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Hematemesis in a Child on Olanzapine

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Abstract The case of a 13-year old boy with hepatic steatosis secondary to atypical antipsychotic use is described. The patient presented with a single episode of moderate-volume hematemesis and was found to have severe fatty infiltration and ductal dilatation of the liver. These changes were attributed to the patient's use of olanzapine for behavioral disorders related to autism spectrum disorder. The differential diagnosis of pediatric hematemesis is described, as well as the importance of considering adverse drug affects in patients maintained on olanzapine and other antipsychotics.

Keywords: *GI bleeding, pediatrics, hepatic steatosis, olanzapine, fatty liver, hematemesis, antipsychotics*

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1. Background

Pediatric gastrointestinal bleeding presents a frequent diagnostic dilemma to emergency providers. Hematemesis, in particular, may be the presenting symptom of severe illness in a child. As such, a thorough differential diagnosis is critical to ensuring comprehensive patient care. We present a case in which a child's hematemesis was thought to be secondary to use of olanzapine for Asperger's Syndrome.

2. Case Report

A 13-year old boy presented our emergency department (ED) with chief complaint of hematemesis. The child had been in his normal state of health until that morning, when he had a single episode of moderate-volume hematemesis. A photograph presented by the patient's mother demonstrated vomitus containing 30-40mL of bright red blood. The patient complained of constant, cramping abdominal pain at the time of presentation. He denied fever, cough, or diarrhea. The remainder of his review of systems was negative, aside from mention of marked weight gain over the past several months. He denied change in eating habits. The patient's medical history was significant for Asperger's Syndrome, for which he had been taking 10 mg of oral olanzapine daily for five months. Review of the patient's social history was negative for drug or alcohol use, and the patient denied smoking or exposure to passive smoke inhalation.

At his ED presentation, the child was noted to be tachycardic with a heart rate of 132 beats/min. The rest of his vital signs were normal with a temperature of 37°C, respiratory rate of 24 breaths/min, and blood pressure of 115/67 mm Hg. He had an otherwise benign physical examination, including a soft and non-tender abdomen and no evidence of upper respiratory or pharyngeal bleeding. Stool guaiac was positive for occult blood. His evaluation included a complete blood count comprehensive metabolic panel, and coagulation factors. Liver function tests were noted to be abnormal with elevated alanine aminotransferase (ALT) of 120 U/l and aspartate aminotransferase (AST) of 43 U/l The remainder of the hematology results were within reference range to include a hemoglobin of 13.9 g/dL and a hematocrit of 39.7% He was hydrated over three hours with intravenous (IV) normal saline, including two boluses of 20mL/kg. He remained persistently tachycardic despite hydration and was admitted to the hospital for observation and serial hemoglobin testing.

During his hospitalization, the patient had ultrasonography of the liver performed, which demonstrated severe hepatic steatosis with intra-hepatic ductal dilatation. Serum testing for viral and autoimmune hepatitis was negative. The patient was seen by pediatric gastrointestinal (GI) disease specialists, and the cause of his hepatic steatosis was felt to be secondary to olanzapine use. The patient's hematemesis was determined to be secondary to olanzapine-induced esophagitis. Olanzapine was discontinued and the patient commenced on proton pump inhibitors with symptomatic relief. Serial hemoglobin and hematocrit testing was stable, and the patient was discharged home on hospital day 2 to follow with pediatric GI specialists. At six-month followup, the patient remained symptom-free, with repeat ultrasonography demonstrated interval improvement in the patient's hepatic steatosis, supporting the assumption that the admitting diagnoses were induced by the patient's olanzapine use.

3. Discussion

Hematemesis may result from swallowed blood or upper gastrointestinal bleeding. Physical examination may be sufficient to rule out non-gastrointestinal sources of bleeding. Severity of the acute presentation is typically determined via a combination of clinical factors, including

hemodynamic stability, skin color and mental status of the patient, and estimate of the volume of blood lost. The differential diagnosis for pediatric hematemesis is listed below in Table 1 [1].

Table 1. Differential Diagnosis of Pediatric Hematemesis

Swallowed blood
-Epistaxis, Breast Feeding, Oral Bleeding
Vitamin K deficiency
Erosive esophagitis
Mallory-Weiss tear
Hemorrhagic gastritis
-Trauma, Surgery, Burns, Severe Stress
Reactive Gastritis
-NSAID use, Alcohol/Drug-induced, Caustic Ingestion, Viral, Crohn's Disease, Vasculitis, Radiation, Ischemic
Peptic ulcer
Variceal bleeding associated with portal hypertension
Submucosal masses
Vascular malformation
Hemobilia

Olanzapine is approved for use in schizophrenia and bipolar disorder. It is frequently used off-label in children for various psychiatric and behavioral conditions, including those related to autism spectrum disorders [2]. An atypical antipsychotic, olanzapine acts via manipulation of multiple neurotransmitters, including 5-HT_{2A} receptor antagonism, dopamine D_2 receptor blockade, as well as significant muscarinic, histaminic, and adrenergic activity [3]. Olanzapine enjoys a relatively innocuous safety profile, with the most common side effect of weight gain, occurring in up to 78% of patients [1]. Other adverse reactions reported include hepatotoxicity and hyperlipidemia, with liver function test (LFT) abnormalities reported in up to 7% of users [4]. While there are no case reports detailing gastrointestinal bleeding as a result of olanzapine use (one reported case of bleeding during post-marketing surveillance was attributed to concomitant aspirin use), the mechanism by which atypical antipsychotics cause GI bleeding has been well described [5]. The anti-muscarinic action of these agents decreases esophageal motility and tone, increasing relaxation of the lower esophageal sphincter and permitting gastro-esophageal reflux [6]. The resultant esophagitis has been seen and reported multiple times with other atypical antipsychotics, particularly with the use of clozapine [6,7].

Though asymptomatic elevation in liver function tests has been reported in many olanzapine users, serious hepatotoxicity or fatty infiltration has rarely been recorded [8,9]. The mechanism of such neuroleptic-induced hepatotoxicity is not well understood, and surveillance of liver function tests is not routinely recommended when prescribing or maintaining patients on atypical antipsychotics. The few case reports that have detailed liver injury due to olanzapine use vary in the reported mechanisms, including eosinophilic infiltration, cholestatic hepatocellular destruction, and toxic hepatitis [10,11,12]. Importantly, however, a strong association has been demonstrated between fatty infiltration of the liver and significant weight gain, as demonstrated in our patient [6].

4. Conclusions

Olanzapine remains a safe and effective option for pharmacologic management of behavioral disorders in children. However, in patients presenting with gastrointestinal complaints who are maintained on olanzapine, it is reasonable to consider esophagitis and hepatotoxicity. Discontinuation of olanzapine can result in normalization of liver enzyme elevation and resolution of gastrointestinal symptoms. Alternative medications or adjunct treatment with proton pump inhibitors or H_2 blockers may improve compliance with prescribed therapy.

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Consent

Written informed consent for publication of their clinical details was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Author Disclosure

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the manuscript.

Authors' Contribution

Richard Pescatore[BEF], Dunisha Ranasuriya[BE], Lisa Drago[B], Julie Whitney[BE], Sandra Nairn[BEF]

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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