

# Navigating Influenza Complications: The Enigma of *Aspergillus Tamaris*-Induced IAPA

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**Abstract:** *Influenza is a devastating respiratory illness that spreads quickly and causes yearly pandemics as well as significant morbidity and mortality worldwide. While majority of influenza illnesses go away without serious problems, some people may develop post - influenza complications such subsequent bacterial or fungal infections. Among these, invasive pulmonary aspergillosis (IPA) has been recognised as a serious condition that can result in higher fatality rates, especially in individuals with impaired immune systems. However, there is not enough information on certain fungi infections, such as Influenza - Associated Invasive Pulmonary Aspergillosis (IAPA), especially regarding the COVID - 19 and H1N1 pandemic influenza strains from 2009 that caused the illness. [1] This article presents a unique and rare occurrence of IAPA caused by the infrequent pathogen *Aspergillus tamaris* in a 33 - year - old male with a history of asthma. The patient's clinical course was noteworthy, as it was preceded by a 50 - day hospitalisation for COVID - 19 pneumonia in August 2020, requiring mechanical ventilation for 37 days. Surprisingly, the patient had no lingering respiratory symptoms after recovering from COVID - 19. In April 2022, the patient was re - admitted to the hospital with fever, cough, and dyspnea, following exposure to a cold environment after a temple visit. High - resolution computed tomography (HRCT) scans revealed progressive lung abnormalities since the previous scan in August 2020, with ground glass opacities (GGOs), crazy paving, nodules, and traction bronchiectasis evident. Subsequent examination identified pandemic (H1N1) 2009 infection through nasopharyngeal swab, and further analysis of expectorated sputum showed thin septate hyphae with acute angle branching, resembling *Aspergillus* species. Serum galactomannan was also positive, leading to a probable diagnosis of IAPA. The patient received Posaconazole (PCZ) treatment following confirmation of *Aspergillus tamaris* as the causative agent, determined through sputum fungal culture and MALDI TOF MS analysis. *Aspergillus tamaris* is an infrequent human pathogen, with previous case reports documenting its involvement in eyelid infections, keratitis, invasive sinonasal infections, and onychomycosis. Sensitivity Minimum Inhibitory Concentrations (MICs) for anti - fungal drugs, Itraconazole, Voriconazole, Posaconazole, and Isavuconazole, were determined. Based on therapeutic drug monitoring (TDM) results, Posaconazole (PCZ) was continued to ensure adequate drug exposure and the patient's clinical improvement. In patients with a history of severe influenza infections, particularly those with underlying respiratory conditions or a history of COVID - 19, this case report emphasizes the importance of considering fungal infections like IAPA into consideration. Given IAPA's rapid progress and high rates of morbidity and mortality, it is crucial to recognize the condition early. In these rare and serious cases of IAPA, on time identification, appropriate diagnostic testing, and targeted anti - fungal medication adapted to the identified pathogen are crucial for improving patient outcomes. Further, more investigation and data gathering are needed to fully recognise the epidemiology, risk factors, and optimal management approaches of IAPA, both in India and internationally. Increased awareness and knowledge sharing among medical professionals can help with quick identification and efficient treatment of this serious illness.*

**Keywords:** Influenza, COVID - 19, *Aspergillus tamaris*, Antifungals

## 1. Introduction

Seasonal outbreaks and sporadic pandemics of influenza, which is brought on by various strains of the influenza virus, remains to be a serious concern for health worldwide. While most cases of influenza results in moderate respiratory symptoms, certain people, especially those with past illnesses or compromised immune systems, might experience severe complications which may require hospitalisation and may raise mortality rates. A notable post - influenza consequence that has evolved in addition to secondary bacterial infections is invasive pulmonary aspergillosis (IPA), which is one of the most serious and life - threatening illnesses. The rare but serious complication known as influenza - associated invasive pulmonary

aspergillosis (IAPA) can develop after infection with pandemic influenza viruses. Although co - infections with bacteria and viruses have been well - documented in influenza cases, information on particular fungal infections like IAPA is scarce. We believe that this case report represents the first incidence of IAPA brought on by *Aspergillus tamaris*, which occurred following pandemic (H1N1) 2009 infection and 20 months after a prior episode of COVID - 19.

In this article, *Aspergillus tamaris* - induced IAPA's distinctive clinical appearance, diagnostic difficulties, and therapeutic issues are discussed. With an emphasis on uncommon fungal diseases like IAPA, we seek to increase healthcare providers' awareness of the possible

consequences that might follow severe influenza infections. Further studies into the prevalence, risk factors, and best care practices for IAPA in other groups, particularly those with scant information on the disorder, are another goal of our study.

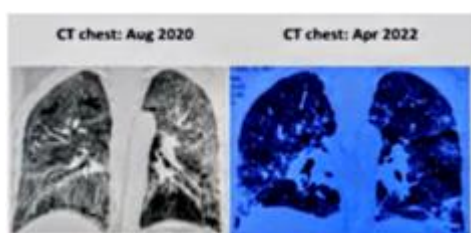
In this article, we give a thorough description of the patient's medical history, clinical symptoms, diagnostic tests, and treatment plan. The findings highlight the necessity for early detection and adequate diagnostic procedures, such as sputum fungal culture and galactomannan assays, to enable quick and precise diagnosis of IAPA. We also examine the reasons for selecting anti-fungal medication, taking into account the uncommon pathogen *Aspergillus tamarii* and the patient's clinical response to therapy.

## 2. Literature Survey

Multiple infections can occur after 2009, pandemic influenza, including fungal and bacterial infections, but data from India are limited. To our knowledge this is the 1<sup>st</sup> reported case of Influenza associated invasive pulmonary aspergillosis (IAPA), caused by *Aspergillus tamarii*, after infection with pandemic (H1N1) 2009 which was preceded by COVID - 19, 20 months before.

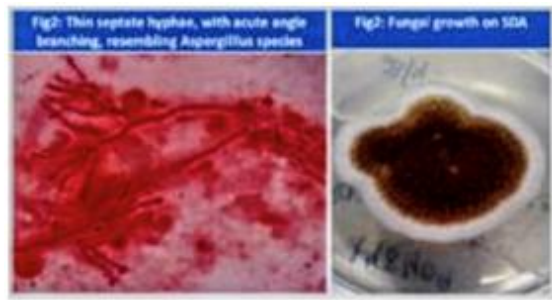
## 3. Methods & Results

A 33 yrs, male, known asthmatic, had been hospitalised elsewhere in August 2020 with COVID - 19 pneumonia for 50 days and had been on mechanical ventilation for 37 days. He had no residual respiratory symptoms 3 months after recovery from COVID - 19. He was admitted to a Hospital in April 2022 with fever, cough, dyspnea for 8 days, which developed after a cold bath in a temple. HRCT (chest) showed ground glass opacities (GGOs), crazy paving, nodules and traction bronchiectasis. Review of previous HRCT showed that only GGOs were present as shown in the picture.



**Figure 1:** HRCT of patient in 2020 and 2022

At admission the Nasopharyngeal swab was positive for pandemic (H1N1) 2009 in the filmarray respiratory panel and no other pathogen was detected. He was treated with Oseltamivir. Expecterated sputum examination showed a heavy load of thin septate hyphae with acute angle branching, resembling *Aspergillus* species as shown in the picture and Serum Galactomannan was positive.



**Figure 2 & 3:** Fungal growth on SDA and showing thin septate hyphae.

Based on these features he was diagnosed as a case of probable IAPA and initiated on Posaconazole (PCZ) treatment. Sputum fungal culture was positive and was identified by MALDI TOF MS as *Aspergillus tamarii*. *Aspergillus tamarii* has been rarely as encountered as a human pathogen. Case report involves eyelid infection, keratitis, invasive sinonasal infection and onychomycosis exist. Sensititre MICs were 0.0625 mcg/ml, 0.125 mcg/ml, 0.0625 mcg/ml, 0.125 mcg/ml for Itraconazole, Voriconazole, Posaconazole and for Isavuconazole respectively. The usually obtained Posaconazole (PCZ) trough level with standard dose is 1.2 mg/l which generates AUC of 200R. The usually obtained Isavuconazole (ISVCZ) trough level with standard dose is 3 mg/l which generates AUC of 100R. The PKPD Index, AUC/MIC of 100, is needed with both these azoles for a therapeutic effect. Therefore, it would be possible to treat this infection with any of these azoles. PCZ was continued in view of easy availability of therapeutic drug monitoring (TDM) to assure adequate drug exposure, lower cost and clinical improvement which had already occurred.

## 4. Discussion

Invasive pulmonary aspergillosis (IPA) has been linked to severe influenza infections, and this is well-established in the medical literature. IAPA, or influenza-associated invasive pulmonary aspergillosis, is a complicated and difficult consequence, especially in people with impaired immune systems or underlying respiratory problems. This case report details a singular and unusual occurrence of *Aspergillus tamarii*-caused IAPA that followed pandemic (H1N1) 2009 infection and occurred 20 months after an earlier COVID - 19 incident.

The invasion of *Aspergillus* species into lung tissue, which causes severe inflammation and sometimes fatal consequences, is what distinguishes IAPA from other lung diseases. Although research into the mechanism of *Aspergillus* infection after influenza is still underway, it is thought that the respiratory epithelial cells' damage from the influenza virus fosters *Aspergillus* colonisation [1].

As IAPA can advance quickly and is linked to high death rates [3], early identification is essential for optimal care. In this instance, the patient's clinical symptoms, which included fever, coughing, and dyspnea, motivated more research that resulted in the discovery of *Aspergillus tamarii* as the culprit responsible for the disease. It should be noted that the patient had a history of COVID - 19, which may have

influenced the development of IAPA because of lingering immunosuppression or lung tissue injury [2]. The exact *Aspergillus* species discovered, and the patient's clinical state determine the choice of anti - fungal treatment for IAPA. Anti - fungal medication sensitivity minimum inhibitory concentrations (MICs) were established to direct treatment choices. Posaconazole (PCZ) was used in this instance because it is therapeutic drug monitoring (TDM) accessible, assuring appropriate.

Our study highlights the significance of taking fungal infections, in particular IAPA, into account in patients who have a history of severe influenza infections or other viral respiratory disorders, including COVID - 19 [1]. Healthcare practitioners need to be aware of the possibility of post - influenza consequences and should look into respiratory symptoms that develop or persist very once. Targeted anti - fungal medication must begin quickly when a timely diagnosis is made using the proper diagnostic techniques, such as sputum fungal culture and galactomannan assays.

A multidisciplinary strategy combining pulmonologists, clinical microbiologists, and infectious disease experts is necessary for the effective management of IAPA. To assess the efficacy of anti - fungal medication and identify any indications of disease progression or unfavourable treatment effects, regular follow - up visits and close monitoring of the patient's clinical response to treatment are essential.

## 5. Conclusion

An uncommon but serious consequence that can follow infection with pandemic influenza viruses is influenza - associated invasive pulmonary aspergillosis (IAPA). In the patient in this article, who had a history of COVID - 19 and asthma, *Aspergillus tamarii* induced IAPA, which is a rare and extraordinary occurrence [1, 5]. The circumstance emphasizes the need of diagnosing and treating uncommon fungal infections in individuals with a history of severe influenza or prior viral respiratory disorders.

It is essential to diagnose IAPA accurately and early in order to start therapy right away. Galactomannan assays and other suitable diagnostic procedures, such as sputum fungal culture, can help identify the pathogen that is causing symptoms including fever, cough, and dyspnea. Targeted anti - fungal medication must be administered promptly to slow the disease's fast course and enhance patient outcomes.

In this case, Posaconazole (PCZ) was chosen as the anti - fungal agent based on its availability of therapeutic drug monitoring (TDM) and the patient's positive clinical response. Isavuconazole (ISVCZ) could have been an alternative treatment option given the susceptibility of *Aspergillus tamarii* to both PCZ and ISVCZ. The achievement of the PKPD index, AUC/MIC of 100, with these azoles further supports their therapeutic effectiveness.

## 6. Future Scope

The future scope of the topic discussed in the article holds significant promise. As our understanding of respiratory illnesses, including the complications associated with

influenza and fungal infections like Influenza - Associated Invasive Pulmonary Aspergillosis (IAPA), continues to evolve, several areas warrant attention:

- 1) **Epidemiology and Risk Factors:** Further research is needed to establish the prevalence and identify specific risk factors for IAPA, especially in different patient populations. Understanding who is most vulnerable to this condition can guide preventive measures and early intervention.
- 2) **Diagnostic Advances:** Ongoing advancements in diagnostic tools, such as improved imaging techniques and molecular diagnostics, can enhance our ability to diagnose IAPA promptly and accurately. This may lead to earlier treatment and better outcomes.
- 3) **Treatment Strategies:** Research into optimal anti - fungal therapies, dosages, and duration of treatment for various fungal pathogens, including uncommon ones like *Aspergillus tamarii*, can improve patient care. Personalised treatment approaches based on the pathogen and patient's condition may become more common.

In summary, the future of this topic involves ongoing research, diagnostic advancements, and collaborative efforts to enhance our ability to detect, prevent, and treat IAPA and other post - influenza complications effectively. This will ultimately improve patient outcomes and reduce the burden of these rare but serious conditions.

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