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Risperidone Associated With Acute Pulmonary Thromboembolism: A Case Report

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Abstract

Antipsychotic drugs (APs) are widely used drugs for schizophrenia. For decades, these agents are frequently associated with some side-effects, including increased the risk of Venous Thromboembolism (VTE). A case of a man (53 years old) with schizophrenia was reported in this study. The man with no identified risk factor for thromboembolism, and developed Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT) after treatment with risperidone 2 years. The current case indicates that use of risperidone for long time can be associated with the risk of PTE and DVT. Risperidone is a Second-Generation Antipsychotic medication (SGA), as a mixed serotonin 5HT2 and dopamine D2 receptor antagonist possibly implicated in this adverse event. As suggested by this observation, VTE and PTE risk not just appears to new users, so they should be vigilant monitored to ensure early detection and prompt treatment of VET and PTE during medication.

Keywords: Venous Thromboembolism (VTE); Pulmonary Thromboembolism (PTE); Antipsychotic agents; Risperidone; Risk factors

Introduction

Antipsychotic drugs (APs) are commonly prescribed to manage behavioural and psychological symptoms. Most of them are used to reduce the symptoms of schizophrenia, including positive and negative symptoms. [1]. The new generation of APs launched after clozapine have been categorized as atypical, which with lower rates of extrapyramidal side effects [2]. The Second-Generation Aps (SGAP) is increasingly prescribed, often replacing conventional drugs. As APs widely used, the safety of APs has also attracted more attention. Schizophrenia patients' life expectancy was 14.5 years shorter compared with healthy population [3]. At the same time, meta-analysis found that unexpected sudden death was associated with multiple APs. [4], which may be related with Pulmonary Embolism (PE).

The association between APs used and sudden death caused by PE had been noticed for decades [5]. However, APs usage and risk with Venous Thromboembolism (VTE) and PE is still controversial. An analysis of UK revealed the risk of idiopathic thromboembolism increased sevenfold in routine or FGAP users [6]. Although the risks between drugs seem to be different, different types of APs lead to similar conclusions. In the SGAP, clozapine presents a higher risk than any other drugs [7]. Risperidone and olanzapine having similar properties and the same 5HT2 receptors antagonism, so some studies showed risperidone also increased the incidence of VTE and PE, which was most pronounced during the first three months of drug use [8]. It is not observed that the VTE risk of Continuing APs users is as high as that of new APs users [3,9].

VTE is serious medical condition, which includes DVT and PE. VTE is a major health problem in the USA occurring in up to 9,00,000 Americans each year. Risk factors can be divided into congenital and acquired [10]. Although, antipsychotics are not an identified risk factor for VTE in the current CHEST guidelines [11], several case reports of VTE among AP users were published in 1950s [12]. Recently, more attention has been paid to the relationship between VTE, PE and APs use. Most VTE were occurs after initiation of APs therapies [3,9]. However, the underlying biochemical mechanism had not been clearly understood. We report 1 case of patient with VTE and PE associated with risperidone therapy for nearly 3 years and discuss its possible role as a risk factor.

Case Presentation

History prior to current admission

Two and a half years prior to current hospitalization at the age of 51, the patient present first-episode psychotic disorder, and been diagnosed with schizophrenia, then admitted to the hospital. Treatment with risperidone (3mg/d) was started, and the dose was gradually increased to 6mg/d. After hospital discharge, the patient continues treated with risperidone for over 2 years.

Current admission

At the age of 53, the patient presented to our hospital with 15 days of worsening psychotic disorder, such as psychomotor agitation, irritability and emotional instability and unable to live and work normally. The patient had no history of trauma or surgery, cancer, peripheral vascular diseases, or myocardium injury recently. He consumed a little alcohol occasionally, and 1 or 2 cigarettes per day. On admission, temperature (36.4℃), pulse (80/min), arterial blood pressure (130/85mmHg) and respiration rate (20breaths/min) respectively. Physical examination, blood chemistry panel and instrumental examinations were all normal. There was no limitation in personal autonomy. Treatment with risperidone 6mg/d, buspirone 30mg/d, lithium carbonate tablets 0.6g/d.

6 weeks after treatment, the patient complained of 2 to 3 days of epigastric discomfort, lacidophilin tablets 4.8g was added. The following week (week 7), he reported acute shortness of breath, palpitations and swollen feet lasting for 2 days. Laboratory tests showed that the C-reactive protein 19.3mg/L (n.v. 0-2.1), d-dimer 19.26mg/l FEU (n.v. 0-0.55), fifibrinogen 5.31g/L (n.v. 2-4), BNP 1400pg/ml (n.v. 0-25). A blood gas test showed pH 7.501, PO_2 58.5 mmHg, PCO_2 25.8 mmHg, bicarbonates 19.7mmol/L. Both sides lobar pulmonary artery thrombosis and both sides lower lobe has pleural effusion shown by computed tomographic pulmonary angiography (Figure 1A). Doppler ultrasound of the lower limbs found popliteal right thrombosis (12mm wide). The diagnosis of PE had been established by aforementioned results and history. After exhaustive investigations, antipsychotics remained the most probable causal factor. Standard anticoagulant treatment was started, and the patient recovered gradually. Laboratory tests showed that the C-reactive protein 1.22mg/L (n.v. 0-2.1), d-dimer 0.4mg/l FEU (n.v. 0-0.55), fifibrinogen 2.36g/L (n.v. 2-4), BNP 16pg/ml (n.v. 0-25). A blood gas test showed pH 7.418, PO_2 80mmHg, PCO_2 33.6mmHg, bicarbonates 21.2mmol/L. Left lobar pulmonary artery thrombosis had been found by computed tomographic pulmonary angiography, pleural effusion in the left lower lobe (Figure 1B). Doppler ultrasound of the lower limbs found popliteal right thrombosis, the width is 8mm. The patient did not appear shortness of breath, palpitations and swollen feet again (Figure 2A & 2B).

Discussion

VTE is serious medical condition, of which, pulmonary embolism (PE) and deep vein thrombosis (DVT) are two clinical expressions. The development of VET is associated with several clinical and environmental factors [13]. Although, literature assessing the risk of VTE in the use of antipsychotics has not been definitive, many sudden death cases caused by PE related to APs exposure had been reported for decades [5]. A study provides a general overview of AP use showing that nowadays SGAPs are more often prescribed (>78%) than FGAPs (10). So, researchers pay more attention to the relationship between SGAPs and VTE.

Risperidone is SGAPs, belonging to the chemical class of benzisoxazole derivatives. It has an affinity for type 2 dopamine receptor that is less than type 2A serotonin receptor (5HT2A). Some studies showed that patients treated with risperidone may affect platelet aggregation induced by 5HT2A, and other studies suggested that platelet aggregation is enhanced by the 5HT2A antagonistic effect of risperidone or due to hyperhomocysteinemia [13,14]. The risk of VTE was most pronounced during the first three months of drug use; meanwhile, the psychiatric symptoms, drug-induced sedation, patient's age, and drug dose might take part in the process of VTE risk [14]. Meanwhile, a meta-analysis indicating continuing APs users were not observed to have as high a risk for VTE as new APS users, indicating that tolerance is increased with longer APS exposure [3]. However, in this case, the patient treatment with risperidone nearly 3 years from present first-episode psychotic disorder, the mechanisms involved in the pathogenesis of this possible adverse reaction are largely unknown.

The patient aged 53, his physical activity and body mass index were normal. After exhaustive investigations, antipsychotics remained the most probable causal factor. Some possible explanation may involve

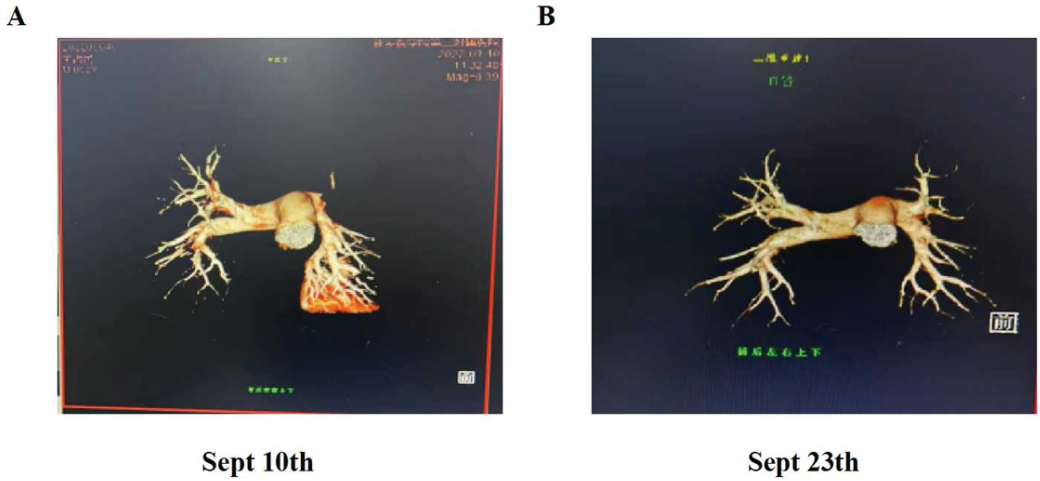

Figure 1: Computed tomographic pulmonary angiography.

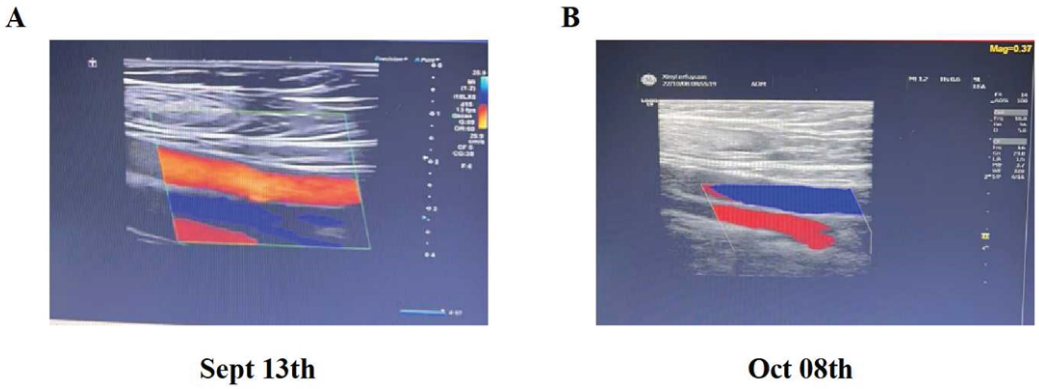

Figure 2: Doppler ultrasound of the lower limbs.

in current case. The worsening psychotic disorder could lead to social withdrawal and immobilization and may relate to VET. These results consistent with Lin CE, et al. [14] study implied psychiatric symptoms might take part in the process of VTE risk. Except risperidone 6mg/d, buspirone 30mg/d and lithium carbonate tablets 0.6g/d were added for treatment. A previous study indicated that for drug associations, the risk associated with how many kinds of APs taken simultaneously [8]. In addition, the VTE test usually was arranged in the first few days of medication treatment, not the entire treatment cycle will be given attention. Despite the absolute risk of VTE being lowed after continuing of antipsychotic therapy, this patient still developed a VTE. We were fortunate to be able to stabilize the patient on psychiatric symptoms and successfully treat the VTEs with anticoagulation agents. The entire treatment cycle should be monitoring, especially in patients with risk factors for VTE.

Conclusion

Although antipsychotic use is not a common influencing factors for VET, which had been associated with the development of VTE in many previous literature. Meanwhile, in current case, it happened in a patient treatment with APs for nearly 3 years. Therefore, vigilant monitored the entire treatment cycle is very important, not just for the new users.

Consent

The patient has provided written informed consent to publish the details of the case.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Statement

No potential conflict of interest was reported by the author(s).

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