

Ultra-early Invasive Pulmonary Aspergillosis after Mild Influenza A

Dandan Weng¹, Minghao Shen², Guancheng Huang³, Juanfen Chu⁴, Jie Lu⁵, Jianfeng Chu⁶, Jian Zhang⁷, Li Zhou⁸, Zhujun Cao⁹

Abstract

Influenza-associated invasive pulmonary aspergillosis (IAPA) is a rare complication, usually affecting critically ill or immunocompromised patients. The case of a patient who first presented on January 2, 2025, with fever, productive cough, and pleuritic chest pain is presented. Imaging showed non-specific viral pneumonia without typical fungal features. Diagnosis was confirmed by positive sputum culture for *Aspergillus fumigatus*, two consecutive elevated serum galactomannan levels, positive fungal nucleic acid testing, and high-load *Aspergillus* reads on bronchoalveolar lavage fluid targeted next-generation sequencing. The patient received Voriconazole for 7.5 weeks with marked clinical and radiological improvement. Follow-up six weeks after discontinuation showed no recurrence. This case highlights the fact that IAPA may occur early in immunocompetent adults with mild influenza. High clinical suspicion and multimodal diagnostic testing are essential for timely recognition.

Keywords: Post-influenza complications, Rapid diagnosis, Public health.

DOI: <https://doi.org/10.47391/JPMA.31622>

Introduction

Influenza A remains a major global health burden.¹ Secondary fungal infection, particularly invasive pulmonary aspergillosis (IPA), is predominantly described in critically ill or immunocompromised individuals, including those with chronic obstructive pulmonary disease (COPD), malignancies, or those admitted in intensive care units (ICU).² However, influenza-associated

invasive pulmonary aspergillosis (IAPA) in immunocompetent adults with only mild influenza symptoms is exceptionally rare. Its non-specific clinical and radiological manifestations often delay recognition, leading to rapid disease progression.³ Reporting such atypical presentations is essential to raise clinical awareness and support timely diagnosis in patients without traditional risk factors. We present this case to raise awareness of unusually early-onset IAPA following mild influenza A infection in an immunocompetent adult without traditional risk factors, a rare presentation that may otherwise be overlooked.

Case Report

A 56-year-old male presented on January 2, 2025 to Yangming Hospital Affiliated to Ningbo University in Yuyao, Ningbo, Zhejiang Province, China, with a four-day history of fever (peak 39°C). He also reported productive cough with thick yellow sputum, chest tightness, and intermittent paroxysmal chest pain that worsened with deep inspiration. He had no significant past medical history, denied smoking, and reported no history of COPD.

On admission, his temperature was 38.4°C, blood pressure 115/76 mmHg, pulse 96 beats per minute, and respiratory rate 20 breaths per minute. Routine blood tests revealed

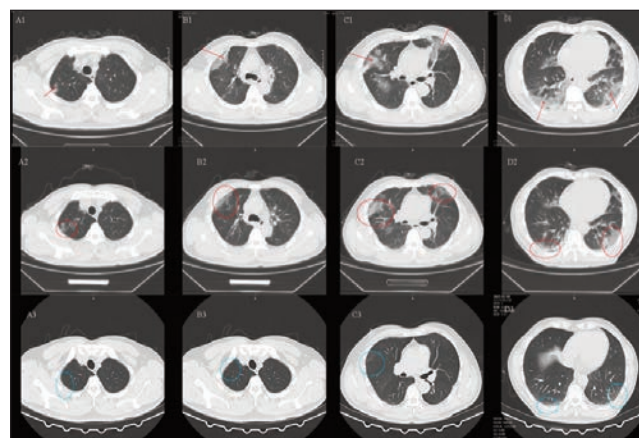


Figure-1: Chest CT scan obtained on January 2, 2025. (A1–D1) Multiple ground-glass opacities and patchy consolidations are observed in both lungs (red arrows), predominantly in the lower lobes.

(A2–D2) Chest CT images obtained on January 6, 2025, after antiviral but before antifungal therapy. (A3–D3) Chest CT images obtained on March 4, 2025, following antifungal treatment. Lesions marked by blue circles showed greater improvement compared to those marked by red circles.

¹⁻⁴Department of Infectious Diseases, Yangming Hospital Affiliated to Ningbo University, Ningbo, China; ⁵Department of Radiology, Yangming Hospital Affiliated to Ningbo University, Ningbo, China; ⁶Department of Pathology, Yangming Hospital Affiliated to Ningbo University, Ningbo, China; ⁷Department of Respiratory Medicine, Yangming Hospital Affiliated to Ningbo University, Ningbo, China; ⁸Department of Laboratory Medicine, Yangming Hospital Affiliated to Ningbo University, Ningbo, China; ⁹Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

Correspondence: Zhujun Cao. e-mail: estherlucifer@163.com

ORCID ID: 0000-0002-8684-2107

Submission completed: 21-07-2025 **1st Revision received:** 25-11-2025

Acceptance: 15-07-2026

Last Revision received: 14-07-2026

Table-1: Changes in Blood Routine Parameters (White Blood Cells, Neutrophils, Platelets, C-Reactive Protein).

Item	Jan 1	Jan 2	Jan 9	Jan 9	Mar 4	Apr 15	Reference Range
WBC($\times 10^9/L$)	4.9	1.7	14.0	10.0	6.1	6.0	3.5–9.5
Neutrophils ($\times 10^9/L$)	1.0	1.2	12.5	8.4	4.3	4.0	1.8–6.3
Plt($\times 10^9/L$)	115	133	161	282	154	140	125–350
hs-CRP (mg/L)	33.9	53.4	3.3	11.9	<0.5	<0.5	<5

WBC, white blood cell; hs-CRP, high-sensitivity C-reactive protein; Plt, platelet.

leukopenia and neutropenia (Table 1). Influenza A nucleic acid test was positive and severity scores (CURB-65 = 0; PSI Class II) indicated mild disease.^{4,5}

A chest computed tomography (CT) scan performed on January 2 demonstrated bilateral inflammatory infiltrates suggestive of viral pneumonia (Figure 1). Despite antiviral and antibacterial treatment, the patient's cough and chest pain remained persistent. These unexplained symptoms prompted fungal evaluation. Serum galactomannan levels on January 4 and 6 were markedly elevated, with values of 1.32 and 2.12, respectively (reference range: <0.5). Sputum culture and fungal nucleic acid testing identified *Aspergillus fumigatus*. Bronchoscopy done on January 6 revealed inflammatory secretions, and targeted next-generation sequencing of Bronchoalveolar Lavage Fluid (BALF) detected 127,025 *Aspergillus* reads, confirming IAPA. A follow-up CT scan obtained on January 6, after antiviral but before antifungal therapy, showed progression of pulmonary lesions (Figure 1).

Voriconazole therapy was initiated intravenously on January 7 at a dose of 0.2 g every 12 hours, and was later switched to oral administration at 0.2 g every 12 hours to complete a 7.5-week course. Oseltamivir was continued until January 7, and Moxifloxacin was discontinued after bacterial infection was excluded. Corticosteroids were tapered gradually in accordance with clinical improvement.

The patient showed steady clinical recovery during antifungal treatment. His cough, sputum production, and chest pain progressively resolved, and inflammatory markers normalised. He was discharged on January 9, 2025, after 7 days of hospitalization. A follow-up CT scan obtained on March 4 demonstrated near-complete resolution of the pulmonary lesions (Figure 1). Routine blood tests also returned to normal (Table 1). At a six-week post-treatment follow-up, the patient remained asymptomatic with no evidence of recurrence.

Discussion

This case highlights an unusually rapid onset of IAPA in an immunocompetent patient with mild influenza, which is in contrast with previously reported cases in which the onset typically occurred much later in the course of the disease. For example, M. Lewis et al. reported a case in 1985, and Oh

Kyung Kwon et al. described a patient who developed IAPA after more than 10 days of illness, presenting with severe hypoxaemia (oxygen saturation dropping to 82%).^{6,7} In contrast, the current patient developed confirmed *Aspergillus* infection within 96 hours while remaining clinically stable, representing an exceptionally early manifestation. To our knowledge, this is the first reported case of early-onset IAPA in an immunocompetent patient following influenza-like illness.

Viral upper respiratory tract infections may facilitate early *Aspergillus* invasion by disrupting epithelial barriers, altering local immune responses, and promoting fungal susceptibility through pro-inflammatory cytokine pathways.² Leukopenia and lymphopenia—frequently observed in influenza—may also signal transient impairment of host defences, thereby increasing vulnerability to fungal superinfection.⁸

Diagnosing IAPA in immunocompetent individuals can be difficult due to the overlap with viral or bacterial pneumonia. In the current case, imaging findings were inconclusive, sputum cultures had contamination risks, and serum GM testing had potential false-positive results. The use of tNGS on BALF was crucial for pathogen identification and helped avoid diagnostic delays. Clinicians should suspect IAPA when there is persistent fever and chest pain, or a GM test comes positive despite standard therapy, even in non-severe influenza cases.

Treatment strategies must balance antiviral, anti-inflammatory, and antifungal approaches. While corticosteroids can reduce airway inflammation, their immunosuppressive effects may exacerbate fungal infections.⁹ Antivirals, such as Oseltamivir, improve influenza outcomes but do not prevent secondary fungal infections. In this case, Voriconazole therapy was essential for recovery, highlighting its role even in immunocompetent patients.

This report is limited by its single-case nature and single-centre origin, which may affect the generalisability of the findings. Moreover, access to advanced diagnostics like tNGS remains restricted in many clinical settings. Future research should explore immune changes post-viral infection and their role in IAPA pathogenesis among immunocompetent hosts. Multicentre studies are needed to evaluate novel diagnostic tools and optimise antifungal treatment strategies, thereby improving early detection, individualised management, and patient outcomes.

Conclusion

IAPA may occur earlier than anticipated in immuno-

competent adults with mild influenza. Prompt consideration of fungal infection in atypical clinical courses can facilitate timely management. Greater clinical awareness is warranted during influenza seasons.

Ethical Approval and Consent to Participate: Informed consent for the publication of medical history and photographs was obtained from the patient. Approval for case publication was granted by the head of the Department of Infectious Diseases at Ningbo University Affiliated Yangming Hospital.

Acknowledgments: The authors thank the patient for his cooperation and support.

Disclosure: None.

Conflict of Interest: None.

Funding Sources: None.

References

1. World Health Organisation (WHO). Influenza (seasonal). News release. The WHO Media Centre. [Online] 2025 [Cited 2025 January 01]. Available from URL: [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))
2. Schauwvlieghe AFAD, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Van Tienen C, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. *Lancet Respir Med* 2018;6:782-92. doi: 10.1016/S2213-2600(18)30274-1.
3. Myszor IT, Gudmundsson GH. Modulation of innate immunity in airway epithelium for host-directed therapy. *Front Immunol* 2023;14:e1197908. doi: 10.3389/fimmu.2023.1197908.
4. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377-82. doi: 10.1136/thorax.58.5.377.
5. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243-50. doi: 10.1056/NEJM199701233360402.
6. Lewis M, Kallenbach J, Ruff P, Zaltzman M, Abramowitz J, Zwi S. Invasive pulmonary aspergillosis complicating influenza A pneumonia in a previously healthy patient. *Chest* 1985;87:691-3. doi: 10.1378/chest.87.5.691.
7. Kwon OK, Lee MG, Kim HS, Park MS, Kwak KM, Park SY. Invasive pulmonary aspergillosis after influenza A infection in an immunocompetent patient. *Tuberc Respir Dis (Seoul)* 2013;75:260-3. doi: 10.4046/trd.2013.75.6.260.
8. Iwasaki A, Medzhitov R. Regulation of adaptive immunity by the innate immune system. *Science* 2010;327:291-5. doi: 10.1126/science.1183021.
9. Martin-Loeches I, Lisboa T, Rhodes A, Moreno RP, Silva E, Sprung C, et al. Use of early corticosteroid therapy on ICU admission in patients affected by severe pandemic (H1N1)v influenza A infection. *Intensive Care Med* 2011;37:272-83. doi: 10.1007/s00134-010-2078-z.

Author Contribution:

DW, MS, GH, JC, JL, JC, JZ, LZ, & ZC: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.