Case Report

Proton Pump Inhibitor (PPI)-Domperidone Induced Anemia and Galactorrhea: A Case Report

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Keywords

Iron deficiency anemia-IDA, Proton pump inhibitors-PPIs, Ferric Carboxy Maltose-FCM, Fermented Oligo, Di, Monosaccharide and Polyols derivative-FODMAP Diet, Tissue transglutaminase-TTG

Abstract

Gastrointestinal disorders are increasingly common among young adults, particularly medical students exposed to chronic stress and irregular dietary habits. Proton pump inhibitors (PPIs) are widely prescribed for the management of gastroesophageal reflux disease (GERD), gastritis, and related acid-peptic disorders. However, prolonged PPI therapy has been associated with impaired iron absorption and may contribute to iron deficiency anemia (IDA).
We report the case of 26-year-old female, unmarried, postgraduate medical student with iron deficiency anaemia and galactorrhea. The patient presented to gastroenterology clinic with a complaint of mild non-colicky epigastric pain, nausea, fatigue and shortness of breath. Comprehensive evaluation included complete blood count with peripheral smear, iron profile study, stool routine and stool for occult blood, serum IgA anti TTG, viral markers, upper gastro intestinal endoscopy (UGIE) & biopsy, H. Pylori ammonia breath test, gastric emptying scintigraphy, USG abdomen and pelvis, and serum prolactin levels. Based on the clinical, laboratory, and radiological findings, a diagnosis of iron deficiency anemia secondary to long-term PPI use and domperidone-induced galactorrhea was established. The patient was treated with intravenous ferric carboxymaltose (1500 mg), advised discontinuation of PPI-domperidone therapy, and initiated on a low-FODMAP diet. Significant clinical and hematological improvement was observed on follow-up, along with resolution of galactorrhea. Although PPIs remain highly effective and generally safe agents for acid suppression, concerns regarding their long-term adverse effects are increasing. Iron deficiency anemia resulting from chronic PPI use and concurrent domperidone-induced galactorrhea occurring in the same patient is rarely reported. This case underscores the importance of meticulous history taking, appropriate diagnostic evaluation, and rational test utilization in identifying uncommon medication-related adverse effects. Clinicians should consider prolonged PPI use as a potential contributing factor when evaluating unexplained iron deficiency anemia, particularly in young individuals receiving long-term therapy.

Background

Iron deficiency anemia (IDA) is a major health issue in India for many reasons[1]. Long-term use of proton pump inhibitors (PPIs) has been associated with impaired iron absorption[2], while domperidone is known to cause hyperprolactinemia due to dopaminergic blockade[3]. The coexistence of these adverse effects is rarely reported. This case highlights on taking clinical history, ordering relevant diagnostic tests to rule out differential causes of IDA in young female and effective test utilization to avoid exhaustive investigations probably invasive GI biopsies.

Case presentation

A 26-year-old unmarried female young medical student presented to the Gastroenterology clinic with a complaint of mild non-colicky abdominal pain and nausea for 8 years. She had localized, dull, non-radiating epigastric pain started 6 years ago, present throughout the day and relieved on taking PPIs (Pantoprazole-Domperidone). She had a complaint of mild to moderate dyspnea on exertion, fatigue for past 3 years and history of white milky discharge from the nipple for the past 1 year. She had intermittent reflux once a week for the previous 9 years. The patient was on long term PPI (pantoprazole/ esomeprazole 40mg daily) and domperidone (30mg daily) combination from 2014 to 2021. For IDA, she was prescribed oral iron supplements in 2018, which she stopped taking after one week owing to non-compliance. Before presentation, she had a history of migraine with aura, for which the patient was on Sodium valproate + Propranolol prophylaxis for around 1.5 years (2017-2018). Valproate side effects had caused her to gain weight in the past. Before to presentation, she reported a 3kg intentional weight loss in 2021. The patient had no comorbidities. She had no history of surgery and menstrual irregularity. She is an occasional smoker, alcoholic, non-vegetarian, non-diabetic and non-hypertensive. She has no known drug allergy. There was no relevant family history in this report. On physical examination, the vital signs were as follows: Body temperature, 36.5°C; blood pressure, 118/72 mmHg; heart rate, 91 beats per min; respiratory rate, 20 breaths per min. There was no noticeable pallor, and the liver was just palpable below the rib. Patient's Laboratory workup, before and after taking treatment are shown in Table 1 below.

Table 1: Showing blood parameters before and after treatment for PPI-DA induced IDA and galactorrhea.

Blood parameters	Before treatment (2014-2021)	3 months after treatment (2022)
1. Hemoglobin (11.5 – 14.5 gm/dl)	**7.8**	**11.8**
2. Erythrocyte count (4.7 – 6.0 mil/cu.mm)	4.1	4.3
3. Packed cell volume (36 – 48 %)	26.1	37
4. Mean cell volume (78- 100 fl)	**60.0**	**81**
5. Mean cell hemoglobin (27 – 31 pg)	18.1	29.9
6. Mean cell Hb# conc. (32 – 36 g/dl)	28.9	33.2
7. Red cell distribution width (RDW) (12 – 14.5%)	21.0	21.5
8. Total Leucocyte count (4000 - 11000/cumm)	11200	10294
9. Platelet count (1.50 – 4.50 × 10^3/ul)	3.91	3.95
10. Peripheral smear	**Microcytic, hypochromic RBCs, anisocytosis seen**	**Normocytic, normochromic RBCs seen**
11. Stool for occult blood	Negative	Negative
12. Stool routine (ova/cyst/larvae/trophozoite segments of any parasites seen)	No	No
13. IgA Anti-TTG# (<4U/ml)	1.29	1.31
14. Iron (70-180ug/dl)	**6.0**	**78**
15. Ferritin (22-32ng/ml)	**2.2**	**24**
16. Vitamin B12 (156-672 pmol/L)	300.0	312.0
17. Folic acid (>5.38ng/ml)	6.63	6.78
18. Anti-HCV Ab (<0.90)	Non-reactive (0.02)	Non-reactive
19. Anti-HIV (<0.90)	Non-reactive (0.08)	Non-reactive
20. HBsAg# (<0.90)	Non-reactive (0.15)	Non-reactive

Blood parameters	Before treatment (2014-2021)	3 months after treatment (2022)
21. HELIC# Ammonia Breath test (<3.0 mm)	**Positive (+) (11.9mm)**	**Negative (-) (2.3mm)**
22. Follicle stimulating hormone (3.85-8.78 mIU/ml Follicular phase)	4.76	4.12
23. Luteinising hormone (2.12-10.89 mIU/ml Follicular phase)	5.22	6.30
24. Estradiol E2 (22.40-115.0 pg/ml Follicular phase)	36.54	37.57
25. Prolactin (2.80-29.20 ng/ml Non pregnant)	**94.01**	**21.02**
26. Inhibin B (21-53 pg/ml)	95.14	44.58

#Hb-Hemoglobin; TTG-Tissue transglutaminase; HELIC-Helicobacter Pylori; HBsAg-Hepatitis B surface antigen

USG abdomen and pelvis showed both ovaries bulky (right; 20cc, left; 18 cc) with echogenic stroma and no other significant abnormality. Upper GI endoscopy revealed a normal study up to duodenum D2, and a biopsy of the body and antrum revealed normal histology. Gastric emptying scintigraphy with 1mCi of Tc99m-Sulphur colloid delivered orally and serial imaging's recorded for 4 hours in both anterior and posterior views, showed no delays with gastric emptying time of t ½ 116 minutes (normal range 70-100 minutes) and 99% emptying after 4 hours.

Diagnosis and treatment

The final diagnosis, based on the patient's medical history and test results, was Chronic GERD/H. Pylori positive/ PPI-associated Iron deficiency anaemia and Domperidone-associated galactorrhea (drug-associated hyperprolactinemia). The patient was advised to avoid PPIs and Domperidone. Because the patient did not respond to oral iron therapy, Ferric Carboxy Maltose 1500 mg (1000 mg initial infusion followed by 500 mg after 10days) as per iron therapy standard dosing protocol, an H. Pylori kit course, folic acid 5mg and methylcobalamine 1500 mg OD were given for three months, and a FODMAP Diet; 1400kcal (low calorie) diet was recommended. On stopping the PPI-Domperidone combination therapy along with injection Ferric Carboxymaltose, IDA and Galactorrhea subsided completely. Follow-up serum iron studies, serum IgA, H. Pylori Ammonia breath test, and Glucose, Fructose, Lactose Hydrogen breath test were indicated, along with food adjustment and physical exercise for 30 minutes each day.

Discussion

Despite being safe for long-term use, Proton pump inhibitors (PPIs) can cause iron deficiency anemia[4]. Omeprazole-Domperidone was the first approved PPI for over-the-counter (OTC) use[5]. PPI-associated Galactorrhea, possibly caused by Domperidone, is rarely reported [6]. This case reported 27-year-old female postgraduate medical student who was taking PPI-domperidone daily for 8 years and experienced mild non-colicky abdomen pain and nausea and suggesting chronic development of iron deficiency.

Dietary iron contains both heme and non-heme iron. Heme iron ($Fe2^{+}$) is more easily absorbed once pancreatic enzymes release it from globin. Since ferric ($Fe3^{+}$) iron is predominant, it absorbs slowly[7]. Iron absorption from the duodenum requires STEAP3 or cytochrome b to reduce $Fe3^{+}$ to $Fe2^{+}$. Over-the-counter PPIs, such as esomeprazole, lansoprazole, and omeprazole, may lead to increased use and dependence. Proton pump inhibitors inhibit gastric H^{+}/K^{+}-ATPase in parietal cells, leading to hypochlorhydria. Gastric acid is essential for solubilizing dietary non-heme iron and reducing ferric (Fe^{3+}) to ferrous (Fe^{2+}) form via duodenal cytochrome b (Dcytb). Reduced gastric acidity impairs this conversion, thereby decreasing iron bioavailability and absorption in the duodenum. Intestinal reduction and absorption of $Fe3^{+}$ decreases. Gastric pH elevates G cell hyperplasia and serum gastrin. Due to a lack of available reduced ferric iron, ferrous iron absorption decreases, resulting in iron insufficiency. Additionally, increased gastric pH may impair release of iron from food matrices and reduce ascorbic acid-mediated reduction[8]. Long term PPI-associated IDA was first reported in 2002. According to Sharma et al. (2004), two patients who used PPI for severe gastritis developed iron deficiency that did not respond to oral iron until the PPI was stopped[9]. In another report, Sarazynski et al. found that 98 patients on PPI for more than a year had significantly lower haematocrit, hemoglobin concentration, and MCV than matched controls. Over 20% experienced a 1 g/dL reduction in hemoglobin concentration. These electronic medical record chart reviews were retrospective, therefore iron deficiency treatment was not discussed[10]. A 25-year-old PPI user in Japan experienced iron deficiency, according to Imai et al. in 2018, which was reverted back on stopping PPI. Anemia was linked with PPI usage in 51% of Japanese cardiac patients, compared to 19% without PPI use ($P < 0.001$). There were no conclusions other than that long-term PPI users may develop IDA[11].

On the other hand, one of the first reports of domperidone-associated galactorrhea came from Great Britain in 1983 and another came from India in 1991[12]. Domperidone is a peripheral dopamine D2 receptor antagonist. Dopamine

physiologically inhibits prolactin secretion from the anterior pituitary. Blockade of D2 receptors removes this inhibitory control, leading to hyperprolactinemia and consequent galactorrhea[13,14]. In our case, with relevant medical history and laboratory results, we found that our patient was a rare case, with coexistence of PPI-DA associated IDA plus galactorrhea. The Naranjo Adverse Drug Reaction Probability Scale has been evaluated for temporal association in this patient and a score of 8 derived[15] attached in Supplemantry file S01.

She had undergone several investigations in Table 1, before PPI- associated IDA was established as her diagnosis, which may be an exhausting experience. The hematological profile demonstrated classical iron deficiency anaemia with microcytosis (MCV 60 fL), hypochromia (MCH 18.1 pg), elevated RDW (21%), and depleted iron stores (ferritin 2.2 ng/mL). Normal B12 and folate levels excluded megaloblastic anaemia. Post-treatment normalization confirms iron deficiency as the primary etiology. Gastrointestinal bleeding excluded (negative stool occult blood, normal endoscopy), Celiac disease excluded (negative anti-TTG IgA), Nutritional deficiency unlikely (mixed diet), Helicobacter pylori was treated, yet anaemia persisted until PPI withdrawal supporting PPI as a contributing factor. Thyroid function was within normal limits. Further, prolactin was elevated (94 ng/mL) but normalized after domperidone withdrawal, and there were no symptoms (like headache, visual defects- absent) excluding pituitary pathology as cause of hyperprolactinemia. Rapid normalization after domperidone withdrawal strongly supports drug- associated etiology.

Finally, as part of her treatment plan, she was prescribed an injection of Ferric Carboxy Maltose 1500 mg (1000 mg initial infusion followed by 500 mg after 10days) as per iron therapy standard dosing protocol, an H. Pylori kit, a FODMAP diet, physical exercise and review after 3 months[16]. At 3-month follow-up Hb improved to 11.8 g/dl, Ferritin increased to 24 ng/mL, Prolactin normalized (21 ng/mL) and complete resolution of galactorrhea and fatigue was observed. A low FODMAP diet was advised to manage persistent functional gastrointestinal symptoms suggestive of IBS overlap, particularly bloating and dyspepsia, after exclusion of structural pathology[17]. The patient's summary of events and treatment history has been provided in Table 2.

Table 2: Showing Timeline of events and treatment course.

Year	Event	Treated
2014	GERD/Gastritis	Started Pantoprazole-Domperidone (*8 years daily)
2018	Anaemia	Oral Iron prescribed (1 week non-compliance stopped)
2020	Progressive fatigue	—
2021	Onset of Galactorrhea	—
2022	Diagnosis made Drug induced IDA with Galactorrhea	Ferric Carboxy Maltose 1500 mg (1000 mg initial infusion followed by 500 mg after 10days) H. Pylori kit course Folic acid 5mg and Methylcobalamine 1500 mg OD* 3 months, FODMAP Diet
2022	Causative drug PPI-Domperidone withdrawal	

This case highlights the importance of balancing comprehensive diagnostic evaluation with judicious test utilization. Although several investigations were normal, but they were helpful to exclude common causes of iron deficiency anemia and hyperprolactinemia, thereby strengthening the association with prolonged PPI-domperidone use. The case reinforces the value of detailed history-taking and systematic exclusion of alternative diagnosis when assessing uncommon drug-related adverse effects.

Conclusion

This case reported that a probable association between long-term PPI use and iron deficiency anaemia, as well as domperidone and hyperprolactinemia[18]. While causality cannot be definitively established from a single case, the temporal relationship and resolution after drug withdrawal support a probable link. Without therapeutic rationale, chronic and improper PPI use raises short- and long-term adverse effects. PPI- associated malabsorption is more common, physician should consider it when diagnosing iron deficiency

without other causes. Over the counter drugs becoming a daily diet are highly alarming serious health concern especially in adolescents, young adults and medical students.

Conflict of Interest

Authors declare no conflict of interest.

Patient Consent

Informed written consent was obtained from the patient for publication of clinical details.

CRediT statement

RB,ST- Conceptualization, Writing – original draft and Writing – review & editing; PP, UKN- Investigation, Methodology, Supervision, Validation, and Visualization.

Funding and Data Availability Statement

No funding is required for this study. No supplemental data available for this study.

Ethical Statement

Informed consent obtained from the patient for clinical history. This case report has been written in compliance with the ethical principles for medical research in accordance with the Declaration of Helsinki.

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Supplementary files

Supplementary Figure 1: Naranjo Adverse Drug Reaction Probability Scale

EVIDENCIO
MEDICAL DECISION SUPPORT

Algorithm-id: 661 | Version: 1.37 | Revision date: 2017-01-25

NARANJO ADVERSE DRUG REACTION PROBABILITY SCALE

The Naranjo ADR Probability Scale was developed to help standardize assessment of causality for all adverse drug reactions. The scale was also designed for use in controlled trials and registration studies of new medications, rather than in routine clinical practice.

Research authors: *Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ*

RESULT 2026-04-29 17:53

Score 8

Based on the following parameters:

1. Are there previous conclusive reports on this reaction?	Yes +1
2. Did adverse event appear after the suspected drug was given?	Yes +2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	Yes +1
4. Did the adverse reaction appear when the drug was readministered?	Yes +2
5. Are there alternative causes that could have caused the reaction?	No +2
6. Did the reaction reappear when a placebo was given?	Not known or not done
7. Was the drug detected in any body fluid in toxic concentrations?	Not known or not done
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Not known or not done
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Yes +1
10. Was the adverse event confirmed by any objective evidence?	Not known or not done

Disclaimer: This algorithm is provided for educational, training and information purposes. It must not be used to support medical decision making, or to provide medical or diagnostic services.