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CASE REPORT

Low-Dose Risperidone-Induced Facial Edema in a Child with Conduct Disorder

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ABSTRACT
Risperidone, a benzisoxazole derivate, is a widely prescribed antipsychotic agent that binds with high affinity to dopamine D2, serotonin type 2 (5-HT2) and α1-adrenergic receptors, and causes antagonism at these receptor sites. Although risperidone has several side effects such as weight gain and sedation, edema is a very rarely observed side effect in children and adolescents. Here, we report a case of facial edema in a child with conduct disorder (CD) who was receiving low-dose of oral solution risperidone. Three days after risperidone discontinuation, the facial edema resolved entirely. Because a plausible mechanism of risperidone-induced edema remains unknown, further investigation is warranted to elucidate the risk factors and potential mechanisms of the edema.
Keywords: Facial edema, risperidone, child, conduct disorder

INTRODUCTION

Risperidone is a widely prescribed second-generation antipsychotic agent in children that is mostly used in the treatment of conduct disorder. It is also used for irritability in context of autism spectrum disorders, tic disorders, and mood disorders in pediatric patients. Risperidone's mechanism of action involves antagonism at the serotonergic (5-HT2), dopaminergic (D2), and α1-adrenergic receptors (1). Although risperidone has several side effects such as weight gain and sedation (2), edema is a very rarely observed side effect in children and adolescents. Here, we report a case of facial edema in a 7-year-old male with conduct disorder (CD) who was receiving low-dose of oral solution risperidone.

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CASE PRESENTATION

A 7-year-old male, was brought to our out patient clinic by his family due to his 'aggressive behaviors to people and animals'. Symptoms of destroyed objects, lying to superiors and cursing at superiors and set fires had first begun approximately two years previously. The patient had no history of any systemic disease and other psychiatric disorder. In the family history, the father was also reported to be impatient, untidy and hyperactive. He was 123 cm tall and weighed 27 kg. His history revealed that the pregnancy was be normal, he was born on term weighing 3300 grams, no complications occurred during delivery but the mother smoked during pregnancy. In the psychiatric evaluation, he told that he did not want to talk and he did not have eye contact. He seemed very nervous and after five minutes in silence, he shut the door and went out. The Turkish versions of the Turgay DSM-IV-Based Screening Scale for DSM-IV Disruptive Behavior Disorders were used to evaluate the severity of his symptoms (the attention deficit score was 9, the hyperactivity/impulsivity score was 11, the oppositional defiant score was 7, the conduct disorder score was 15) (3). The patient was diagnosed with conduct disorder

(CD) at psychiatric evaluation based on DSM-5 diagnostic criteria and was started on risperidone. WISC-R was used to evaluate the intelligence test (the verbal IQ score was 88, the performance IQ score was 94, the total IQ score was 90. The clinical global impression-severity of illness (CGI-SI) score was 6. Risperidone was initiated at 0.25 mg/ day and then the dose was increased to 0.5 mg/ day. Within a week of increasing risperidone, he developed swelling over the face and lips. On examination, he was found to have facial edema and swollen lips. Symptoms of facial edema was neither preceded or accompanied by intake of any other medications, insect sting, fever, local or generalized itching, pain, jaundice, distension of abdomen, malnutrition, difficulty in breathing, palpitation, urinary symptoms, past history of any allergic reaction, food-related allergies or asthma. There was no past history of cardiac failure, hepatic dysfunction, renal disease and thyroid disorder. Then, risperidone was stopped and his routine investigation (complete blood cell count, serum electrolytes, albumin, thyroid function, renal function, liver function, urinalysis, electrocardiogram) provided no explanation for the edema. The Immunoglobulin E (Ig E) levels were detected to exclude any allergic reactions against to the risperidone or an angioedema that demonstrated no abnormalities. Complement assays also were not examined. Subsequently, a diagnosis of risperidone-associated edema was made. His Naranjo adverse drug reaction probability scale score was 7 for the drug (4). It suggests a probable association between risperidone and edema. Three days after risperidone discontinuation, the facial edema resolved entirely. He was switched to aripiprazole 5 mg/day. We are managing CD symptoms with the same dose of aripiprazole for the last three months with no signs of edema.

DISCUSSION

We report a 7-year-old male patient with CD developing facial edema following risperidone use. The edema resolved entirely following discontinuation of risperidone. Cases, albeit few in number, of edema developing in association with risperidone and other antipsychotics, have been reported in the literature;although these are quite rare in children and adolescents than in adults. Two of these involved adolescents and one a child of 8 (5-7). Bilateral ankle edema developed in an autistic male adolescent using carbamazepine, sodium valproate and melatonin following the addition of 2 mg/day risperidone (5). In the case of a 15-year-old male under observation due to schizophrenia, facial edema developed with 2 mg/day risperidone monotherapy (6). In these adolescent cases, edema was observed with risperidone at relatively high doses of 2 mg/day, while bilateral pedal edema was reported in an 8-year-old girl receiving risperidone oral solution monotherapy at 0.5 mg/day due to aggressive behavior (7). Our case differs from those other children and adolescents in that our patient was a 7-year-old male and edema developed in the facial region.

The mechanism by which risperidone causes edema in child, adolescent, and adult cases has not generally been determined (at hematological and immunological examinations). Also, we could not clearly determine the etiology of the edema present in this case, but there are several explanations that may account for the onset of edema due to risperidone therapy. First, reduced dopaminergic activity due to risperidone plays a role in producing edema by altering the renal regulation of fluid and electrolytes (8). Second, Type I and type IV allergic reactions were considered to be responsible in one patient (9). Third, allergic reactions, supersensitivity of receptors and complex drug interactions (10). Fourth, supersensitivity of the α-receptors of neurons (5). Fifth, risperidone-induced 5-HT2 receptor blockade which can potentially increase the plasma cyclic adenosine monophosphate levels that relax the vascular smooth muscle through the phosphorylation of myosin light chain kinase (11). Sixth, C4-C2 activation due to a previous C1 inhibitor deficiency (7). Seventh, the action of risperidone as a vasodilator on the α-receptors of the peripheral vascular system, which would result in tissue edema (12).

The side-effect of risperidone-associated edema emerged in adolescent and adult cases at dosages of 2

mg/day and above (1,5,6). Therefore, if discontinuing risperidone therapy in cases developing edema will represent a problem in terms of prognosis of the disease, reducing the dosage of risperidone may be a useful option in terms of edema control. However, edema may even be observed with risperidone therapy at low doses of 0.5 mg/day as in a previous child patient (7) and in our own case. Clinicians must therefore be aware that this rare side-effect may appear even at low dosages. Under such conditions, treatment may be modified to another antipsychotic with a different effect mechanism. In our case we stopped risperidone and initiated aripiprazole at 5 mg/day. No edema-associated side-effect was observed over 3-month follow-up.

However, the use of risperidone has become widely common in treating behavioral problems associated with CD, thus, this case report indicates that the need monitor the possibility of edema precipitated by risperidone is increasingly important.

In conclusion, because a plausible mechanism of risperidone-induced edema remains unknown, further investigation is warranted to elucidate the risk factors and potential mechanisms of the edema.

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REFERENCES

1. Tamam L, Ozpoyraz N, Unal M. Oedema associated with risperidone: a case report and literature review. Clin Drug Investig 2002;22(6):411–14. [CrossRef]
2. Stigler KA, Potenza MN, McDougle CJ. Tolerability profile of atypical antipsychotics in children and adolescents. Paediatr Drugs 2001;3(12):927-42. [CrossRef]
3. Ercan ES, Amado S, Somer O, Çıkoğlu S. Development of a test battery for the assessment of attention deficit hyperactivity disorder. Turkish Journal of Child And Adolescent Mental Health 2001;8:132-45. (Turkish)
4. Kose S, Akin E, Cetin M. Adverse drug reactions and causality: the Turkish version of Naranjo Adverse Drug Reactions Probability Scale. Psychiatry and Clinical Psychopharmacology 2017;27(2):205-6. [CrossRef]
5. Feroz-Nainar C, Selvaraj P, Roy M. Risperidone induced oedema in a child with learning disability and autism. Autism 2006;10(3):308-10. [CrossRef]
6. Soumya RN, Frover S, Dutt A, Gaur N. Angioneurotic edema with risperidone: a case report and review of literature. Gen Hosp Psychiatry 2010;32:646.e1- 646.e3. [CrossRef]
7. Akdag ST, Fettahoglu EC, Ozatalay E. Pedal edema induced by low-dose risperidone monotheraphy in a child. J Child Adolesc Psychopharmacol 2009;19(4):481-2. [CrossRef]
8. Franco K, Tamburrino M, Campbell N, Pentz J, Evans C. Dopaminergic activity and idiopathic edema. Hosp Community Psychiatry 1991;42(3):309-10. [CrossRef]
9. Terao T, Kojima H, Eto A. Risperidone and allergic reactions. J Clin Psychiatry 1998;59(2):82-3. [CrossRef]
10. Knox ED, Stimmel GL. Clinical review of a long-acting, injectable formulation of risperidone. Clin Ther 2004;26(12):1994-2002. [CrossRef]
11. Yaluğ I, Ozten E, Evren Tufan A, Alemdar M, Cerit C. Bilateral pedal edema associated with olanzapine use in manic episode of bipolar disorder: report of two cases. Prog Neuropsychopharmacol Biol Psychiatry 2007;31(7):1541-2. [CrossRef]
12. Yang HN, Cheng YM. Peripheral edema associated with risperidone oral solution: a case report and a review of the literature. J Clin Psychopharmacol 2012;32(1):128-30. [CrossRef]