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CASE REPORT

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Is there association of olanzapine and pulmonary embolism: A case report

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Abstract

Olanzapine is a second-generation antipsychotic drug that is often used to treat schizophrenia and manic attacks. An increasing number of cases in recent years have shown that olanzapine is associated with vascular thromboembolic disease (VTD). Here, we reported a case of patient with history of taking aripiprazole, benzhexol, olanzapine, and sertraline for 5 years. He was admitted because of aggravated chest tightness, chest pain, and shortness of breath sustaining for 3 days. Laboratory examination and computed tomography angiography of the chest revealed new pulmonary embolus which involved the main trunk of the pulmonary artery and bilateral pulmonary arteries, with pneumonic infiltration in the left upper lobe. After thrombolytic therapy, the patient was out of danger.

KEYWORDS

antipsychotics, case report, olanzapine, VTD

1 | INTRODUCTION

Currently, venous thromboembolic disease (VTD) caused by antipsychotics had attracted increasing attention. Reports of related cases were increasing.[1-7] VTD was a multifactorial disease including deep venous thrombosis (DVT) of the lower extremity and pulmonary embolism (PE). There were many risk factors for VTD, such as tumor, old age, obesity, sedentary, hypercoagulable state, and a history of DVT. Studies showed medication with inefficient antipsychotics was an important risk factor for development of PE.[8,9] We reported a patient who developed PE after taking olanzapine for 5 years.

2 | CASE HISTORY

A 36-year-old man who had taken olanzapine(15mg, once a day, with no interval), aripiprazole, sertraline, and trihexyphenidyl for nearly 5 years because of

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schizophrenia. He had experienced repeated shortness of breath and chest tightness without obviously chest pain for one month. After his vaccination with 600SU inactivated COVID-19(Corona Virus Disease 2019) vaccine, his symptoms got worse appearing chest pain. So, he was admitted to pneumology department. He had been smoking for 10 years (half a pack of cigarettes a day) with no history of hypertension, diabetes, or atrial fibrillation. On examination, the patient was conscious and coherent. The physical examinations were unremarkable. The heart rate was 92 beats per minute, respiratory rate was 21 beats per minute, and blood pressure was 120/96 mmHg. Pulmonary examination revealed clear breath sounds and no signs of respiratory distress. The patient had a regular cardiac rhythm with no additional heart sounds. Despite maintaining outdoor exercise for 2 h per day, his weight had increased irresistibly to 100 kg combined with hyperlipidemia in recent years.

Laboratory examination revealed an elevated d-dimer of 6.16 mg/L, an elevated C-reactive protein (CRP) level of 119.55 mg/L, and high fibrin degradation product (FDP) level of 16.9 μg/ml. The prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), and fibrinogen levels were all normal. The arterial gas showed a pH of 7.45, partial pressure of oxygen (PO_2) of 78 mmHg, partial pressure of carbon dioxide (PCO_2) of 36.0 mmHg, and oxygen saturation (SaO_2) of 96%. Laboratory examination excluded the common causes of pulmonary embolism such as blood diseases, vascular diseases, autoimmune diseases, tumors, and thromboembolism. Electrocardiography showed that heart-related disease was excluded. Chest computed tomography angiography showed a new pulmonary embolus that involved the main trunk of the pulmonary artery and bilateral pulmonary arteries with pneumonic infiltration in the left upper lobe, as showed in Figure 1. No thrombus was observed on ultrasound of the lower extremities.

Anticoagulant therapy and interventional thrombolysis were performed. Two weeks later, the computed tomography pulmonary angiography (CTPA) suggested a

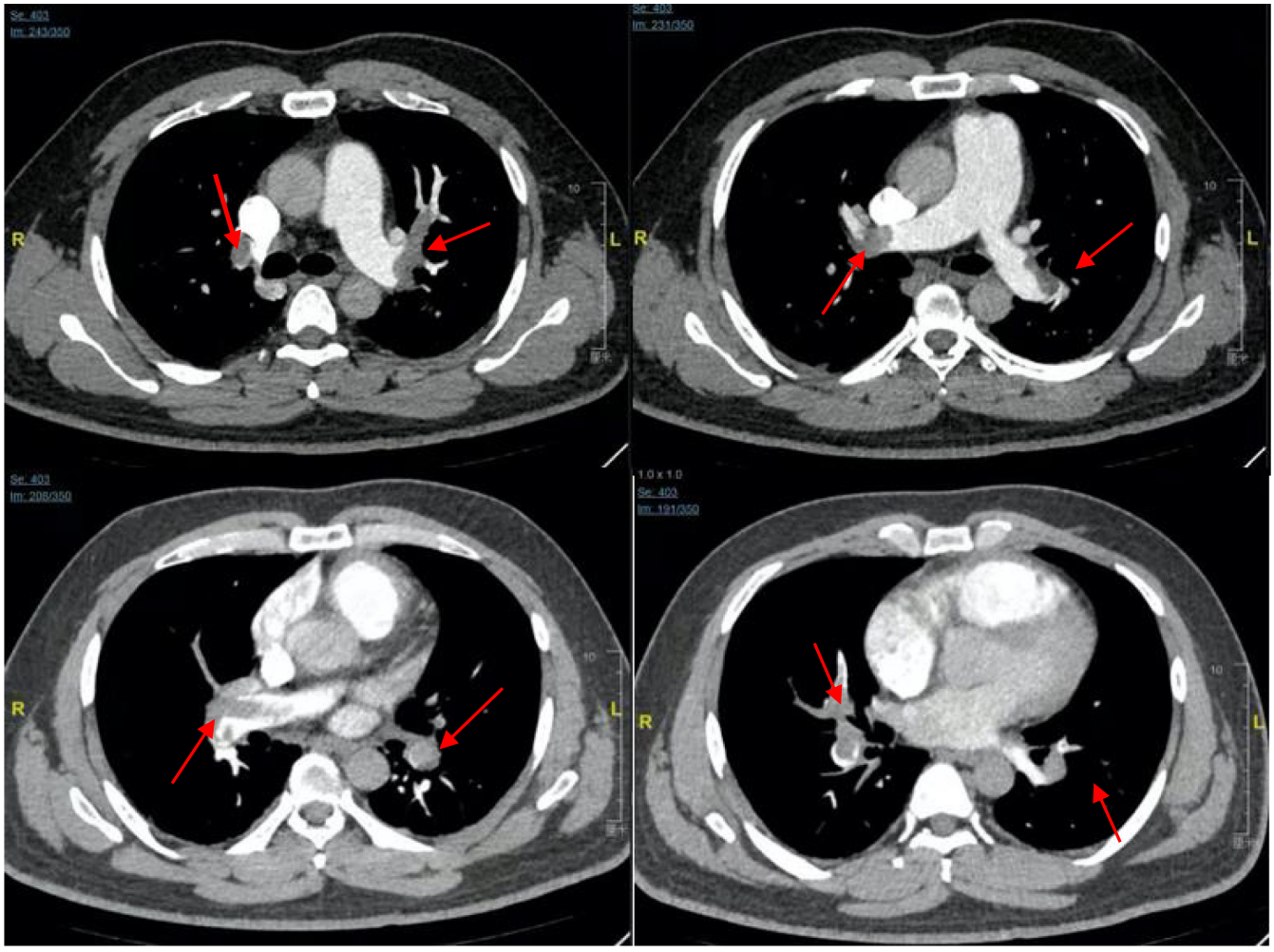

FIGURE 1 Computer tomography angiography of pulmonary artery (CTPA): Embolus involves the main trunk of pulmonary artery and bilateral pulmonary arteries, red arrow

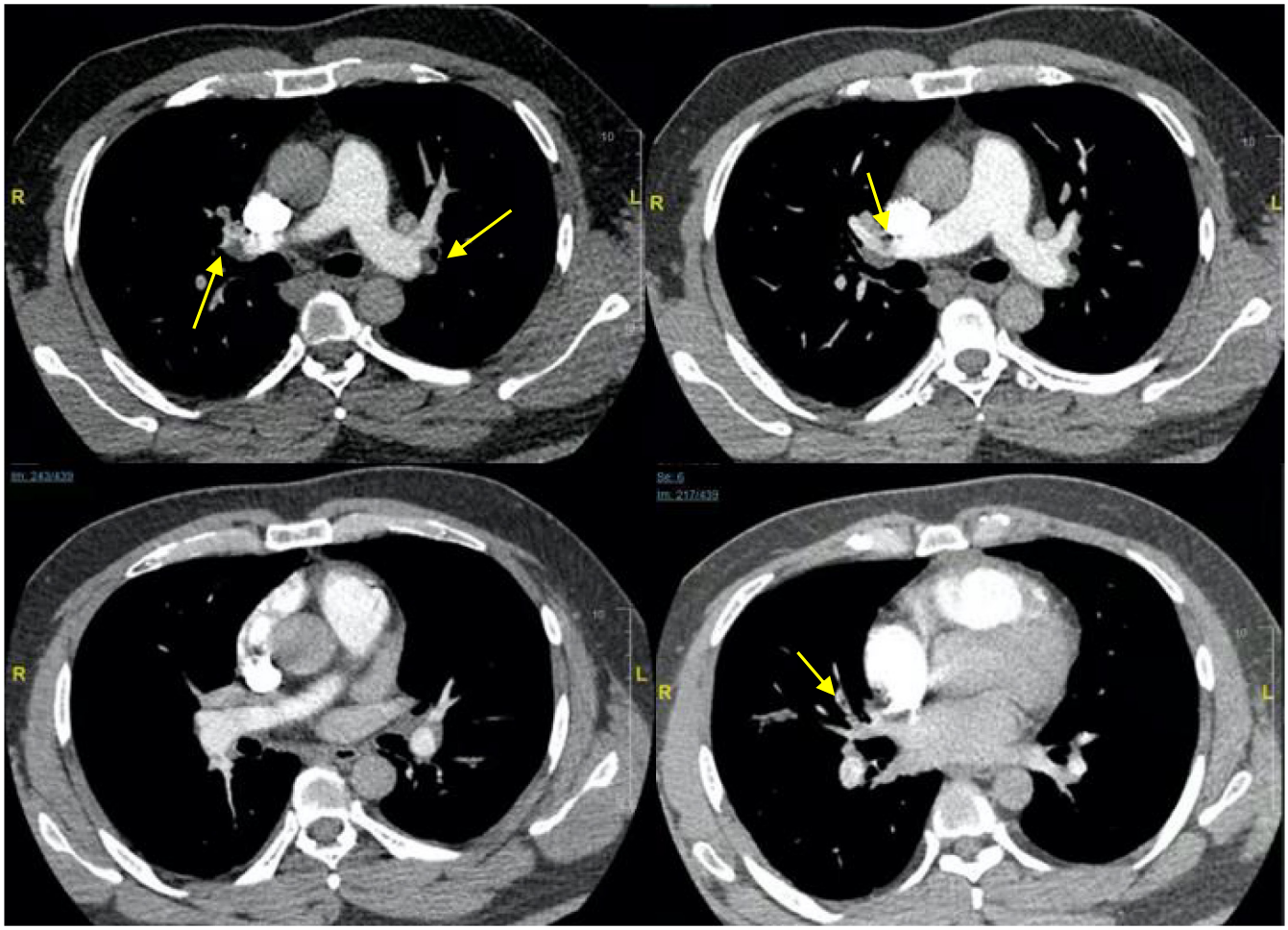

FIGURE 2 Computed tomography angiography of the pulmonary artery (CTPA) after 2 weeks: a significant size reduction of emboli in the bilateral pulmonary arteries, yellow arrow

significant size reduction of emboli, as showed in Figure 2. The d-dimer decreased to normal level. The patient was discharged on rivaroxaban (20 mg, daily).

3 | DISCUSSION

In this case, the patient was treated with four antipsychotic drugs: aripiprazole, benzhexol, olanzapine, and sertraline. He experienced repeated shortness of breath and chest tightness for one month. After his COVID-19 vaccination, his symptoms got worse and appeared chest pain.

Aripiprazole is a second-generation antipsychotic drug with serotonin-2A (5-HT2A) antagonism. Chen Hong's meta-analysis[9] shows that exposure to non-classical antipsychotic aripiprazole will not increase the risk of VTD and PE. Whether it is related to aripiprazole's special mechanism of action needs to be confirmed by more studies. The results of meta-analysis conducted by Yinzhao Liu[10] showed that the use of haloperidol, risperidone, olanzapine, or prochlorazine would significantly increase the risk of VTD, but chlorpromazine, quetiapine, or aripiprazole would not increase the risk of VTD. Generally, selective serotonin(5-HT) reuptake inhibitors are often related to bleeding, not to thromboembolic events.[11]

The central anticholinergic and antiparkinsonian drug benzhexol selectively blocks the cholinergic pathway in the striatum but has little peripheral effect. There was no related research or reports linking sertraline to VTD.

The inactivated COVID-19 vaccination made the symptoms worsened which should remind us that vaccination was not appropriate when we are not in good health. Or maybe the inactivated COVID-19 vaccine was the induce of PE, but it lacked related research and reports. Before the patient vaccinated he had repeated shortness of breath and chest tightness for one month. The vaccine worsened the symptoms.

Olanzapine is a second-generation antipsychotic drug. In 1997, Walker et al.[12] conducted a retrospective cohort study and proved that olanzapine can significantly increase the risk of fatal PE. A retrospective study in the

World Health Organization database showed that VTD occurred more frequently in the olanzapine and clozapine groups than in other groups, and 60% of cases occurred in the first 3 months of treatment. The patient was 36-year-old who was young enough to have a good physical condition. His dosage of olanzapine was adequate without interruption which reduced the risk of PE occurrence. This maybe the reason why PE occurred at the fifth year after olanzapine taking.

The metabolic symptoms caused by olanzapine represent an indirect mechanism of VTD development. In olanzapine treatment, metabolic disorders symptoms such as hyperglycemia, hyperleptinemia, dyslipidemia, and weight gain often occur.[13,14]

The patient in this case had additional thrombosis risk factors such as smoking, uncontrolled obesity, and hyperlipidemia. The uncontrolled obesity and hyperlipidemia were considered relative to antipsychotic drugs which may lead to PE.[15] The obesity and hyperlipidemia progressed slowly which made the PE occurred slowly in the fifth year of antipsychotic drugs.

During oral antipsychotic drugs in patients with schizophrenia, if obesity and hyperlipidemia exist, regular follow-up of d-dimer is recommended. Moreover, if appearance of hypoxic manifestations such as chest tightness or other respiratory symptoms was observed, CTPA is recommended as soon as possible.[16] Early detection and management is necessary to avoid life-threatening (in high-risk group) embolism.

4 | CONCLUSION

This case report did not show that olanzapine is associated with VTD directly. Clinicians should consider this aspect when using antipsychotic drugs for patients, especially those with risk factors for VTD. Patients using antipsychotic drugs should try to improve their living habits, reduce individual risk factors, and avoid iatrogenic factors as much as possible. The mechanism of olanzapine as a cumulative factor in VTD needs to be further explored.

AUTHOR CONTRIBUTIONS

Lumin Wang wrote the introduction and discussion, made the submission, and revised the paper. Yijiao Xu wrote the medical history and revised the paper. Weiwen Jiang analyzed the medication history. Jiaxin Liu analyzed the medical history. Chang Cao analyzed the medication history. Yun Shen modified the article. Xiong Xiao provided the case. Yanrong Ye modified the article.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding this study.

DATA AVAILABILITY STATEMENT

The data used to support the findings of this study are available from the corresponding author upon request.

ETHICAL APPROVAL

Institutional review board approval of our hospital was obtained for this study.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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