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Risperidone Induced Isolated Thrombocytopenia: A Rare Adverse Event

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TO THE EDITOR

The rare odds, combined with a relatively safe hematological profile, often deter the physicians from making the connection between Risperidone and isolated thrombocytopenia. Quite possibly, this is the singular reason as to why an up-to-date scrutiny of medical literature revealed only one case of isolated thrombocytopenia with Risperidone.¹ Thereby, it is our endeavor here to shed light on this potentially life-threatening and extremely rare adverse effect of Risperidone through this case report.

A 42-year-old patient of paranoid schizophrenia, diagnosed at 14 years of age, presented to the psychiatry outpatient department (OPD) in August, 2015 with delusions of persecution and reference, anger outbursts and multiple episodes of intentional self-harm, since the past 6 months. Despite being on chronic treatment, a definitive drug history could only be ascertained from February 2015 when the patient was hospitalized and initiated on tablet Risperidone 2 mg twice daily and tablet Lorazepam 4 mg once daily. At that time patient's hemoglobin was 9 g/dL (11–15 g/dL), white blood cell counts – 3,700 cells/cu.mm. (4,000–11,000 cu.mm.) and platelets – 1.8 lacs/cu.mm (1.5–4.5 lacs/cu.mm). Thereafter, routine follow ups until the episode in August 2015 revealed that the patient was maintaining well with Risperidone and Lorazepam for his underlying condition of paranoid schizophrenia.

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Subsequently, when the patient presented with an acute exacerbation of his underlying psychiatric illness in August 2015, routine hematological investigations revealed hemoglobin –8 g/dL, whereas the white blood cell counts had remained static at 3,700 cells/cu.mm. A dramatic decline in platelet counts from 1.8 lacs to 0.7 lacs/cu.mm was observed. Considering the severity of his symptoms, the patient was hospitalized and the management of the psychiatric status was accorded maximum priority. Risperidone was continued at the same dose and Haloperidol 50 mg was administered intramuscularly monthly. Tablet Trihexyphenidyl 2 mg twice daily and Lorazepam was administered on a SOS basis. Additionally, parenteral vitamin B12 supplementation was administered, with the dual purpose of benefiting with patient's psychiatric symptoms as well as improving upon patient's anemia. A switch over from Risperidone to another antipsychotic was not considered as the patient showed improvements with the above-mentioned modifications to the treatment regimen and was discharged within a few days.

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When the patient returned 3 months later with a similar episode, his blood picture revealed improvements in hemoglobin (10 g/dL) and white blood cell counts (6,200 cells/cu.mm.). Thrombocytopenia continued with 0.71 lacs/cu.mm of platelets. Further inquiry with the relatives revealed that the patient had been compliant with the prescribed drugs in the past 3 months. At this point of time, Risperidone was withdrawn in view of a possibility of Risperidone inducing thrombocytopenia, since the other possible causes like genetic predispositions, sepsis, dehydration, vitamin B12 deficiency, dengue, Idiopathic Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura (TTP) were absent within the patient. Despite the patient being on Haloperidol, an agent which has been associated with thrombocytopenia,² the sequence of events seemed to implicate Risperidone as the more likely agent for producing thrombocytopenia. Thereafter, the patient was initiated on Clozapine 300 mg twice daily and Flupenthixol 20 mg once daily with Haloperidol continuing as before due to the perceived better symptomatic control. Nonetheless, further evaluation of patient's hematological picture was not possible as the patient was discharged on request, despite the psychiatrist's advice. Naranjo's score,³ despite the absence of the 'de-challenge' information, was 6; the presence of other documented reports of this reaction, positive temporal association, absence of other possible causes like previous comorbidities or alcoholism history and presence of an objective evidence (laboratory values) contributed to the causality. This rendered a probable causality to Risperidone producing thrombocytopenia in the present case.

Despite the reporting of a few accounts of Risperidone associated thrombocytopenia,^{4,5} it would be pertinent to note that in both these

instances, thrombocytopenia has inevitably been accompanied by leukopenia which is more suggestive of a picture resembling Risperidone induced myelosuppression translating into bicytopenia/pancytopenia. However, till date, isolated thrombocytopenia with Risperidone, as seen in our case, has only been observed once.¹ Selective inhibition of the megakaryocytes suggests platelet antibody formation as the more likely cause of thrombocytopenia. Further light can be shed on this issue using dedicated mechanistic studies. But, given the serious implications of this extremely rare adverse effect, it bears merit to investigate the possibility and (if) the manner of antibody generation with Risperidone. Unfortunately, the paucity of post-marketing reports in this regard has possibly led to research into thrombocytopenia associated with Risperidone remaining an uncharted territory. However, since thrombocytopenia, either alone or as bicytopenia/pancytopenia, has been reported within scientific literature, the suggestion of platelet counts monitoring of such patients is not bereft of scientific merit, especially until further clarity is obtained on the association between Risperidone and thrombocytopenia. ❖

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CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Semba J, Okui S. Risperidone-induced thrombocytopenia: a case report. *Gen Hosp Psychiatry*. 2009; 31:97–98.
2. Balon R, Berchou R, Zethelius M. Thrombocytopenia associated with chlorpromazine, haloperidol and thiothixene: a case report. *Can J Psychiatry*. 1987;32(2):149–150.
3. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239–245.
4. Assion HJ, Kolbinger HM, Rao ML, Laux G. Lymphocytopenia and thrombocytopenia during treatment with risperidone or clozapine. *Pharmacopsychiatry*. 1996;29(6):227–228.
5. Kairav S, Muhammad R. Bicytopenia: Adverse effect of Risperidone. *Current Psychiatry*. 2014;13(4):E1.