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Case Report

Iron Deficiency Anemia-Induced Lymphocytopenia in a Young Female

Elabbass A. Abdelmahmuod[a] Mohamed A. Yassin[b]

[a]Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar; [b]Department of Medical Oncology, National Center for Cancer Care and Research, Doha, Qatar

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Abstract
Iron deficiency anemia is the most common type of anemia, and it occurs when the human body does not have enough of the mineral iron (https://www.healthline.com/health/iron-deficiency-anemia#diagnosis). Iron deficiency anemia is caused by blood loss, insufficient dietary intake, or poor absorption of iron from food. Sources of blood loss can include heavy periods, childbirth, uterine fibroids, stomach ulcers, colon cancer, and urinary tract bleeding (https://www.nhlbi.nih.gov/health-topics/iron-deficiency-anemia). Poor absorption of iron from food may occur as a result of an intestinal disorder such as inflammatory bowel disease or celiac disease, or surgery such as a gastric bypass (https://www.who.int/nutrition/topics/ida/en/). Little is known about the association between iron deficiency anemia and lymphocytopenia. Here, we report on a 17-year-old female who presented with iron deficiency anemia and was found to have lymphopenia. She recovered after having received intravenous iron therapy.

Introduction

Iron deficiency anemia (IDA) arises when the balance of iron intake, iron storage, and the body's loss of iron are insufficient to fully support the production of erythrocytes. IDA rarely causes death, but the impact on human health is significant [1]. Symptoms of IDA are related to decreased oxygen delivery to the entire body and may include the following: unexplained fatigue or lack of energy; shortness of breath or chest pain, especially with activity; unex-

Elabbass A. Abdelmahmuod
Department of Internal Medicine
Hamad Medical Corporation Alrayan street
P.O. Box 3050 Doha (Qatar)
abbassrex280@gmail.com

Table 1. Complete blood count upon presentation

Group	Detail	Date	Value	Flags	Normal range	Comment Ind
General hematology	WBC	03/12/2018 13:20:00 AST	7.5×10^3/μL		4.0–10.0	
General hematology	RBC	03/12/2018 13:20:00 AST	4.1×10^6/μL		3.8–4.8	
General hematology	Hgb	03/12/2018 13:20:00 AST	5.2 g/dL	CRIT	12.0–15.0	Y
General hematology	Hct	03/12/2018 13:20:00 AST	21.2%	LOW	36.0–46.0	
General hematology	MCV	03/12/2018 13:20:00 AST	51.2 fL	LOW	83.0–101.0	
General hematology	MCH	03/12/2018 13:20:00 AST	12.6 pg	LOW	27.0–32.0	
General hematology	Platelet	03/12/2018 13:20:00 AST	302×10^3/μL		150–400	
General hematology	Absolute neutrophil count auto# (ANC)	03/12/2018 13:20:00 AST	6.19×10^3/μL		2.00–7.00	
General hematology	Lymphocyte auto#	03/12/2018 13:20:00 AST	0.74×10^3/μL	LOW	1.00–3.00	

Table 2. Iron profile >> severe iron deficiency anemia

Group	Detail	Date	Value	Flags	Normal range	Comment Ind
Blood chemistry	Iron	07/08/2019 10:40:00 AST	5.23 μmol/L	LOW	5.90–18.30	
Blood chemistry	TIBC	07/08/2019 10:40:00 AST	70 μmol/L		45–80	
Blood chemistry	Fe% saturation	07/08/2019 10:40:00 AST	7%	LOW	15–45	
Endocrinology	Ferritin	07/08/2019 10:40:00 AST	3 μg/L	LOW	6.0–44.0	

plained generalized weakness; a rapid heartbeat; headache, especially with activity; craving for ice or clay ("picophagia"); a sore or smooth tongue; and brittle nails or hair loss [2]. According to the WHO, the criterion for anemia is a hemoglobin level <13 g/dL in adult males and <12 g/dL in adult females. As the iron deficiency worsens, both hemoglobin and PCV decline together [3]. The diagnosis of iron deficiency to be confirmed by any one of the following findings in the appropriate clinical setting: serum ferritin <30 ng/mL; transferrin saturation <19%, mostly used in patients for whom the ferritin level is thought to be unreliable due to an inflammatory state; or anemia that resolves upon iron administration or absence of stainable iron in the bone marrow (provided that adequate staining controls are performed [4]).

IDA presents with thrombocytosis; however, there rarely is an association between IDA and lymphocytopenia. Here, we would like to shed light on this rare presentation.

Case Presentation

A 17-year-old female who presented with dizziness and fatigability was found to have severe anemia (hemoglobin 5.2 g/dL; normal value 12–15). Her menstrual cycle was normal, but she had poor nutrition; she denied other symptoms. On examination, she showed severe pallor, but no hepatosplenomegaly. For her laboratory results, see Tables 1–4.

Peripheral Smear

Red blood cells showed mild anisopoikilocytosis with few ovalocytes/elliptocytes and occasionally schistocytes. Leukocytes occasionally showed reactive lymphocytes. Monocytes were slightly prominent. Platelets were adequate.

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Table 3. Vitamin B12, folate and thyroid function test

Group	Detail	Date	Value	Flags	Normal range	Comment
Endocrinology	Vit. B12	15/09/2019 18:50:00 AST	250.0 pmol/L		145.0–596.0	
Endocrinology	Folate	07/08/2019 10:40:00 AST	17.74 nmol/L	HIGH	2.70–16.30	
Endocrinology	TSH	28/01/2019 08:32:00 AST	2.260 mIU/L		0.700–3.400	Y
Endocrinology	fT_4	28/01/2019 08:32:00 AST	10.7 pmol/L		7.9–13.6	Y

Table 4. Laboratory results after therapy

Group	Detail	Date	Value	Flags	Normal range	Comment Ind
General hematology	RBC	07/08/2019 10:40:00 AST	5.0×10^6/μL	HIGH	3.8–4.8	
General hematology	RBC	07/08/2019 10:40:00 AST	5.2×10^6/μL	HIGH	3.8–4.8	
General hematology	Hgb	07/08/2019 10:40:00 AST	11.0 g/dL	LOW	12.0–15.0	
General hematology	Platelet	07/08/2019 10:40:00 AST	408×10^3/μL	HIGH	150–400	
General hematology	Platelet	07/08/2019 10:40:00 AST	392×10^3/μL		150–400	
General hematology	Lymphocyte auto#	07/08/2019 10:40:00 AST	1.41×10^3/μL		1.00–3.00	
Endocrinology	Ferritin	07/08/2019 10:40:00 AST	31.9 μg/L		6.0–44.0	

The patient received IV ferric carboxymaltose (Ferinject) at 1,000 mg in 2 doses. Her symptoms, anemia, and lymphocytopenia dramatically improved after therapy.

Discussion

Iron plays an essential role in immunosurveillance, because of its growth-promoting and differentiation-inducing properties for immune cells and its interference with cell-mediated immune effector pathways and cytokine activities [5].

IDA is a problem of serious public health significance that impacts mental and physical development, health maintenance, and work performance. It is the most common micronutrient deficiency worldwide. It exceeds 50% in developing countries and is usually attributed to inadequate nutrition [6]. IDA due to nutritional deficiency is not just a disease of developing countries, but it can also be seen in developed countries. Worldwide, over 40% of cases of children who have iron deficiency anemia are frequently associated with infections [7].

IDA impairs thyroid metabolism in animals and humans and may negatively affect the growth and development of children. On the other hand, both overt and subclinical hypothyroidism are associated with anemia, and adding iron to thyroxine therapy improves both conditions compared to thyroxine therapy alone. In addition, patients with chronic hemolytic anemia requiring repeated blood transfusion have a high prevalence of hypothalamic-pituitary-thyroid axis disturbances. Both primary hypothyroidism and central hypothyroidism occur in these patients with increasing prevalence with age and severity of the anemia [8]. It appears that all forms of chronic anemia have a negative effect on linear growth during all stages of growth (infancy, childhood, and adolescence). Although infants with chronic IDA may have delayed cognitive, motor, and affective functions [9], the effects on male fertility explored by Soliman et al. [10] in a study showed that correction of IDA with IV iron is associated with significant enhancement of sperm parameters and increased concentrations of serum LH, FSH, and T. These effects on spermatogenesis are reached by an unknown mech-

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anism and suggest a number of pathways that need further human and/or experimental studies. In another study looking for the effects of IDA on glucose metabolism, Soliman et al. [11] suggest that among nondiabetic and diabetic individuals, IDA is associated with higher concentrations of HbA_{1c}. Iron replacement therapy decreases HbA_{1c} in both diabetic and nondiabetic individuals. This implies that the iron states must be considered during the interpretation of HbA_{1c} concentrations in diabetic or nondiabetic patients. Early diagnosis and treatment of IDA in diabetic patients can improve their glycemic control and may prevent or delay complications.

Worldwide, over 40% of children have IDA, frequently associated with infections. Certain cytokines are involved in both immune activation of/response to infection and iron transport/metabolism. An increased susceptibility to infections has been reported in some IDA patients, the etiology of which is not well known [5].

Iron is required for monocyte/macrophage differentiation, while macrophages require iron as a cofactor for the execution of important antimicrobial effector mechanisms, including the nicotinamide adenine dinucleotide phosphate hydrogen-dependent oxidative burst [12].

Little is known concerning the effect of clinical iron deficiency on cytokines, although it has been reported that in vitro production of cytokines by lymphocytes in iron-deficient patients may be impaired [5] and thus may make people with IDA more susceptible to infections.

Conclusion

IDA commonly presents with typical signs and symptoms. However, it rarely can present with atypical presentation, lymphocytopenia being one of them. There is a lack of clinical research regarding the effect of IDA on white blood cells. However, the clinician should pay attention to such a presentation as it can lead to infection because of lymphocytopenia.

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Statement of Ethics

This case report was approved by the Hamad Medical Corporation's Medical Research Center, and the patient consented to the publication of her case.

Conflict of Interest Statement

The authors have no conflicts of interest.

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Author Contributions

Both authors contributed equally to writing and editing.

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