



International Journal of Medical and Pharmaceutical Case Reports

14(3): 25-28, 2021; Article no.IJMPCR.74721
ISSN: 2394-109X, NLM ID: 101648033

Case Report: Risperidone Induced Peripheral Edema

Farzana Faruki^{1*}, Uma Datta Gupta², Adeel Anwar¹ and Saral Desai¹

¹One Brooklyn Health System, United States of America.

²Chittagong Medical College, Bangladesh.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2021/v14i330136

Editor(s):

(1) Dr. Erich Cosmi, University of Padua School of Medicine, Italy.

Reviewers:

(1) Priyal Shrivastava, Jawaharlal Nehru Medical College, India.

(2) Marcel Vasconcellos, Centro Universitário Serra dos Órgãos (UNIFESO), Brazil.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/74721>

Case Study

Received 13 July 2021
Accepted 23 September 2021
Published 28 September 2021

ABSTRACT

Risperidone is the first line of treatment for bipolar disorder, atypical depression, and Schizophrenia. We present a 55-year-old male with a history of schizoaffective disorder with bipolar type I presented with aggressive behavior and suicidal ideation. Our patient was treated with low-dose Risperidone; after that, he gradually developed leg pain and edema. His leg pain hampers his ambulation, which is clinically improved after a week of medication discontinuation; however, his leg edema did not resolve completely. In addition, we evaluated our patient's compliance with an empathic verbal interview that shows edema and leg pain hampers his quality of life. We have found that not informing edema as one of the possible side effects increases medication non-compliance in our case. There are several case reports about the side effect of Risperidone (such as leg edema) in combination with other medications, but there is no recommendation about patient counseling of forthcoming leg edema and mobility issues.

Keywords: *Bipolar disorder; schizoaffective disorder; mental disorder; risperidone.*

*Corresponding author: E-mail: ffaruki@bhmcny.org;

1. INTRODUCTION

Schizoaffective disorder is a condition where Schizophrenia co-exists with a mood disorder such as bipolar disorder Type I or major depressive disorder. Patients usually present with hyperactivity, irritability, distractibility, grandiosity, decreased need for sleep, and talkative with acute suicidal ideation [1]. Second-generation atypical antipsychotic antidepressants are the treatment option for bipolar disorder, Schizophrenia, and atypical depression. Risperidone is a Benzisoxazole derivative; this is a combination of Serotonin and Dopamine antagonism. Risperidone was approved in 1993 by FDA to use in patients with Schizophrenia; however, it is also effective for manic and mixed episodes of Bipolar I disorder [2]. Although British National Formulary added edema as one of the side effects, it is not usually a common one, e.g., weight gain and sedation [3]. According to Hossain S. et al., there were reported six cases so far where complex drug interaction with Valproate, benzodiazepine, and Risperidone cause leg edema to patients mild to moderate severity [4].

Although the effect of leg edema is dose-dependent, there is only one case reported that leg edema occurs in low doses of Risperidone as similar to our case. However, after a week of low-dose medication, our patient had edema, and discontinuation of the drug did not improve his leg edema for 2 weeks [5].

2. CASE HISTORY

We present a 55-year-old African American male presented by EMS activated by his sister in the emergency department with aggressive behavior and suicidal ideation for one week. For a month, the patient's sister reported a gradual worsening of his manic symptoms (easy distractibility, increased energy levels, and slept less than 4 hours/night). His speech was rapid and pressured. Additionally, he had a tangential thought process. We noted that our patient had a past medical history of hypertension (on Amlodipine) for the last five years and past psychiatric history of schizoaffective disorder with bipolar type I disorder for the previous 12 years. His home medications included Sodium Valproate 500 mg BID, Atorvastatin 10 mg QD, Amlodipine 5 mg QD, Escitalopram 10 mg QD, Mirtazapine 30mg QD, Lurasidone 80 mg QD that he was taking for the past six months. According to the caregiver, he was compliant

with the medication. On his recent course of hospitalization, we started Risperidone 1mg BID and titrated up to a total of 3 mg per day, and we increased the dosage of Sodium Valproate to 500 mg TID to control his aggressive behavior and manic symptoms.

The patient's caregiver mentioned that he had multiple hospitalizations (more than ten times) in the psychiatry unit for 12 years and his last hospitalization was six months ago due to manic episodes. His family history of psychiatric disease is insignificant. Mild impairment of his intellectual function affects his ability to complete high school and currently he is on social security. He did not have a history of substance abuse.

After a week of hospitalization, the patient develops sudden foot pain on a scale of 6/10. He also developed moderate bilateral leg edema and could not walk. The patient denied any shortness of breath, chest pain, cough, fever, and abdominal pain. However, his behavior was getting better and less aggressive on medication. We consulted with a cardiologist and nephrologist to rule out any pathology. The cardiologist recommended switching Amlodipine to Lisinopril 5 mg to exclude Calcium channel blocker-induced leg edema. On his subsequent consult, the cardiologist also suggested adding Hydrochlorothiazide 12.5 mg. Nevertheless, we did not notice significant changes in his symptoms. In addition, he gradually developed leg edema with pain and discomfort, and DVT was excluded after extensive workup. Multi-disciplinary opinions were taken to rule out other medical causes of edema, but we did not find any medical reasons so far.

On physical examination, his vitals are stable; the general appearance was disheveled but cooperative with no apparent distress. There was 2+ edema in the lower limb. His edema is localized in his foot, pitting in nature, and associated with no overlying skin changes. A review of his other system was normal.

Other laboratory examinations, including complete blood count, comprehensive metabolic panel, renal function test, thyroid function test, rheumatological test, immunological examination, and urinalysis, were within normal limit except for low platelet count. In addition, ECG, Echo, and duplex venous ultrasonography for bilateral lower limb did not reveal any pathology.

According to the collateral history of previous drug reactions, our patient had a history of ankle

edema with Risperidone which was self-limiting in nature two years ago. At that time, his edema gets worse with prolonged treatment with Risperidone. As a result of his positive drug reaction history and reviewing the literature, we decided to reduce the dose of Risperidone to 2 mg/day in four days and gradually discontinued the medication.

Table 1. The figure of 8 ankle measurements

| Date | On Risperidone | Without Risperidone |
|-------|----------------|---------------------|
| Day 1 | 26.0 cm | 26.8 cm |
| Day 3 | 26.8 cm | 26.3 cm |
| Day 7 | 27.0 cm | 25.9 cm |

After a week of Risperidone discontinuation, the leg pain gradually subsided and entirely resolved, but he had bilateral pitting leg edema. The patient was ambulatory after discontinuation of the medication. Therefore, we evaluated his probable adverse drug reaction with Risperidone. According to Naranjo Adverse Reaction, the rating was seven which proves the association of leg edema and the use of Risperidone.

3. DISCUSSION

First-line treatment for psychosis and mood disorder is second-generation antipsychotics such as Risperidone, Clozapine, and Olanzapine. However, several medical conditions can cause bilateral leg edema, such as heart failure, chronic or acute renal failure, and chronic liver failure. Therefore, our patient undergoes all possible lab tests and procedures to rule out other relevant medical conditions of his newly developed leg edema.

The second-generation antipsychotics block the D2 receptor, 5HT-2A receptor, Alpha 1 receptor, and H1 receptor. It has been found that these D2 receptor has contributed to edema by influencing the renin-angiotensin system in the kidney [6]. It has been shown that 5-HT2A blockade increases cyclic AMP, which causes vasodilation and leads to edema [7]. Risperidone also influences the alpha one receptor in a post-capillary system that causes peripheral vascular dilation and subsequently edema [8]. Facial or pedal edema with signs of disseminated skin eruption could be considered an allergic drug reaction or hypersensitivity. We can exclude this condition with blood C3, C4, and IgE levels [9]. However, the combination of Sodium Valproate and

second-generation antipsychotic is usually safe with fewer adverse effects.

After an extensive search in PubMed and Google Scholar, we have found a total of nine cases of pedal edema with Risperidone. However, six of these cases are associated with other medications such as Quetiapine, Valproate, and Benzodiazepine [10]. However, in our case, the patient has been on sodium valproate and Lurasidone for a long time, and the administration of Risperidone for a week causes leg edema. In addition, we have found that the edema is associated with leg pain and discomfort.

Additionally, due to added distress and uncertainty about the cause of leg edema, we believe the drug compliance of patients is affected in our case.

4. CONCLUSION

Atypical antipsychotic-induced edema is not rare, but symptoms like the pain, heaviness, discomfort associated with edema are new in our case. Several cases were reported with leg edema after Risperidone or with a combination of Valproate or Lurasidone; however, in our case, leg edema is persistently present for two weeks with discomfort and pain. We need to identify the risk factors before prescribing antipsychotics and properly monitor daily changes (like weight gain) in hospital-admitted chronic psychotic patients to ensure better medication compliance in the future, especially in a long-term history of antipsychotic use.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline, patient's consent and ethical approval have been collected and preserved by the authors

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. American Psychiatric Association. Bipolar disorder. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: Author; 2013.

2. Stahl S. Essential Psychopharmacology, Cambridge University Press, Cambridge, UK; 1996.
3. Stigler KA, Potenza MN, McDougle CJ. Tolerability profile of atypical antipsychotics in children and adolescents. *Pediatric Drugs*. 2001;3(12): 927–42. [PubMed] [Google Scholar]
4. Hosseini SH, Ahmadi A. Peripheral Edema Occurring during Treatment with Risperidone Combined with Citalopram. *Case Rep Med*. 2012;2012: 540732.
DOI: 10.1155/2012/540732
PMID: 23251178; PMCID: PMC3510775.
5. Tamam L, Ozpoyraz N, Unal M. Oedema associated with Risperidone. *Clin Drug Invest*. 2002;22(6):411–14.
DOI: 10.2165/00044011-200222060-00011 [Crossref], [Web of Science ®], [Google Scholar]
6. Knox ED, Stimmel GL. Clinical review of a long-acting, injectable formulation of Risperidone. *Clin Ther*. 2004;26(12):1994–2002. [PubMed] [Google Scholar]
7. Sanders RD, Lehrer DS. Edema is associated with the addition of Risperidone to valproate treatment. *J Clin Psychiatry*. 1998;59(12):689–90.
DOI: 10.4088/JCP.v59n1208e [Crossref], [Web of Science ®], [Google Scholar]
8. Terao T, Kojima H, Eto A. Risperidone and allergic reaction. *J Clin Psychiatry*. 1998;59(2):82–3.
DOI: 10.4088/JCP.v59n0207c [Crossref], [Web of Science ®], [Google Scholar]
9. Akdag ST, Fettahoglu EC, Ozatalay E. Pedal edema induced by low-dose risperidone monotherapy in a child. *J Child Adolesc Psychopharmacol*. 2009;19(4): 481–2.
DOI: 10.1089/cap.2008.0104 [Crossref], [Web of Science ®], [Google Scholar]
10. Case Notes. Pedal Oedema Associated with Atypical Antipsychotics. Available: <http://www.progressnp.com/SpringboardWebApp/userfiles/esprog/file/Casenotespedaloedema.pdf>

© 2021 Faruki et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://www.sdiarticle4.com/review-history/74721>