

Pulmonary Aspergilloma: A Case Report

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Chronic pulmonary aspergillosis (CPA) is a rare disease. It is usually diagnosed in immunocompromised patients with other chronic respiratory disorders. Diagnosis can be challenging due to non-specific symptoms. It is based on clinical, radiological, and microbiological criteria and excludes other causes of the symptoms. The outcomes of antifungal treatment may be unpredictable as optimal treatment duration has not yet been standardized.

This is the case of a 74-year-old male who presented via teleconsultation with hemoptysis. GeneXpert for pulmonary tuberculosis was negative. Chest radiograph showed a cavitary lesion with an aspergilloma within. This led to a longstanding treatment effort with voriconazole, as he was a poor candidate for surgical resection due to the risk of post-operative complications. Three months into the treatment, the patient unexpectedly suffered from a severe episode of dyspnea, culminating in cardiac arrest. While the patient has been resuscitated with no residuals, it is only one of the many steps on his road to recovery and his second lease on life, this time coming to terms with his own preferences and values regarding his medical care. The patient showed clinical improvement and the promise of a cure in his fifth month of treatment. Learning points include the role of family physicians in a patient's well-being even in specialized cases, the value of individualized care and the application of technology in hybrid consultation and monitoring.

Key words: Aspergillosis, aspergilloma, hemoptysis, voriconazole

INTRODUCTION

Chronic pulmonary aspergillosis (CPA) is a relatively rare condition.³ It is usually diagnosed in immunocompromised patients with other chronic respiratory disorders, such as emphysema, chronic lung illness, a history of pulmonary tuberculosis, non-tuberculous infection, or lung cancer.² Due to the non-specific symptoms, it can be difficult to diagnose CPA. The diagnosis is made using clinical, radiological, and microbiological criteria, and other more common causes of the reported symptoms are excluded.³ Itraconazole, voriconazole, and amphotericin B can be given as a single or combination therapy in a few circumstances.⁵ There is no current set duration of therapy, but a minimum of six months is recommended. The length of the treatment should depend on the improvement in clinical and radiological results.² Surgery may be employed to address certain conditions, such intractable hemoptysis or recurrent aspergillosis, in patients with good functional status and a singular lesion.⁵

THE CASE

The patient is a 74-year-old male with a known case of hypertension, diabetes mellitus type 2 controlled, and COPD. Ongoing

daily medications consisted of Losartan 100mg, Atorvastatin 20mg, Metformin 1000mg, Amlodipine 5mg and Aspirin 80mg. He completed 6-month treatment for pulmonary tuberculosis a year ago. He presented at the virtual clinic with mild hemoptysis (<5 ml) upon slight coughing. The blood was bright red and did not have any clotted portions. There was no weight loss, body pain, persistent cough, chest pain, fever, or chills. The patient was hospitalized in 2009 and 2018 for community-acquired pneumonia. He has a 40-pack-year smoking history and quit five years ago. He is a former occasional alcoholic beverage drinker. The patient's diet consists mostly of balanced, home-cooked meals. He considers himself a picky eater, especially with his ill-fitting dentures. The patient lives in a rural area of central Luzon in a well-ventilated one-story house with his wife, son, daughter-in-law, and granddaughter. The family belongs to the low-middle-income class.

Clinical Findings

During the teleconsultation, vital signs were as follows: RR= 18 cpm, PR = 76 bpm, O₂ saturation 95% at room air. The patient was conscious, coherent, and not in distress. He had no pallor, non-distended neck veins, no visible retractions, adynamic precordium, no abdominal distension and no pedal edema.

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Table 1. Timeline of events.

	Initial Teleconsult	Reaction to Diagnosis	Major Therapeutic Efforts	Adjustment to Outcomes
Subjective	2 episodes hemoptysis <5ml, no dyspnea, occasional mild cough	Psychosocial: Patient in shock about his diagnosis Family supportive of patient management	No hemoptysis. no dyspnea, no cough, no fever, no chills	Psychosocial: Financial constraints
			3rd month of treatment Sudden dyspnea → Cardiac arrest → Revived without residual deficits	Occasional pain over intercostal area, no hemoptysis, occasional dyspnea
Objective	RR 18 bpm, PR 76 bpm, O ₂ sat 95% at room air. Conscious, coherent, not in distress. No pallor, moist lips, nondistended neck veins, no visible retractions, adynamic precordium, no abdominal distension and no bipedal edema.	RR 24 bpm, PR 76 bpm, O ₂ sat 93% at room air, temperature 37.1 degrees Celsius, BMI 18.5 Rest of PE: unremarkable Sputum GeneXpert - MTB not detected CXR: Cavitory lesion with aspergilloma	Stable PE FBS 121 mg/dL →106.7 mg/dL HbA1C 7.6% Other labs within normal limits	RR 24 bpm, PR 72 bpm, O ₂ sat 93% at 2-3 LPM 36.7 Rest of PE: unremarkable Geriatric Depression Scale 5 →7
Assessment	Hypertension stage II, Diabetes Mellitus type 2, controlled, COPD, t/c PTB relapse	Hypertension stage II, Diabetes Mellitus type 2, COPD, Pulmonary Aspergillosis, Presumptive PTB	Status quo s/p cardiac arrest without residuals	Hypertension stage II, Diabetes Mellitus type 2, COPD, Pulmonary Aspergillosis, PTB ongoing treatment
Management	Continue present medication, request sputum GeneXpert, chest x-ray PA view	Requested CBC with platelet, serum Na, K, creatinine, FBS, HbA1C, Lipid profile and Urinalysis., continued present medication, adjusted Metformin to 500mg/tab TID HRZE regimen initiated. Psychoeducation of patient and family	Continue voriconazole 200mg/tab 2 tablets once a day, adjustment of metformin to 500mg/tab to TID, vitamin B complex 1 tablet daily Reassurance and counselling, education on the side effects and prognosis, advance care planning introduced Navigated to Malasakit Center for financial support Referred to Pulmonology management Referred to TCVS Contemplated lung resection but was deferred due to being a poor surgical candidate	Continue medications, confirmed advance care directives oxygen supplementation. Psychoeducation, emotional support and counseling

Diagnostic Assessment

Hemoptysis mimics the clinical presentation of pulmonary tuberculosis, which is a more common disease entity in the local setting given the patient's past history. The diagnosis can be confirmed through sputum examination (GeneXpert, AFB stain, MTB culture) and/or chest imaging. The patient's chest x-ray showed the presence of aspergillomas or fungus balls within a cavitation. A diagnosis of aspergilloma can be made through x-ray, CT or MRI. Any of these can demonstrate the presence of cavitations and aspergillomas.^{2,3} Kousha, et al.³ noted that bronchoscopy is the gold standard yet the most invasive procedure. This might have been helpful to obtain a biopsy and lavage sample for culture and sensitivity to determine the drug resistance profile of the offending organism.

Therapeutic Interventions

As stated by Denning, et al. in their clinical guidelines, the management of CPA aims at preventing disease progression, preventing life-threatening hemoptysis, and improving the patient's quality of life.⁵ Surgical resection of aspergillomas in symptomatic patients with low surgical risk is strongly recommended. Resection is most recommended in patients who possess a singular aspergilloma, have good functional status or low surgical risk, have persistent hemoptysis, or have lesions unresponsive to pharmacologic management.⁵ Treatment of Chronic Cavitory Pulmonary Aspergillosis (CCPA) can also be achieved through

pharmacologic means. Oral itraconazole at 100 to 200 mg twice daily is the initial drug of choice² but Voriconazole at a dose of 200mg twice daily is also an acceptable alternative.³ The duration of treatment is at least 6 months, with periodic reassessments every 3-6 months.² Patient response and survival rates in patients treated with voriconazole were 20% higher if the antifungal was started upon the initial detection of radiological signs of invasive pulmonary aspergillosis.⁵

In some cases, Tranexamic acid, an antifibrinolytic agent, can be used in mild to moderate hemoptysis. Massive, intractable hemoptysis may require bronchial artery embolization.⁹

Besides biomedical management, it is also important to consider the patient's quality of life. Cardio-pulmonary assessment identified the patient as a poor surgical candidate despite the indication, due to the increased risk for operative and postoperative mortality and morbidity. Hence, pharmacologic treatment was maximized.

Non-pharmacologic management included dietary supplements to address malnutrition and increase the patient's BMI, proper sanitation of the household; mask wearing to limit contact with agents that may exacerbate cough; and counseling coupled with education on the patient's episodic concerns. Malnutrition was found by de Sire, et al. (2022) to be associated with poorer health outcomes in older adults, so it must be addressed through supplementation and increased intake.⁷

Family APGAR and SCREEM-RES assessment tools showed a moderately functional family with adequate resources. It would be most prudent to continue monitoring the family, as the patient's condition may continue to cause psychosocial distress for the family over time.

Table 2. Patient-family-community matrix for the patient.

Patient	Family	Community
<p>Biomedical Continue medications : HRZE 150 mg+75 mg+400 mg+275 mg 4 tabs once a day Metformin 500mg/tab three times a day Losartan 100mg/tab once a day Amlodipine 5mg/tab once a day Voriconazole 200mg/tab 2 tabs once a day Vitamin B complex (B6 50mg/tab) once a day Multivitamins + amino acids once a day Oxygen supplementation as needed at 2-4 LPM Ensure good oral intake of food/fluids; balanced diet Paracetamol 500mg/tab every 6 hour for pain Incentive spirometry</p> <p>Wellness</p> <ul style="list-style-type: none"> • Regular geriatric syndrome screening and quality of life assessments • Immunization • Physical activity • Multisensory stimulation <p>Psychosocial</p> <ul style="list-style-type: none"> • Depression screening and interventions • Individual counseling • Emotional support • Spiritual health assessment and support • Advance Directive - Review as deemed necessary. 	<p>Family Meetings - Continue to monitor family members for signs of dysfunction and provide psychosocial support</p> <p>Help family navigate the system (Malasakit Center) Facilitate the acquisition of oxygen compressor</p> <p>Regular caregiver assessment</p>	<p>Identify other support agencies</p> <p>Facilitate navigation: Medication from health centers</p> <p>Mobilization of community resources including church, relevant groups</p>

In line with the Patient-Family-Community (PFC) approach, the patient's family and community were tapped in order to optimize the patient's care. The patient's family was informed of the disease as well as the prognosis with an appropriate level of complexity and tact in order to maximize their knowledge. They were asked to help keep the patient in good spirits to prevent the descent into depression as well as to tap resources such as their religious community and other funding options in order to address the patient's needs. Lastly, local and national resources were involved. The national Malasakit program was utilized to alleviate the financial burden on the family. The local government unit was able to provide services such as the sputum GeneXpert test as well as access to some of his medications.

Follow Up and Outcomes

The patient has another month to complete the 6 month treatment prior to a comprehensive reassessment of his condition. He remains stable, ambulatory, mostly independent, and without signs of depression. He maintains his previous lifestyle consisting of household affairs, being an advisor to the family business, and taking part in religious activities. There were no adverse effects from his current treatment regimen.

DISCUSSION

Lordan, et al. (2023) advised that non-massive hemoptysis of less than 1000 ml is generally self-limiting in 90% of cases and will not usually require specific intervention.⁸ Larici, et al. (2014) stated that for determining the etiology of the hemoptysis, the initial diagnostic procedure of choice is chest x-ray but may be followed up with CT angiography if the radiographic result is nonlocalizing or negative.⁹ In the current patient's case, the hemoptysis was intermittent and relatively small in volume, hence, there was no active intervention done for the hemoptysis. The x-ray was done as an initial diagnostic to determine the cause of the hemoptysis.

Kanj and Soubani (2018) stated that antibodies against aspergillus can be measured in blood samples, presenting with positive IgG results.² It is not completely reliable, however, and some studies show that immunoglobulin levels fluctuate over time and may sometimes present as a negative result.³ Test kits usually detect the most common species, *Aspergillus fumigatus*, and may not test positive when a different species is the pathogen.² Skin tests for *Aspergillus* antigens are available; however, these are largely considered to be more for confirmatory testing rather than diagnostic.³ These tests were not performed on the patient, as the radiologic evidence was deemed sufficient.

Aspergillus is a genus of saprophytic mold that is ubiquitous and present in a wide range of environments. They have been isolated in soil, as well as in hospitals.² *Aspergillus* is an opportunistic pathogen with the majority of infection attributed to the species *Aspergillus fumigatus*. This study divided the manifestations of pulmonary aspergillosis into three main types: allergic bronchopulmonary aspergillosis, chronic pulmonary aspergillosis and invasive pulmonary aspergillosis. To summarize, allergic bronchopulmonary aspergillosis is an inflammatory process

of the airways caused by a hypersensitivity reaction to *Aspergillus* spores. Its signs and symptoms include chronic cough, wheezes, chronic pulmonary infiltrates and possibly bronchiectasis on radiologic imaging. It is most commonly associated with bronchial asthma and cystic fibrosis patients. Invasive pulmonary aspergillosis on the other hand, affects severely immunocompromised patients, such as patients on chemotherapy or immunosuppressive therapy for transplantation or autoimmune conditions.³ Kanj and Soubani (2018) defined it as a direct invasion of lung tissue by aspergillus molds and is an acute condition that presents initially with signs and symptoms similar to bacterial pneumonia and can cause complications such as hematogenous spread of the molds or embolism.² In the current patient's case, the type of pulmonary aspergillosis that developed is chronic pulmonary aspergillosis. First described in the literature in 1981, this term refers to several clinical syndromes presenting with chronic productive cough, weight loss, and hemoptysis with nodules. On imaging, cavitation or fungal balls may be visualized. To make the diagnosis, the patient must present with symptoms for at least three months prior to diagnosis. This is a relatively rare condition and most of the literature is composed of case studies and case series. It is most associated with underlying chronic lung diseases such as COPD, previous pulmonary tuberculosis, thoracic surgery, radiation therapy, pneumoconiosis, cystic fibrosis, lung infarction or sarcoidosis.³ It may also occur in patients who are mildly immunocompromised due to diabetes mellitus, alcoholism, chronic liver disease, low-dose corticosteroid therapy, malnutrition, or connective tissue diseases.^{2,3} Jhun, et al. (2017) also identified advanced age with a median of 65 years, male sex, low BMI (<18.5) and present or past smoking as risk factors, as observed in the current case.¹⁰ Kousha, et al. (2011) determined that mortality for CCPA varies on the data with as high as 39% in American studies to as low as 10% in European studies.

A point of improvement is how the patient, early in the course of treatment, was initially prescribed rifampicin and isoniazid. As Moon, et al. (2015) concluded, rifampicin is a potent cytochrome p450 inducer, with the potential to reduce serum concentrations of azole antifungals.¹⁴ Hayes and Novak-Frazer (2016) found that pulmonary aspergillosis has a moderate mortality rate of 27% at 30 months and 50% at 5 years¹, thus, it was deemed prudent by the attending physician to establish advance care directives. Despite the absence of hemoptysis during the course of treatment, the unexpected cardiac arrest of this patient was a result of an obstructing blood clot that was dislodged during the intubation. Hence, occult bleeding in the airways should be closely monitored.

Anderson, et al. (2015) noted that morbidity after cardiopulmonary resuscitation is mostly found in the central nervous system. This is because the brain is highly sensitive to cardiac arrest due to its lack of ATP stores and anaerobic metabolism. Reperfusion may also cause an increase in oxygen free radicals that may result in subsequent damage.¹² The key elements of the general supportive care of post-cardiac arrest patients are similar to patients in the intensive care setting. They may require airway protection, mechanical ventilator support, seizure precaution and stringent monitoring to ensure adequate oxygenation and ventilation. Over-oxygenation may lead to the formation of free radicals, so it is recommended to titrate the oxygen supplementation to achieve an oxygen saturation of 95%. Monitoring of arterial blood gas,

electrolytes, and blood glucose is advised, as is screening for possible nosocomial infection.¹¹

Fortunately, the patient suffered only a relatively short delay between the identification of dyspnea and being resuscitated. Due to this and the prompt intervention, the patient did not suffer from any overt residual disability after resuscitation. As primary care physicians, they can contribute to the patient's well-being and ultimate recovery, even in patients who require specialist management. This can be achieved by providing individualized care for each patient, as they each have different characteristics and circumstances. They can also see the importance of having a multidisciplinary team work in concert to maximize the patient's care. This case emphasizes the value of consistent hybrid patient and family engagements. While telemedicine was not widely utilized prior to the COVID pandemic, its utility can be seen in cases that require monitoring and supervision, such as this one.

Patient Perspective

The patient finds his current situation dismal. He expressed a desire to get cured as much as possible but also worries that this may put undue financial burden on his family, and he would prefer to leave them financially stable if he expires. While he still feels hope that he can recover completely, he believes that he has already lived a long and fulfilling life and accepts that there is a possibility of his demise as part of God's work. Though the patient seems to have overcome depression, counseling, and emotional support were still provided to him and his family members.

Informed Consent

The patient has given his full consent to document his illness in the form of a case report.

REFERENCES

1. Hayes GE, Novak-Frazer L. Chronic pulmonary aspergillosis - where are we? and where are we going? *J Fungi* 2016; 2(2): 18. doi: 10.3390/jof2020018.
2. Kanj A, Abdallah N, Soubani AO. The spectrum of pulmonary aspergillosis. *J Respir Med* 2018; 1(141): 121-31. doi: 10.1016/j.rmed.2018.06.029.
3. Kousha M, Tadi R, Soubani AO. Pulmonary aspergillosis: a clinical review. *Eur Resp Rev* 2011; 20(121): 156-74. doi: 10.1183/09059180.00001011.
4. Flores GP, Alberto IR, Eala MA, Canal JP. The social determinants of tuberculosis in the Philippines. *Lancet Global Health* 2022; 10(1). doi: 10.1016/S2214-109X(21)00516-7
5. Denning DW, Cadranel J, Beigelman-Aubry C, Ader F, Chakrabarti A, Blot S, Ullmann AJ, Dimopoulos G, Lange C. Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management. *Eur Respir J* 2016; 47(1): 45-68. doi: 10.1183/1393003.00583-2015
6. Douglas AP, Smibert OC, Bajel A, Halliday CL, Lavee O, McMullan B, Yong MK, van Hal SJ, Chen SC. Consensus guidelines for the diagnosis and management of invasive aspergillosis. *Internal Medicine Journal* 2021; 51(7): 143-76. doi:10.1111/imj.15591
7. de Sire A, Ferrillo M, Lippi L, Agostini F, de Sire R, Ferrara PE, Ragusa G, Riso S, Rocuzzo A, Ronconi G, Invernizzi M, Migliario M. Sarcopenic Dysphagia, Malnutrition, and Oral Frailty in Elderly: A Comprehensive Review. *Nutrients* 2022; 14(5): 982. doi: 10.3390/nu14050982
8. Lordan JL, Gascoigne A, Corris PA. The pulmonary physician in critical care Illustrative case 7: Assessment and management of massive haemoptysis. *Thorax* 2023; 58(9): 814-9. doi: 10.1136/thorax.58.9.814
9. Larici AR, Franchi P, Occhipinti M, et al. Diagnosis and management of hemoptysis. *Diagn Int Radiol* 2014; 20(4): 299-309. doi: 10.5152/dir.2014.13426
10. Jhun BW, Jung WJ, Hwang NY, Park HY, Jeon K, Kang ES, Koh WJ. Risk factors for the development of chronic pulmonary aspergillosis in patients with nontuberculous mycobacterial lung disease. *PLoS One* 2017; 12(11). doi:10.1371/journal.pone.0188716
11. Girotra S, Chan PS, Bradley SM. Post-resuscitation care following out-of-hospital and in-hospital cardiac arrest. *Heart* 2015; 101(24): 1943-9. doi: 10.1136/heartjnl-2015-307450
12. Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-hospital cardiac arrest: A review. *J Am Med Assoc* 2019; 321(12): 1200-10. doi: 10.1001/jama.2019.1696
13. Sandherr M, Maschmeyer G. Pharmacology and metabolism of voriconazole and Posaconazole in the treatment of invasive aspergillosis: review of the literature. *Eur J Med Res* 2011; 16(4): 139-44. doi: 10.1186/2047-783x-16-4-139.
14. Moon SM, Park HY, Jeong BH, Jeon K, Lee SY & Koh WJ. Effect of rifampin and rifabutin on serum itraconazole levels in patients with chronic pulmonary aspergillosis and coexisting nontuberculous mycobacterial infection. *Antimicrobial Agents and Chemotherapy* 2015; 59(1): 663-5.
15. Department of Health. (2020). National Tuberculosis Control Program Manual of Procedures 6th edition. Department of Health National Tuberculosis Control Program. <https://ntp.doh.gov.ph/download/ntp-mop-6th-edition/>