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Available online at: http://www.iajps.com ***A Case Report***

EPISTAXIS AS A RARE SIDE EFFECT OF RISPERIDONE ENCOUNTERED IN A PATIENT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER; A CASE REPORT

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Abstract:

Risperidone is an atypical antipsychotic drug that works as an antagonist of multiple neurotransmitters; mainly serotonin and dopamine. It is used for a wide range of indications. One of the diseases that risperidone is used for is Attention deficit hyperactivity disorder (ADHD), a psychiatric condition usually affects children. Risperidone is generally considered as a safe drug that might have some gastrointestinal, neurological and metabolic side effects. Although thrombocytopenia is a recognized side effect of risperidone; abnormal bleeding in the background of normal platelet count is very uncommon.

In the present case, we report the incidence of a rare side effect of risperidone that is seldomly reported in literature; which is epistaxis or nose bleed. This adverse event occurred in an 18-your-old male, known to have ADHD and intellectual disability. He was started on risperidone 2mg tablet once daily for having an exacerbation of his condition. Thirty minutes after taking the first dose, he had profuse bleeding from the nose.

This was not associated with any evidence from history, physical examination or labs suggesting other explanations. Very few related cases were reported; with similar presentation and circumstances. In this report, along with presenting our case, we discuss the possible explanations for epistaxis related to risperidone use.

Key words: *risperidone, epistaxis, attention deficit hyperactivity disorder, psychopharmacology.*

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INTRODUCTION:

Attention Deficit Hyperactivity Disorder (ADHD) is a psychiatric condition usually encountered in children, and characterized by decreased ability to concentrate, impulsivity, increased activity or restlessness. The disease severity varies from one child to another, and in some advanced cases it can lead to major problems to the child himself and his family [1]. ADHD can be managed by different modalities; including the use of pharmacological agents, psychoeducation and behavioral therapies. Among different pharmacological agents used in the management of patients with ADHD, Risperidone is one of the commonly used medications [2]. Risperidone is an atypical antipsychotic that acts by modulating the transport of many neurotransmitters. It is a selective monoaminergic antagonist for serotonin, 5HTR2, dopamine D2, and to some extent, it antagonizes α-1, α-2 and histamine H1 receptors [3.4]. Risperidone is generally considered as a safe medication, yet, it can cause some side effects including sedation, headache and metabolic effects, such as weight gain, increased appetite, glucose intolerance and lipid abnormalities [5-7]. Increased bleeding tendency was rarely reported in literature as an adverse event of risperidone. In both adults and children, it occurred either in the form of nasal or gastrointestinal bleeding [8,9]. In this case, we are reporting the incidence of epistaxis in an 18-year-old male, known to have ADHD and intellectual disability on 2mg Risperidone tablets.

CASE PRESENTATION:

This is an 18-year-old male patient, known to have attention-deficit hyperactivity disorder (ADHD) and intellectual disability diagnosed at the age of six. Since the time of diagnosis, he tried multiple agents in different periods, including methylphenidate, olanzapine, valproic acid and paliperidone. Although he was regularly following-up and compliant to his medications, he did not show adequate response to any of them. So, as a result, the family decided to discontinue his medications. He was off medications for around one year, after which he had a two-month period of excessive irritability, aggressiveness and hyperactivity, therefor, the family came back to the psychiatry clinic asking for a new management. As he already used many different agents, the treating team decided to start him on Risperidone 2mg oral tablets, once daily at bedtime. On the first day of treatment, and thirty minutes following the ingestion of risperidone tablet, his father noted seeing a large amount of blood on his pillow. This bleeding was from the nose, spontaneous, and not preceded by any trauma. Bleeding continued for around fifteen minutes and stopped by itself. The parents attributed this to risperidone, and thus, they stopped it and did not seek medical advice at that time. He did not have any other episodes after that one. The family stated that this was his first episode of nose bleed in his lifetime. He was not taking any concurrent medications and he is not known to have any chronic medical condition. The family did not give any history of bleeding elsewhere in the body or easy bruising. No history of dark urine or stool as well. No significant family history of bleeding disorders.

One month after this incidence, the family came on their regular follow up appointment. Full physical examination was performed at that time, including careful examination of the nasal cavity, and all was unremarkable. Additionally, complete blood count (CBC), prothrombin time (PT), and partial thromboplastin time (aPTT) were done, and all were within normal ranges.

The patient was seen three months after this visit, and throughout that time, he did not experience any episode of epistaxis. So the impression of epistaxis as a rare side effect of Risperidone was proposed.

DISCUSSION:

Risperidone related epistaxis was rarely reported literature. According to Harrison and Clark (2004), World Health organization (WHO) reported 54 cases in this regard, among which 37 had sufficient information for causality assessment. 60% of these cases developed epistaxis within the first three weeks after the initial dose of Risperidone [8].

In the following table (table1), we summarize the cases reported in literature; in terms of diagnosis, risperidone dose used and onset of epistaxis after initiating risperidone. All the cases in the table were not diagnosed with any chronic medical illness, and all their laboratory findings were within normal ranges.

Table1: Summary of few reported cases regarding Risperidone-related Epistaxis

	Report Author Year of Publication	Age	Sex	Diagnosis	Dose	Onset of epistaxis	Comments
1	Harrison and Clark. 2004.[8]	57	Female	-	1mg daily	Immediately after 1st dose	- Epistaxis was associated with significant headache - Discontinued risperidone after 4th day of use, then epistaxis stopped
2	Coskun and Mukaddes. 2007.[9]	11	Male	ADHD, oppositional defiant disorder and sleep disturbance.	0.5mg per day (At bed time)	5th day of treatment	- Epistaxis occurred during sleep, about two hours after taking the medication. - Another episode occurred two days later during the day. - Patient continued on the same dose, and had another episode two days later.
3	Binici and Güney 2017.[10]	5	Male	ADHD	0.5mg twice daily	5th day of treatment	-Patient continued on the same dose, and had 2-3 further episodes of epistaxis.
4		7	Male	ADHD and DMDD*	2mg	2nd week of treatment	-He had 1-2 episodes of epistaxis for the next three days

In the table above (table1), we summarize the cases reported in literature. We can note that all of these cases developed epistaxis within two weeks of starting risperidone

*DMDD: Disruptive mood dysregulation disorder

Along with the cases described above, Coskun and Mukaddes (2008) reported the incidence of blood mixed with stool in a six-year-old male, known to have Borderline mental capacity and Disruptive Behavioral Disorder (DBD). This happened on the 6th day of treatment with 0.25mg of risperidone twice daily. Three days later, testing for occult blood (TOB) in feces was positive. This was in the absence of any other abnormal lab findings, chronic medical conditions or use of other medications [9].

An additional case of risperidone related epistaxis was reported by Harrison and Clark, with no further information regarding the diagnosis, dose and onset of epistaxis [8].

This rare side effect of risperidone, i.e. epistaxis, can be explained by different mechanisms. Thrombocytopenia (low platelet count) is a recognized side effect of atypical antipsychotics, and was reported during risperidone treatment [11,12]. Yet, in our patient, and other reported relevant cases, platelet count was within normal ranges; so other possible better explanations and mechanisms should be considered.

Another possible mechanism can be comparatively explained by Sarpogrelate; which is a drug used for cardiovascular indications. Its mechanism of action is by antagonizing 5HT2A receptors. These are serotonin receptors; and by blocking them, it inhibits serotonin-induced platelet aggregation. Sarpogrelate also inhibits the release of vasoconstrictors from platelets at the level of microcirculation [13,14]. Given the fact that risperidone is a serotonin antagonist and has a high affinity for 5HT2A receptors [8], we can presume that risperidone can have antithrombotic effects in the microcirculation. And thus, can increase bleeding tendency and cause nasal bleeding.

In conclusion, it is still difficult to state that this bleeding was definitely the result of risperidone use. Nevertheless; considering that all the cases described in literature did not have any medical explanation for epistaxis. Additionally, the onset of symptoms was shortly after the use of risperidone. So, risperidone induced epistaxis remains the most probable explanation. And as the case is rarely described in literature, we recommend further studies in this regard, and more attention to be paid for rare side effects identification and documentation. This can enrich clinician's awareness and patients' compliance to the medication.

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