

Invasive Pulmonary Aspergillosis Following Influenza Infection: Diagnostic and Therapeutic Challenges

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Background: Invasive pulmonary aspergillosis (IPA) is traditionally considered a disease of profound immunocompromising conditions (e.g., transplantation). Yet influenza-associated pulmonary aspergillosis (IAPA) is an emerging threat affecting ~10-20% of critically ill influenza patients, with ~50% mortality despite antifungal therapy. Diagnosis can be obscured by concurrent bacterial infection, and first-line antifungals carry major drug interactions and toxicity risk. We report a case of IAPA in a patient with minimal immunosuppression, complicated by concurrent pneumococcal pneumonia.

Case: A 74-year-old woman with chronic obstructive pulmonary disease, obstructive sleep apnea, and depression presented with two weeks of progressive dyspnea, cough, and fatigue following influenza. She had completed outpatient courses of prednisone and doxycycline. On examination, she was afebrile but hypotensive (84/53 mmHg), with oxygen saturation of 92% on room air, coarse breath sounds, and wheezing. Computed tomography (CT) demonstrated nodules with surrounding ground-glass attenuation (halo sign) and early cavity changes, concerning for invasive fungal infection. A positive *Streptococcus pneumoniae* urinary antigen led to an initial diagnosis of bacterial pneumonia, and ceftriaxone plus azithromycin were started. However, sputum culture grew *Aspergillus fumigatus*.

Pulmonology and infectious diseases were consulted. Bronchoscopy with bronchoalveolar lavage (BAL) was performed; serum beta-D-glucan, BAL galactomannan, BAL polymerase chain reaction, and BAL pathology were positive for *Aspergillus*, confirming IPA. Allergic bronchopulmonary aspergillosis was excluded. Voriconazole 250 mg twice daily was initiated. Follow-up CT showed left-sided resolution, but new right lower lobe opacities and bronchiectasis, showing the dynamic nature of IPA despite treatment. The patient was discharged with close outpatient follow-up.

Discussion & Conclusions: This case illustrates how IPA can mimic and coexist with bacterial pneumonia following influenza. Concurrent pneumococcal pneumonia initially anchored the diagnostic evaluation, delaying IAPA recognition. Lack of improvement on antibacterial therapy was the pivotal clue prompting further investigation. This patient's risk factors were limited to recent influenza, structural lung disease, and brief corticosteroid exposure, highlighting that profound immunosuppression is not required for IAPA to occur.

Voriconazole's CYP3A4 inhibitory profile necessitated close monitoring. She later developed voriconazole toxicity (supratherapeutic levels, transaminitis, visual disturbances) and transitioned to posaconazole, underscoring the need for ongoing antifungal surveillance in polypharmacy patients. In influenza patients with steroid exposure or structural lung disease, do not let a positive bacterial test end the diagnostic search; co-infection with IAPA is possible, and lack of clinical improvement should prompt early evaluation.

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