RISPERIDONE-INDUCED THROMBOCYTOPENIA

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ABSTRACT

Thrombocytopenia is an uncommon side effect of antipsychotics medication that can lead to bleeding symptoms threatening the vital prognosis. We are presenting a documented case of drug induced-thrombocytopenia in a 29 year-old male with psychiatric history of undifferentiated schizophrenia who was treated with Risperidone and we are discussing it with the literature data. Although this complication is rare, psychiatrists should be aware of the hematological risk of Risperidone by performing periodic blood-profile monitoring.

Keywords: Blood dyscrasia, Risperidone, Side Effect, Thrombocytopenia.

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Introduction

Antipsychotics rarely cause thrombocytopenia [1]. Among them, Risperidone, an atypical antipsychotic, is known to have a low risk of hematotoxicity [2]. However, some authors have reported cases of thrombocytopenia as an uncommon complication of treatment with this treatment. On September 2016, 16 428 patients reported to have side effects while taking Risperidone. Among them, 359 (2.19%) had thrombocytopenia [3]. In this article, we report a case report of Risperidone induced-thrombocytopenia in a 29-year-old patient diagnosed with schizophrenia that was accidently discovered while he was hospitalized for a complication of Tetralogy of Fallot.

Case report

Mr. S is a 29-year-old male with a history of tetralogy of Fallot and undifferentiated schizophrenia that was diagnosed nine years ago. The psychiatric symptoms consisted on persecutory delusion which mechanism was auditory and visual hallucinations and dissociative behavior. After neurologic intolerance to haloperidol, the switch to Risperidone was initiated.

Despite good compliance with treatment, his prominent psychotic symptoms have responded poorly justifying the augmentation of posology until the dose of 6 mg/day and to 8 mg daily 2 weeks before the accident (Table 1). Mr. S, who has no history of hematological disorder, was brought to the emergency room for faintness and a generalized convulsion. An atrial flutter related to his cardiovascular disease had been diagnosed and reduced by external electric shock. However, during hospitalization in cardiology department, a thrombocytopenia had been discovered with a controlled platelet count of 54,000/µl then 23,000/µl. The WBC and RBC count stayed normal. We did not find any external or internal hemorrhagic complication. Since there was no other medical cause for the thrombocytopenia, Drug-Induced Thrombocytopenia was suspected according to the criteria reported by Aster et al. [3]; Risperidone was immediately discontinued and platelet count was monitored on a daily basis. After six weeks, the count had recovered to 150,000/µl. At the 2-month follow-up his platelet count was 157,000/µl. Treatment with Olanzapine had been initiated with a favorable evolution of psychiatric symptoms, the monitoring of blood count showed no abnormalities.

Discussion

Drug-induced immune thrombocytopenia (DITP) can be caused by several drugs. According to epidemiologic studies conducted in the United States and Europe, about 10 persons per million present DITP every year [5]. Through this case, we notice that risperidone can also lead to this uncommon side effect. Risperidone is, in fact, an atypical antipsychotic acting as antagonist of 5HT2 and D2 receptors. It has low incidence of extrapyramidal symptoms and improves negative symptomatology. Placebo-controlled studies had shown no significant abnormal results for patients treated with

this drug [6]. There are even some authors who suggested that Risperidone might be considered as a good alternative when blood dyscrasia occurs with classic antipsychotics [7]. In our case, we concluded that the use of this antipsychotic was associated with thrombocytopenia since there was a chronological relationship between the time of the suspension of the treatment and the normalization of the platelet count. In fact, the rapid recovery of the platelet count within few days supported this causal relationship. In the other side, no other clinical or iatrogenic parameters seemed to account for the onset of thrombocytopenia. George and al., after analyzing cases of drug-induced thrombocytopenia, devised a set of four clinical criteria to assess the likelihood that individual drugs are capable of causing DITP [8]. In our case, three criterions were met suggesting that the diagnosis of DITP is probable. To our knowledge, thrombocytopenia induced by antipsychotics was more found with the use of quetiapine, olanzapine and clozapine and reported cases of thrombocytopenia associated with Risperidone were contrariwise rare [9,6].

This effect occurs usually 5 to 15 days after beginning the treatment and disappears within a week after discontinuation [10]. Even if remission was rapid in our case, the onset of thrombocytopenia occurred after 8 years of treatment exposure which is uncommon (0.85%) [3]. The augmentation of the posology of the treatment was suggested to be the cause for the occurrence of this effect after many years of therapy. Still according to Semba et al., thrombocytopenia is not directly related to the doses of responsible drugs [10]. On the other hand, no other drug taken by the patient may cause a thrombocytopenia and there were no other changes in the patient's pharmacotherapy. All these arguments plead for the accountability of Risperidone in this incident.

Thrombocytopenia induced by Risperidone was often described in male patients (68.56%) and more observed in the 40-49 year-old age group (36.31%) [3]. However, the explication of these ascertainments is still unknown. Similarly, how drugs cause platelet decrease after exposure to the drug is still barely understood. The pathogenesis of DITP is complex. Researchers have proposed at least six different mechanisms by which drug-induced antibodies can destroy platelets. Identifying antibodies that react with platelets in the presence of the sensitizing drug can be possible, but required testing is difficult to provide and not widely available [4].

After normalization of the platelet count, we substituted the antipsychotic treatment with 10 mg per day of olanzapine. Although this one can cause the same complication [11], the follow-up of the platelet count still be normal.

Table1: Therapeutic sequences prescribed according to each period

Period	Therapeutic sequence
From June 2007 to August 2010	Haloperidol (15mg daily) + chlorpromazine (300mg daily)
From August 2010 to March 2011	Haloperidol (25mg daily) + chlorpromazine (100mg daily)
From March 2011 to April 2010	Risperidone (2mg daily)
From April 2010 to July 2013	Risperidone (4mg daily)
From July 2013 to April 2016	Risperidone (6mg daily)
From April 2016 to Mai 2016	Risperidone (8mg daily)
From May 2016	Olanzapine (10mg daily)

Conclusion

To summarize, this case raises the issue of rare abnormalities of thrombocytes under treatment with Risperidone. So, psychiatrists should be aware of this effect and blood-profile monitoring should be conducted periodically.

Ethical approval and consent for publication

The patient's and his father oral consents were obtained to report the case.

Availability of data and material: Data for blood count are available.

Conflicts of interest: None

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Authors' contributions

Prof Lotfi Gaha , Dr Badii AMAMOU and Prof Ferid ZAAFRANE designed the study.

Dr Soumayya FATHALLAH, Dr Wafa CHEBBI, Dr Badii AMAMOU and Dr Ahmed Mhalla managed the literature searches.

Dr Nadia BEN FRADJ and Prof Karim AOUAM managed the verification of the relation between the thrombocytopenia and the Risperidone intake.

Dr Badii AMAMOU and Dr Wafa CHEBBI wrote the first draft of the manuscript.

All authors contributed to and have approved the final manuscript.

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