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Olanzapine-Induced Pulmonary Embolism: A Case Report

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Abstract | **Case Report**

Background: Atypical antipsychotics, particularly olanzapine, are widely used first-line agents for psychotic and mood disorders due to their favorable neurological side-effect profile compared to first-generation antipsychotics. However, their association with severe systemic adverse events, such as venous thromboembolism (VTE) and pulmonary embolism (PE), is an increasingly recognized but underdiagnosed risk. ***Case Presentation:*** A 30-year-old male with no prior psychiatric or medical history was admitted for schizophreniform disorder and initiated on olanzapine (10 mg/day). After five weeks of successful psychiatric stabilization, the patient acutely developed bilateral chest pain and exertional dyspnea. Electrocardiography (ECG) demonstrated sinus tachycardia and an S1Q3T3 pattern. A computed tomography pulmonary angiogram (CTPA) confirmed a right proximal pulmonary embolism. A comprehensive workup for inherited and acquired thrombophilia - including antithrombin, protein C, protein S activities, and antiphospholipid antibodies - was entirely negative. No classic immobility or lifestyle risk factors were present. Olanzapine was discontinued, and the patient was successfully cross-tapered to aripiprazole while receiving apixaban. Complete resolution of the PE was radiologically confirmed at three months. ***Conclusion:*** This case highlights the necessity of maintaining a high index of clinical suspicion for thromboembolic complications in patients treated with olanzapine, even in young individuals without baseline risk factors. Early recognition and interdisciplinary management are vital to preventing mortality.

Keywords: Atypical antipsychotics, Olanzapine, Venous thromboembolism, Pulmonary embolism, Schizophreniform disorder, Drug-induced thrombosis.

INTRODUCTION

Atypical antipsychotics (second-generation antipsychotics, SGAs) have revolutionized the treatment of schizophrenia, bipolar disorder, and other psychotic conditions. While they carry a significantly lower risk of extrapyramidal symptoms compared to first-generation agents, they are heavily linked to metabolic side effects, including weight gain, dyslipidemia, and altered glucose metabolism [1].

Beyond these metabolic concerns, growing epidemiological evidence over the last two decades has connected SGA use with an increased risk of venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and its life-threatening complication, pulmonary embolism (PE) [2]. Among the atypical agents, low-potency medications and specific clozapine- or olanzapine-based regimens appear to carry the highest relative risk [3]. The risk is particularly pronounced during the initial months of treatment initiation [4].

Despite these documented associations, the routine monitoring of hematological and vascular risks during olanzapine therapy remains underemphasized in clinical guidelines compared to metabolic parameters. This case report describes a young, physically active 30-year-old male who developed an acute proximal pulmonary embolism during the sixth week of low-dose olanzapine monotherapy, in the absence of any genetic, acquired, or situational prothrombotic risk factors.

CASE PRESENTATION

Patient History & Clinical Presentation

Mr. B.A., a 30-year-old single male employed as a security guard, presented to our psychiatric department with a history of recent behavioral changes, social withdrawal, and marked irritability. He had no notable personal or family history of psychiatric illness, cardiovascular disease, or coagulopathies.

The onset of symptoms began in December 2024 with the emergence of auditory-verbal hallucinations. The patient reported hearing the voices of

his coworkers harassing and criticizing him for his solitude and lack of emotional or sexual experience. This triggered a poorly systematized persecutory delusion, causing profound mistrust toward his professional environment, severe irritability, and social isolation. Concurrently, he increased his tobacco and cannabis use and engaged in frequent workplace interpersonal conflicts.

In February 2025, attempting to resolve his perceived inadequacies, the patient approached female pedestrians on three separate occasions to abruptly ask for their hands in marriage. The systematic rejections he faced resulted in a collapse of self-esteem, intense self-deprecation, and suicidal ideation without a specific plan. This was accompanied by classic features of a major depressive episode, including anhedonia, loss of interest in hobbies, refuge hypersomnia, and persistent asthenia. Following an evaluation by a general practitioner, he was referred to the psychiatric emergency department and hospitalized in April 2025.

Evaluation and Initial Management

Upon admission, the psychiatric evaluation revealed an anxious, irritable patient with labored rapport, though personal hygiene was preserved. He exhibited hypomimia, a distinctly dysphoric and depressed mood, persecutory delusions centered on his workplace, and auditory hallucinations delivering pejorative commentary. His judgment was impaired, and he experienced anorexia alongside hypersomnolence.

Based on a symptom duration of greater than one month but less than six months, a diagnosis of schizophreniform disorder was established according to DSM-5 criteria. Treatment was initiated with olanzapine, gradually titrated up to 10 mg/day, and alprazolam (2 mg/day). The therapeutic response after five weeks was highly favorable; the patient achieved complete insight into his delusional ideas and perceptual phenomena, and his mood normalized.

Systemic Adverse Event: Pulmonary Embolism

During the sixth week of treatment, while still hospitalized but fully ambulatory, the patient acutely developed bilateral chest pain and exertional dyspnea. Immediate cardiopulmonary examination revealed sinus tachycardia. An ECG demonstrated the classic S1Q3T3 pattern (deep S wave in lead I, Q wave in lead III, and inverted T wave in lead III). A computed tomography pulmonary angiogram (CTPA) was urgently performed and confirmed a right proximal pulmonary embolism.

The patient was immediately transferred to a specialized unit, and a comprehensive etiological workup was initiated to screen for underlying thrombophilia or compounding risk factors:

- **D-dimer:** 1800 ng/mL (elevated)
- **Standard Coagulation Profile:** Prothrombin time (PT) activity at 79%; INR at 1.19
- **Immunological Screening:** Antinuclear antibodies (ANA) were negative
- **Inherited Thrombophilia Panel:**
  - Protein C activity (chromogenic assay): 88% (Normal)
  - Protein S activity (clotting assay): 122% (Normal)
  - Antithrombin activity: 95% (Normal; reference range: 80–120%)
- **Antiphospholipid Syndrome (APS) Screening:**
  - Lupus anticoagulant: Negative
  - Anti-beta-2-glycoprotein I IgG antibodies: < 7 U/mL (Normal: < 7)
  - Anti-cardiolipin IgG antibodies: 10 GPL U/mL (Normal: < 20)
  - Anti-cardiolipin IgM antibodies: 13 MPL U/mL (Normal: < 20)

Therapeutic Adjustment and Follow-Up

Given the entirely negative thrombophilia and autoimmune screen, alongside the complete absence of typical provoking factors - such as prolonged immobilization, recent surgery, trauma, obesity, or long-haul travel - olanzapine was strongly suspected as the primary etiological driver.

An interdisciplinary management strategy was enacted:

1. **Cardiovascular Intervention:** Anticoagulant therapy was initiated utilizing a direct oral anticoagulant (DOAC), apixaban, at a dose of 5 mg twice daily.
2. **Psychiatric Intervention:** Olanzapine was gradually cross-tapered and discontinued. It was replaced with aripiprazole, which was titrated to a target maintenance dose of 20 mg/day.

The switch to aripiprazole maintained psychiatric stability with no recurrence of psychotic or depressive symptoms. A follow-up CTPA performed three months after starting the anticoagulant therapy revealed a complete resolution of the proximal pulmonary embolism, with no residual radiological abnormalities. Both his cardiovascular and psychiatric outcomes remained completely favorable over medium-term follow-up.

DISCUSSION

This case highlights a critical and potentially fatal complication of second-generation antipsychotic therapy. While olanzapine is frequently selected for its low risk of extrapyramidal symptoms, its propensity to induce venous thromboembolism presents a clear clinical challenge. Large pharmacoepidemiological studies indicate that patients exposed to atypical antipsychotics face an approximate 1.5- to 2.5-fold increased risk of developing VTE compared to non-users [5]. Among

these agents, olanzapine and clozapine consistently exhibit the highest risk profiles [3,5].

Several mechanisms have been proposed to explain how olanzapine induces a prothrombotic state:

- **Sedation and Hypersomnolence:** Olanzapine induces marked sedation and, as seen in our patient, can cause severe hypersomnolence. This leads to prolonged periods of physical immobility, promoting venous stasis in the deep veins of the lower extremities [6].
- **Platelet Aggregation:** Olanzapine is a potent antagonist of the 5-HT2A serotonin receptor. Blockade of these receptors can upregulate platelet activation and accelerate aggregation, directly contributing to thrombus formation [7].
- **Metabolic and Adipokine Alterations:** Olanzapine induces rapid weight gain and metabolic syndrome. It elevates levels of plasminogen activator inhibitor-1 (PAI-1) and increases pro-inflammatory cytokines, which impair endogenous fibrinolysis and damage vascular endothelial cells [8].
- **Hyperprolactinemia:** Antipsychotic-induced elevations in prolactin have also been associated with platelet hyper-reactivity, further compounding the hypercoagulable state [9].

A particularly crucial observation in this case is the timeline of event onset. The pulmonary embolism occurred during the sixth week of treatment. This aligns precisely with existing literature indicating that the risk of antipsychotic-induced VTE is highest within the first 1 to 3 months of initiating therapy [4,10]. The acute nature of this window suggests an immediate drug-induced hypercoagulable trigger rather than a slow, long-term accumulation of metabolic risk factors like obesity or diabetes.

When managing antipsychotic-induced PE, discontinuing the offending agent is a priority if clinically feasible. In this case, olanzapine was cross-tapered with aripiprazole. Aripiprazole features a distinct mechanism of action as a partial D2 and 5-HT1A agonist and a 5-HT2A antagonist, but it carries a minimal sedative footprint and negligible risk of weight gain or thromboembolic events [11]. Combining a switch to aripiprazole with direct oral anticoagulant therapy (apixaban) allowed for complete clot resolution within three months while successfully protecting the patient from psychiatric relapse.

CONCLUSION

Olanzapine therapy can precipitate life-threatening pulmonary embolisms even in young, active patients entirely devoid of conventional genetic or environmental thromboembolic risk factors. Clinicians must maintain a high index of suspicion, particularly during the first two months of treatment initiation. When a patient on olanzapine presents with unexplained dyspnea, tachycardia, or chest pain, an immediate diagnostic workup for VTE is mandatory. Recognizing this adverse effect early, discontinuing the drug, and switching to an antipsychotic with a lower thromboembolic profile, like aripiprazole, is paramount to ensuring patient safety.

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