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Unusual combination and existence of hemolytic anemias; Thalassemia and G6PD deficient anemia in female patient

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Abstract

Beta-thalassemia intermedia exhibits feature of ineffective erythropoiesis and hemolytic anemia. Diagnosis can be made via hemoglobin electrophoresis. G6PD deficiency is an X-linked recessive disorder commonly affecting males while females are carrier. Diagnosis is made by measuring G6PD level. A 19-year old pregnant lady, known case of β-thalassemia intermedia, had been presented with episode of acute hemolytic anemia. Investigations were highly suggestive of G6PD deficient anemia. This was confirmed with low G6PD level. Back to her immediate history, consumption of broad bean was ascertained. After appropriate therapy, the patient felt better and her medical derangement was normalized. She delivered normally and kept on life-long folic acid therapy. The importance of recording such a case report is to expect unusual combination of hemolytic anemia despite the uncommon finding of Xlinked recessive disorder in women. This was the first case recorded in Karbala province

Keywords: Beta-thalassemia; Erythropoiesis; G6PD; Hemolytic anemia

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Introduction

Beta-thalassemia of intermediate severity (β^+ β^+ or β^0 β^+) is a common and prevalent condition in the Mediterranean area [1]. Mechanisms behind its development are reduction in the synthesis of beta chain due to point mutation and unbalanced accumulation of globulin subunits [2]. This ultimately gives rise to hypochromic microcytosis, ineffective erythropoiesis and hemolytic anemia [3].

Patients with β-thalassemia intermedia usually presented with hepatomegaly, splenomegaly, hypochromic microcytosis, some target cells, and raised level of HbF, HbA_2, or both. These are stigmata of ineffective erythropoiesis [4]. Patients can survive

without the need for regular blood transfusion. Diagnosis can be made via hemoglobin electrophoresis and genetic study [5].

Glucose-6-phosphate dehydrogenase (G_6PD) is the key enzyme in the hexose monophosphate shunt pathway. Deficiency of G_6PD is the commonest red blood cell enzyme defect [6]. It is inherited in an X-linked recessive fashion: males are affected while females are carrier. Females can manifest the abnormality if they are homozygous or heterozygous in the presence of extreme lyonisation [7, 8].

Most patients with G_6PD deficiency remain clinically asymptomatic throughout their lifetime; however, all of them have an increased risk of developing neonatal jaundice and a risk of developing acute hemolytic anemia [7, 8].

Acute hemolytic anemia can develop as a result of three types of triggers [9, 10, 11]:

(1) Favabeans
(2) Infections
(3) Drugs (definite risk is associated with primaquine, sulfamethoxazole, dapsone, cotrimoxazole, nalidixic acid, nitrofurantoin, phenazopyridine, naphthalene).

Diagnosis is usually made by measuring G_6PD level [12]. During an acute hemolytic episode, care has to be taken because immature erythrocytes and reticulocytes released during hemolytic attack may have normal enzyme level and give rise to a falsely normal result.

Aim of this case report

The aim of this case report is to expect X-linked recessive hemolytic anemia in female and to anticipate even unusual combination of hemolytic anemia.

Case Presentation

A 19 year old female 9 MP pregnant patient presented with malaise, generalized weakness, and mild form of exertion dyspnea. She experienced this attack as gradual sense of weakness started two days ago and maximized few moments prior to consultation. She indeed described her urine turned cola-color and her body turned yellowish.

Detailed history had shown that she had few clinic visits due to attacks of anemia of mild severity with only one attack requiring blood transfusion (two pints). The reason for blood transfusion was not known and not recorded. She denied recent feeling of fever or taking medicines.

She was born in Nasiriya governorate and travelled to live in Karbala after her marriage. She had a previous medical history of thalassemia. She had therefore, given advice to be kept on folic acid but she was non-complaint for her medical follow-up. Her father was incapacitated and blind with unknown medical history and her mother having thalassemia too.

No known allergies and no surgical history of note. Physical examination showed jaundice, pallor, no cyanosis, no digital clubbing, no edema, and no lymphadenopathy.

The vital signs were recorded as follow:

Blood pressure	100/65 mmHg
Pulse rate	105
Respiratory rate	30 breaths/minute
Temperature	37 ^{O}C
Oxygen saturation	98%

Her abdomen was distended due to pregnancy. Her cardiorespiratory status was unremarkable apart from increased respiratory rate. Neurologic examination was perfect. Admission was advised for further analysis and management. She received folic acid, fluid, and blood; investigations had been sent prior to blood transfusion. A previous medical report including the results of hemoglobin electrophoresis performed few years ago was obtained on admission and was as follow:

Hb A	Hb A_2	Hb F	Hb C	Hb S
60	5	35	-	-

The report suggested a moderately severe form of β-thalassemia (β-thalassemia intermedia). Because the severity of the clinical course of β-thalassemia intermedia remains mostly unpredictable even in known genotypes, her previous silent history was accepted. Initial hematologic investigations were as follow:

No.	Parameter		Value	Interpretation
1	Hemoglobin concentration (Hb)		6 g/dl	Low
2	Packed cell volume		26	Low
3	White blood cell count		10 x 10^{9}/l	Normal
	Neutrophil	3.5 x 10^{9}/l	(60%)	Normal
	Lymphocyte	3 x 10^{9}/l	(30%)	Normal
	Monocyte	0.2 x 10^{9}/l	(6%)	Normal
	Eosinophil	0.08 x 10^{9}/l	(3%)	Normal
	Basophile	0.06 x 10^{9}/l	(1%)	Normal
4	Platelets count		300 x 10^{9}/l	Normal
5	Reticulocyte count		10	High
6	Corrected reticulocyte count		6.5	High

The basic hematologic investigations well refer to anemia due to peripheral cause (bleeding or hemolysis) due to high corrected reticulocyte count. In the presence of clinical jaundice, one should consider hemolysis. Blood film is also sent and the result presented later. Biochemical screening was sent at the time of admission and the results obtained were as follow:

No.	Parameter	Value	Interpretation
1	Random plasma glucose	110 mg/dl	Normal
2	Blood urea	82 mg/dl	Raised
3	Serum creatinine	0.9 mg/dl	Normal
4	Total serum albumin	5 mg/dl	Raised
5	Direct albumin fraction	0.2 mg/dl	Normal
6	SGPT	15 U/L	Normal
7	SGOT	16 U/L	Normal
8	Alkaline phosphatase	89 U/L	Normal
9	Total serum protein	5.7 g/L	Normal
10	Serum albumin	3.4 g/L	Normal
11	Bile pigment	Negative	Normal

Biochemical investigations showed that this pregnant lady had indirect hyperbilirubinemia and renal impairment. Together with her blood indices, this was due to hemolysis. Raised blood urea was attributed to hemolysis as a cause of prerenal renal failure; lower normal limit of albumin and aminotransferases enzymes as well as slightly raised alkaline phosphatase were all attributed to normal physiological changes of pregnancy.

Blood film revealed two populations of cells; hypochromic microcytosis and macrocytosis. Target cells were also seen together with many bite cells (red cells with a 'bite' of membrane missing) and blister cells (red cells with surface blistering of the membrane). A suggestion of G_6PD deficiency was surprisingly made by lab hematologist. The blood film had been seen and red by two lab hematologists. Back to patient's history, we asked her about broad bean (fava bean) intake. She remembered that she ate it two days before admission. Additional investigations were also appeared and were as follow:

NO.	Parameter	Value	Interpretation
1	Lactate dehydrogenase	650 U/L	Raised
2	Prothrombin time	10 seconds	Normal
3	Activated partial thromboplastin time	30 seconds	Normal
4	D-dimer	150 µg/L	Normal
5	Bleeding time	5 minutes	Normal

EKG and echocardiography were normal apart from sinus tachycardia and trivial physiologic tricuspid regurgitation and pulmonary regurgitation. Infectious screen was negative. Despite the fact that G_6PD level may be normal close to a hemolytic episode, we requested a G_6PD level and the result was 6 U/g Hb (low); an ultrasound was also

requested and showed a single viable fetus with mild hepatomegaly and mild splenomegaly. Hepatosplenomegaly was attributed to ineffective erythropoiesis due to β-thalassemia intermedia. Splenomegaly may be attributed to chronic hemolytic state of G6PD deficiency but this is rather less common.

We discussed her condition with a lab hematologist and an obstetrician; the decision was to continue her pregnancy and to target her hemoglobin to 10 g/l. She kept four days inside the hospital where she received four pints of blood. Her condition after that became well as her hemoglobin level approaches 10 g/l and biochemical profile normalized. On discharge, she was given advice of she had to avoid fava beans, some drugs, and to be kept on folic acids together with close medical supervision. Her family was given advice to perform hemoglobin electrophoresis.

Three months after delivery, the patient returned back for medical follow-up. In addition to basic investigation, hemoglobin electrophoresis was requested which confirmed the basic diagnosis of β-thalassemia intermedia, G6PD level was requested which was low and an abdominal ultrasound also confirmed the existence of hepatosplenomegaly.

The final treatment strategy included life-long folic acid supplementation, periodic blood transfusion support and/or splenectomy, as indicated.

In conclusion, this case report was obviously a combined disorder of β-thalassemia intermedia and asymptomatic G6PD deficient hemolytic anemia that is exacerbated by broad bean intake. The current case emphasizes the importance of expecting unusual combination of hemolytic anemia and to anticipate uncommon existence of X-linked recessive hemolytic anemia in female. This was the first case recorded in Karbala province.

Competing interests

The authors declare that there is no conflict of interest.

Author Contributions

All authors wrote, read and approved the final case report.

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