lesions of pulmonary tuberculosis (PTB). Every year, 112,000 to 160,000 people worldwide will develop post-PTB CPA. The simultaneous occurrence of CPA with the first episode of PTB is rare. During the COVID-19 pandemic, COVID-19-associated invasive aspergillosis (CAPA) occurred in patients receiving high doses of corticosteroids and mechanical ventilation. However, CPA and COVID-19 are rarely reported simultaneously. This case study presents a patient with CPA in the first episode of PTB during hospitalization for COVID-19. The favorable evolution is highlighted, including the resolution of the cavitation and fungal ball with appropriate and early treatment.

**Case presentation:** A 48-year-old female patient from the Central West of Brazil was admitted with a history of cough, yellow sputum, fever, and significant weight loss for two months. The respiratory symptoms worsened one week before admission. She tested positive for COVID-19 by RT-PCR. She had a history of hypertension and diabetes. Clinical examination revealed tachypnea, slurred speech, and hypoxia. She presented with hyperglycemia, obesity, hypertension, and an episode of hemoptysis. Chest CT revealed cavitation in the right upper lobe with a 45 mm aspergilloma, multifocal morning opacities, and nodular opacities. Laboratory tests confirmed the PTB with positive sputum for acid-fast bacilli and positive culture for *Mycobacterium tuberculosis*. The sputum culture also showed *Aspergillus* spp. She received early treatment for bacterial pneumonia with ceftriaxone, dexamethasone, enoxaparin, an anti-TB regimen, and itraconazole. There was a progressive clinical improvement and the patient was discharged after 15 days. She completed six months of anti-TB therapy and 13 months of itraconazole treatment for CPA, with complete resolution of the cavitation and aspergilloma.

**Discussion and conclusion:** This case study presents a unique case of CPA that manifested as simple aspergilloma and was diagnosed concurrently with the initial episode of PTB in a COVID-19 patient with obesity, hypertension, and diabetes. Remarkably, the fungal ball and cavitation regressed spontaneously. The favorable clinical and radiological results highlight the importance of comprehensive treatment approaches for concurrent respiratory infections and emphasize the need to investigate CPA and PTB during COVID-19 hospitalization.

**Key words:** Pulmonary tuberculosis, chronic pulmonary aspergillosis, SARS-COV-2, COVID-19, aspergilloma

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## Introduction

The occurrence of chronic pulmonary aspergillosis (CPA) in residual cavities, mainly due to pulmonary tuberculosis (PTB), is widely described in the literature. Each year, it is estimated that 112,000–160,000 people worldwide will develop CPA after therapy for PTB, according to the annual incidence rates reported for this disease [1]. Concomitant occurrence with the initial episode of PTB is uncommon [2].

COVID-19 associated invasive aspergillosis (CAPA), characterized by invasive aspergillosis (IA), was frequently reported in patients who underwent high doses of corticosteroids and mechanical ventilation (MV) during the COVID-19 pandemic [3]. On the other hand, cases of CPA and COVID-19 have been rarely reported [4–6]. Therefore, we report a single case where both CPA and the initial episode of PTB occurred concomitantly in a patient hospitalized for COVID-19. The patient presented a favorable outcome with the established treatment.

## Case presentation

A 48-year-old female patient was admitted to a high-complexity hospital in the Central-West region of Brazil, presenting with a chief complaint of a cough accompanied with yellowish sputum, daily afternoon fever, and weight loss of 17 kg over the course of two months. A week before, her respiratory complaints worsened, progressing to dyspnea on exertion and ventilatory-dependent pain in the left posterior thoracic region. Three days prior to hospitalization, the

rapid antigen test for COVID-19 yielded a positive result, and this was subsequently confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) in a nasal swab upon admission. She was undergoing treatment with metformin and losartan for systemic arterial hypertension (SAH) and diabetes mellitus (DM).

Upon clinical examination, she exhibited a regular general condition, maintaining consciousness and orientation. She was tachypneic, with a respiratory rate of 22 breaths per minute, had choppy speech, and was using a nebulizer (with nasal oxygen [O<sub>2</sub>]) set at a 2 L/min flow rate, with an O<sub>2</sub> saturation of 99%. Her heart rate was 110 beats per minute and blood pressure was 130/70 mmHg. Lung auscultation revealed reduced vesicular breath sounds on the right, diffuse rhonchi in both hemithoraces, and crackling rales in the bases.

Computed tomography (CT) of the chest showed the following abnormalities: 1) Heterogeneous lung consolidation in the right upper lobe, associated with cystic bronchiectasis and 45 mm excavation, with amorphous content inside (aspergilloma); 2) Multifocal pulmonary opacities, with ground-glass attenuation, associated with thickening of interlobular septa and consolidation foci, scattered throughout both lungs; and 3) Small, adjacent, nodular opacities, with soft tissue attenuation, observed in the upper lobes of both lungs and in the upper segment of the right lower lobe.

Her laboratory test results were as follows: hemoglobin (Hb) concentration of 10.9 mg/dL, hematocrit (Ht) value of 31.6%, 10,400 leukocytes, 312,000 platelets, a C-reactive protein (CRP) level of 25.6 mg/L (reference value <5mg/L), and no significant changes in the arterial blood gas analysis. Her sputum smear

microscopy was positive for acid-fast bacilli (AFB) in two samples. The rapid molecular test (RMT) was positive for *Mycobacterium tuberculosis* (MTb) sensitive to rifampicin. Culture in Lowenstein-Jensen medium was positive and MTb was phenotypically identified. Susceptibility testing using the Mycobacteria Growth Indicator Tube (MGIT) revealed sensitivity to streptomycin, isoniazid, rifampin and ethambutol. Hyaline septate hyphae were identified in the sputum, and the culture was positive for *Aspergillus* spp. Serology for *Aspergillus* by enzyme linked immunosorbent assay (ELISA) was negative (4.53 AU/mL), and double immunodiffusion in agar gel (DID) was non-reactive. HIV serology yielded a negative result. The measurement of total and specific Immunoglobulin E (IgE) against *Aspergillus fumigatus* was not performed.

With the diagnosis of PTB, COVID-19, and the presence of an aspergilloma, the following medications were administered: ceftriaxone 2 g intravenously (IV) daily for seven days, dexamethasone 6 mg orally daily until hospital discharge, prophylactic subcutaneous enoxaparin, four tablets a day of rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg and ethambutol 275 mg (weight at admission was 64 kg), and itraconazole at a dose of 200 mg orally every 12 hours.

The patient was kept in surveillance based on respiratory precautions against aerosols and contact. During hospitalization, she developed periods of hyperglycemia (blood glucose levels ranging between 400-500 mg/dl) and NPH (neutral protamine Hagedorn) insulin was started. She also presented small episodes of hemoptysis, with no history of its occurrence before hospitalization. With progressive improvements in respiratory complaints and without O<sub>2</sub> dependence, she was discharged from hospital after 15 days and referred for outpatient follow up in our outpatient service at the Esterina Corsini Day Hospital.

She was maintained on a PTB regimen for six months, showing improvements in clinical, microbiological, and tomographic aspects, resulting in a complete cure. Itraconazole treatment for CPA was continued for 13 months and suspended due to complete resolution of cavitation and aspergilloma observed in a chest CT scan (Figure 1). A new chest CT was performed 14 months after the suspension of treatment, without recurrence of pulmonary aspergillosis

(Figure 1). The patient remained asymptomatic at the time of outpatient follow up.

## Discussion

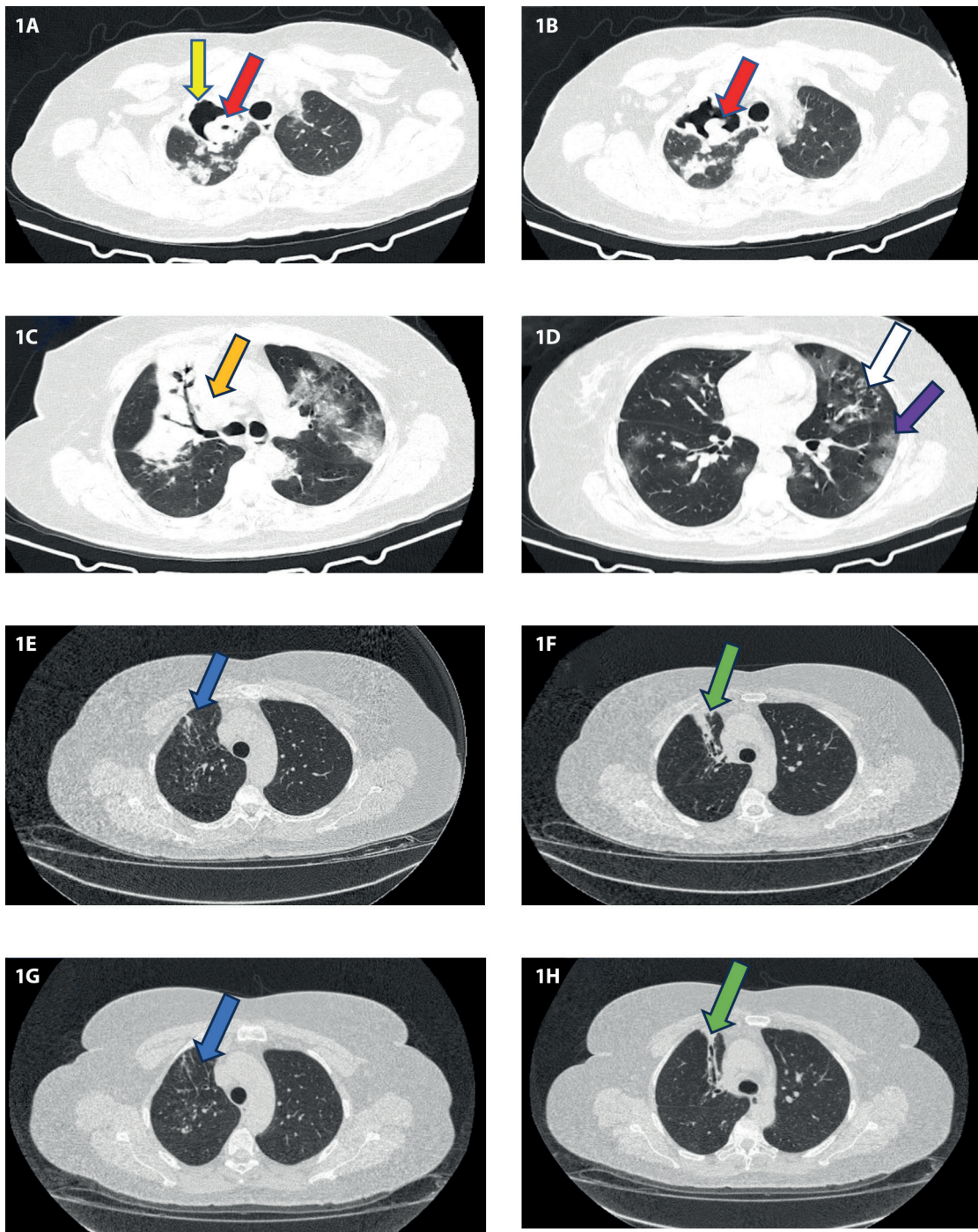
We report a unique case of CPA presenting as a simple aspergilloma in a cavity of a patient experiencing an initial episode of PTB associated with recent symptoms of COVID-19. The patient, from the Central-West region of Brazil, exhibited a favorable outcome, with complete resolution of the fungal ball and cavitation. To the best of our knowledge, this is the first report to describe the simultaneous occurrence of all three diseases.

The occurrence of CPA as a consequence of pulmonary tuberculosis is well defined and studies estimating local and global prevalences have been reported [1,7,8]. Therefore, we believe that the symptoms presented by the patient in the initial two months were due to PTB. Despite its short evolution, the presence of cavitation facilitated the *Aspergillus* colonization and the swift progression to CPA, in the form of simple aspergilloma characterized by a single fungal ball within a lone lung cavity. This condition differs from chronic cavitary pulmonary aspergillosis (CCPA), which may or may not contain an aspergilloma in multiple cavities and the presence of symptoms and inflammatory markers, with an evolution of at least 3 months [9].

Diagnosing CPA is challenging, and its diagnostic criteria are based on expert opinion, taking into account clinical, microbiological, serological, and tomographic findings [9], as well as criteria published in 2018, which can be used in resource-poor countries [10]. It is worth noting that many case definitions consider ruling out active PTB to diagnose CPA [10,11], making it difficult to diagnose CPA that occurs simultaneously with active PTB, like in the present case.

Studies on the prevalence of CPA have demonstrated rates of around 2.3 to 13.7% [1,2]. Similarly, in the city of residence of the reported case, our team demonstrated a prevalence of 10.9% [2].

An important point in the case description is the presentation of CPA, with a fungal ball (aspergilloma) measuring approximately 45 mm. We assumed the aspergilloma to be recent, considering that the patient



**Figure 1.** Chest computed tomography performed at the diagnosis of a patient with chronic pulmonary aspergillosis, pulmonary tuberculosis, and COVID-19. A, B, C and D: January 2017; Figures E and F: September 2018; Figures G and H: October 2019. Yellow arrow: cavitation; red arrow: fungal ball; white arrow: budding tree; purple arrow: peripheral ground-glass infiltrate (COVID -19); Orange arrow: consolidation. Chest CT at 13 months after the start of treatment (1E and 1F) and after 14 months of treatment suspension (1G and 1H). Blue arrow: multiple centrilobular pulmonary nodules; yellow arrow: fibroatelectasis, segmental atelectasis, and subsegmental atelectasis in the anterior and apical segments of the right upper lobe.

**Table 1.** Articles published with the identification of chronic pulmonary aspergillosis in patients with the first episode of pulmonary tuberculosis.

Authors/Year of publication	Country of study	Number of patients diagnosed with CPA	Number of patients with first episode of PTB	Prevalence of CPA in first episode of PTB
Volpe-Chaves et al., 2022 [2]	Brazil	2	129	1.6%
Setianingrum et al., 2022 [11]	Indonesia	Start of treatment: 12 (confirmed) and 5 (probable) End of treatment: 10 (confirmed) and 7 (probable)	Start of treatment: 216 End of treatment: 128	Start of treatment: 7.9% at the beginning of treatment (confirmed and probable) End of treatment: 13.3% (confirmed and probable)
Ocansey et al., 2022 [12]	Ghana	5	134	3.7%
Ekwueme et al., 2016 [13]	Nigeria	1	1	Case report

CPA, chronic pulmonary aspergillosis; PTB, pulmonary tuberculosis.

had no previous history of treatment for PTB and the length of time since symptoms appeared in the clinical case was around two months. The prevalence rate of CPA increases with the time since diagnosis of the first tuberculosis episode, with a higher prevalence observed after four years [2]. Few studies have identified CPA with the first episode of PTB [2,11-13] with an incidence/prevalence ranging between 1.6 % and 13.3% (Table 1).

Aspergilloma is one of the most frequent findings on chest CT scans [2]. Its presence facilitates the diagnosis of CPA; however, it is present in only 1/3 of cases [1].

The occurrence of hemoptysis in our patient during hospitalization led to the discussion of an important manifestation of CPA, which can be present in up to 76.5% of cases with surgical indication and can lead to death [14]. Its pathogenesis is associated with multiple factors [15] and the administration of higher doses of anticoagulants during the COVID-19 pandemic in 2020 may have contributed to this event [16]. In a 2022 prevalence study, the chance of presenting hemoptysis was approximately 10 times greater in patients with CPA than in patients with an isolated diagnosis of PTB [2].

The presence of diabetes mellitus (DM) and its association with TB, as observed in our report, has been well defined and its presence increases the probability of developing PTB by four fold, with a prevalence of DM of 6.9% in patients with TB [17,18].

There are few reports on the association between CPA and COVID-19 and in Table 2 we describe the main characteristics of these studies [4-6,19,20].

All cases that reported an association with COVID-19, with the exception of one study [4], were not correlated with PTB. Our report defines the occurrence of CPA in the initial episode of PTB, where the diagnosis of COVID -19 only contributed to the diagnosis.

In our report, the diagnosis of CPA was made based on the modified criteria outlined by Denning et al. [2,10]: 1) Microbiological: septate hyphae are identified combined with a positive culture for *Aspergillus* sp. in sputum; and 2) Radiological findings: presence of an image compatible with a fungal ball. Unfortunately, ELISA serology was negative and agar gel double immunodiffusion was non-reactive, which classifies our case as probable chronic pulmonary aspergillosis in the form of simple aspergilloma [10].

The complete resolution of tuberculosis cavitation, accompanied by the complete resolution of the fungal ball in our report, caught the team's attention. The occurrence of cavitation after PTB treatment is identified in 20-30% of patients [1,21] and its complete resolution after treatment is rarely observed. There is evidence demonstrating the association between the inflammatory response, which is dependent on host proteases, and the destruction of lung tissue leading to the formation of cavities in TB. Therefore,

**Table 2.** Clinical characteristics of published studies identifying chronic pulmonary aspergillosis in association with COVID-19.

Authors/Year of publication	Number of cases	Clinical form of COVID-19 during CPA diagnosis	CPA presentation	Time between the first episode of TB and CPA	Treatment	Outcome
Horiuchi et al., 2022 [5]	2	1st case: severe convalescence from COVID-19 2nd case: severe convalescence from COVID-19	1st case: CPA not defined - multiple cavitations 2nd case: CPA not defined - multiple cavitations	No reports of PTB	Itraconazole for both cases	Satisfactory response for both cases with transfer to long-term hospital
Patti et al., 2020 [6]	1	During hospitalization for COVID-19	Invasive subacute pulmonary aspergillosis	No reports of PTB	Voriconazole	Satisfactory response with transfer to long-term hospital
Chaurasia, Thimmappa, Chowdhury, 2021 [14]	1	Severe form with recovery during hospitalization	Previous simple aspergilloma that progressed to CCPA after initial improvement in the severe form of COVID-19	20 years	Voriconazole	Satisfactory clinical and radiological response
Coşgun, Zeren, Kocatürk et al., 2022 [19]	1	Unreported form - diagnosis after discharge due to COVID-19	Simple aspergilloma	No reports of PTB	Complete resection No pharmacological treatment reported	Not reported
Razafindraso et al., 2022 [20]	1	After three months of discharge due to COVID-19	Invasive subacute pulmonary aspergillosis (cited as chronic necrotizing pulmonary aspergillosis) associated with chronic fibrosing pulmonary aspergillosis	No reports of PTB	Itraconazole	Loss of tracking

CPA, chronic pulmonary aspergillosis; PTB, pulmonary tuberculosis; CCPA, cavitary chronic pulmonary aspergillosis.

immunomodulatory therapy as an adjuvant to TB treatment has been proposed [22].

Despite the satisfactory evolution of our patient with an asymptomatic presentation of CPA (simple aspergilloma), more advanced forms, such as CCPA, have five-year mortality rates ranging from 17.5% to 85% [1,23], demonstrating the need for early diagnosis of this disease.

In our patient, itraconazole treatment for CPA was discontinued after 13 months, and she is currently asymptomatic, underdoing quarterly monitoring in our outpatient clinic. Itraconazole is considered the drug of choice for CPA [24] and its use has been recommended for a period of between six to 12 months or even indefinitely if there is the presence of advanced

forms of CPA [9]. One study demonstrated that itraconazole treatment for 12 months was superior in reducing relapses within two years [25].

Although the measurement of total and specific IgE was not performed in our study, the elevation of IgE appears to be an immune response in some patients with CPA. Further studies are needed to define future therapeutic strategies [26,27].

The patient underwent treatment with a standardized TB regimen in association with itraconazole. O<sub>2</sub> supplementation, introduction of corticosteroids, and prophylaxis with anticoagulants recommended for COVID-19 were also administered. There was a quick response with hospital discharge within 15 days and adherence to the prescribed regimens contributed to

clinical, laboratory, and tomographic improvements. The use of itraconazole and the complete resolution of the fungal ball visualized on chest CT (Figure 1), accompanied by clinical and laboratory improvement, raised some questions for the team: 1) Does early diagnosis of CPA interfere with the clearing of *Aspergillus* and complete resolution of the fungal ball?; 2) Could recent TB cavitation together with the recent diagnosis of CPA have contributed to the cure?; 3) Did the association between rifampicin and itraconazole interfere with the resolution of the fungal ball, due to the effects of this drug interaction, and could a lower dose be used in these cases?; and 4) Could the concomitant use of dexamethasone in the initial period of treatment for the three pathologies have assisted the complete resolution of the cavitation?

## Conclusion

In conclusion, we describe a rare case of CPA diagnosed during the initial episode of PTB, while the patient required hospitalization for COVID-19. This case study underscores the importance of early TB diagnosis and the timely investigation of CPA, recognized as a late complication of PTB. The favorable outcome of this case can be attributed to the early initiation of treatment for all three pathologies and the patients' adherence to specialized outpatient follow up.

## Abbreviations

CPA: chronic pulmonary aspergillosis  
 PTB: pulmonary tuberculosis  
 TB: tuberculosis  
 CT: Computed tomography  
 RMT: rapid molecular test  
 CAPA: COVID-19 associated invasive aspergillosis  
 IA: invasive aspergillosis  
 MV: mechanical ventilation  
 RT-PCR: reverse transcriptase-polymerase chain reaction  
 SAH: systemic arterial hypertension  
 DM: diabetes mellitus  
 CRP: C-reactive protein  
 AFB: acid-fast bacilli  
 RMT: rapid molecular test  
 MTb: *Mycobacterium tuberculosis*  
 MGIT: Mycobacteria Growth Indicator Tube

ELISA: enzyme-linked immunosorbent assay  
 DID: double immunodiffusion in agar gel  
 IV: intravenously  
 CCPA: chronic cavitary pulmonary aspergillosis  
 NPH: neutral protamine Hagedorn

## References

1. Page ID, Byanyima R, Hosmane S, Onyachi N, Opira C, Richardson M, et al. Chronic pulmonary aspergillosis commonly complicates treated pulmonary tuberculosis with residual cavitation. *Eur Respir J* 2019; 53:1801184.
2. Volpe-Chaves CE, Venturini J, Castilho SB, Fonseca SSO, Nunes TF, Cunha EAT, et al. Prevalence of chronic pulmonary aspergillosis regarding time of tuberculosis diagnosis in Brazil. *Mycoses* 2022; 65:715-723.
3. Verweij PE, Brüggemann RJM, Azoulay E, Bassetti M, Blot S, Buil JB, et al. Taskforce report on the diagnosis and clinical management of COVID-19 associated pulmonary aspergillosis. *Intensive Care Med* 2021; 47:819-34.
4. Chaurasia S, Thimmappa M, Chowdhury S. Case report: chronic cavitary pulmonary aspergillosis after COVID-19. *Am J Trop Med Hyg* 2021;106(1):105-7.
5. Horiuchi H, Utada S, Shinomiya Y, Miyagawa T, Sogo A, Niida S, et al. Chronic pulmonary aspergillosis during convalescence from severe COVID-19 treated with oral itraconazole: a report of two cases. *Cureus* 2022; 14:e27281.
6. Patti RK, Dalsania NR, Somal N, Sinha A, Mehta S, Ghitan M, et al. Subacute aspergillosis "fungal balls" complicating COVID-19. *J Investig Med High Impact Case Rep* 2020; 8:2324709620966475.
7. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull World Health Organ* 2011; 89:864-72.
8. 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.
9. Denning DW, Cadranell 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.
10. Denning DW, Page ID, Chakaya J, Jabeen K, Jude CM, Cornet M, et al. Case definition of chronic pulmonary aspergillosis in resource-constrained settings. *Emerg Infect Dis* 2018; 24:e171312.
11. Setianingrum F, Rozaliyani A, Adawiyah R, Syam R, Tugiran M, Sari CYI, et al. A prospective longitudinal study of chronic pulmonary aspergillosis in pulmonary tuberculosis in Indonesia (APICAL). *Thorax* 2021; 77:821-8.
12. Ocansey BK, Otoo B, Adjei A, Gbadamosi H, Kotey FCN, Kosmidis C, et al. Chronic pulmonary aspergillosis is common among patients with presumed tuberculosis relapse in Ghana. *Med Mycol J* 2022; 60:myac063.

13. Ekwueme C, Otu AA, Chinenye S, Unachukwu C, Oputa RN, Koruboet 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; 4:432–6.
14. Bongomin F, Olum R, Kwizera R, Baluku JB. Surgical management of chronic pulmonary aspergillosis in Africa: A systematic review of 891 cases. *Mycoses* 2021; 64(10):1151–8.
15. Kanj A, Abdallah N, Soubani AO. The spectrum of pulmonary aspergillosis. *Respir Med* 2018;141:121–31.
16. Sadeghipour P, Talasaz AH, Rashidi F, Sharif-Kashani B, Beigmohammadi MT, Farrokhpour M, et al. Effect of intermediate-dose vs standard-dose prophylactic anticoagulation on thrombotic events, extracorporeal membrane oxygenation treatment, or mortality among patients with COVID-19 admitted to the intensive care unit: The INSPIRATION Randomized Clinical Trial. *JAMA* 2021; 325:1620–30.
17. Bridson T, Matthiesson A, Owens L, Govan B, Norton R, Ketheesan N. Diabetes: A contributor to tuberculosis in Tropical Australia. *Am J Trop Med Hyg* 2015;93: 547–8.
18. Dos Santos Feltrin AF, Vendramini SHF, Neto FC, Correa APV, Werneck AL, Sasaki NSGMS, et al. Death in patients with tuberculosis and diabetes: associated factors. *Diabetes Res Clin Pract* 2016; 120:111–6.
19. Coşgun T, Zeren H, Kocatürk C. Ciliated muconodular papillary tumor masked by COVID-19 infection and aspergilloma COVID-19. *Turk Gogus Kalp Damar Cerrahi Derg* 2022; 30(4):635–40.
20. Razafindrasoa ZA, Ravahatra K, Tiaray HM, Nandimbinaina AM, Andriamahenina FPP, Razafimpihaninaet SM, et al. COVID-19 complicated with chronic necrotizing pulmonary aspergillosis and aspergilloma progressing to fibrosing aspergillosis: A case report. *Clin Case Rep* 2022; 10:e05814.
21. World Health Organization. WHO Global tuberculosis report. WorldHealth Organization, 2017. ([http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/)).
22. Ong CWM, Elkington PT, Friedland JS. Tuberculosis, Pulmonary Cavitation, and Matrix Metalloproteinases. *Am J Respir Crit Care Med* 2014; 190(1):9–18.
23. 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; 49:1601062.
24. Sehgal IH, Dhooria S, Prasad KT, Muthu V, Aggarwal AN, Chakrabarti A, et al. Anti-fungal agents in the treatment of chronic pulmonary aspergillosis: systematic review and a network meta-analysis. *Mycoses* 2021; 64:1053–61.
25. Sehgal IS, Dhooria S, Muthu V, Prasad KT, Aggarwal AN, Chakrabarti A, et al. Efficacy of 12-months oral itraconazole versus 6-months oral itraconazole to prevent relapses of chronic pulmonary aspergillosis: an open-label, randomised controlled trial in India. *Lancet Infect Dis* 2022; 22:1052–61.
26. Sehgal IS, Choudhary H, Dhooria S, Aggarwal AN, Garg M, Chakrabarti A, et al. Is there an overlap in immune response between allergic bronchopulmonary and chronic pulmonary aspergillosis? *J Allergy Clin Immunol Pract* 2018; 7:969–74.
27. Sehgal IS, Dhooria S, Muthu V, Rudramurthy SM, Prasad KT, Chakrabarti A, et al. Identification of distinct immunophenotypes in chronic pulmonary aspergillosis using cluster analysis. *Mycoses* 2023; 66: 299–303.

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