Case scenarios in Pediatric Hematology and Oncology

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Objectives

* To discuss and learn initial features of childhood leukemia.
* To discuss about differential diagnosis of iron deficiency anemia.
* Understand about thalassemia carrier.
* Discuss and learn treatment of iron deficiency anemia.
* Discuss what could you do in acute severe anemia

Burden of Anemia in children in UAE

Saudi Med J. 2003 Jun;24(6):609-13.

* **A hematological survey of preschool children of the United Arab Emirates.**

Miller CJ[1], Dunn EV, Berg B, Abdouni SF.

Abstract

* **OBJECTIVE:**

Anemia is common worldwide, particularly in developing countries including states of the Arabian Peninsular. The purpose of this study was to produce a hematological profile of preschool national children of the United Arab Emirates (UAE).

* **METHODS:**

From April 2000 to October 2000, a cross-sectional community clinic-based capillary blood survey was carried out on a convenience sample of 1-5-year-old Emirati children attending a Primary Health Care Center in Al-Ain, UAE. Those children with capillary hemoglobin (Hb) and mean corpuscular volume (MCV) values below predetermined cutoffs were offered venous blood hematological workup. A random sample of children with values above those cutoffs were also offered the same workup. All venous blood sampling was completed by May 2001.

* **RESULTS:**

Four hundred and ninety six children were surveyed. The mean Hb and adjusted MCV rose with increasing age but were not significantly different by gender. **Two hundred and sixty-two children with Hb or MCV below the cutoffs** and 50 children above the cutoffs were venous blood tested. The estimated abnormalities for this population of children were as follows: **anemia 36.1%; iron deficiency anemia 9.9%; glucose-6-phosphate dehydrogenase (G6PD) deficiency 9.1%; sickle cell trait 4.6%; and beta thalassemia 8.7%.**

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* **α-Thalassemia syndromes in the United Arab Emirates.**

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* α-Thalassemia (α-thal) is usually due to deletions within the α-globin gene cluster, leading to loss of function of one or both α-globin genes. α-Thalassemia is prevalent in the Arabian Peninsula, particularly in the United Arab Emirates (UAE) and Saudi Arabia. There are no large-scale reports regarding the prevalence of α-thal in the Arabian populations apart from sporadic surveys in the mid-1980s on red cell indices from Saudi Arabia and a more recent study from Kuwait. Several studies were conducted in an attempt to elucidate the frequency of α-thal in the UAE. **Cord blood samples were collected from 419 consecutive newborns of UAE national mothers.** The study involved polymerase chain reaction (PCR)-based analysis of the α-globin genes and sequencing using an ABI Genetic Analyser 3130. **The findings demonstrated that 49% of the neonates had α-thal, one of the highest in the world.**

7-year-old girl
7 days of progressive pallor, abdominal distension, multiple bruises and fever

Hepatosplenomegaly
No lymphadenopathy

What investigations we could do at this point?

What investigations we could do at this point?

* CBC, peripheral smear
* CRP or ESR
* PT/PTT
* LDH

Hb 2.4
WBC 6.4
Neutrophil 0.62
Platelet 12

Peripheral Smear Blast
LDH 926

Bone Marrow Examination reveals this child has Acute Lymphoblastic Leukemia

What we can learn from this experience

- How the symptoms and signs develop in ALL?
- What are the clinical features of ALL?
- What are the differential diagnosis of ALL in children?
- What are the basic investigations you could do ?

Clinical Features

Clinical Features

* Anemia
* Bleeding and bruises
* Infection
* Bone Pain
* Hepatosplenomegaly
* Lymphadenopathy
* Abdominal distension
* Breathing difficulty

Differential diagnosis

Differential diagnosis

* Aplastic Anemia
* Idiopathic Thrombocytopenic Purpura
* Viral infection
* Infectious Mononucleosis
* Juvenile Chronic Arthritis
* Neuroblastoma

Current Outcome of ALL

Study group	Trial	Years	ALL subtypes	No. of patients	Age	EFS, % (year)	OS, % (year)	Reference
AIEOP/BFM	AIEOP-BFM	2000–2006	B-ALL	4016	1–18	80.4 (7)	91.8 (7)	Conter et al. [2]
	ALL 2000		T-ALL	464		75.9 (7)	80.7 (7)	Schrappe et al. [3]
MRC	UKALL 2003	2003–2011	All	3126	1–24	87.2 (5)	91.5 (5)	Vora et al. [5]
			B-ALL	2731		–	–	
			T-ALL	388		–	–	
DCOG	DCOG Protocol	1997–2004	All	859	1–18	81 (5)	86 (5)	Veerman et al. [5]
	ALL-9		B-ALL	701		82 (5)	–	
			T-ALL	90		72 (5)	–	
EORTC-CLG	EORTC CLG	1998–2008	All	1947	1–18	82.7 (5)	89.7 (5)	Domenech et al. [6]
	58591		B-ALL	1650		–	–	
			T-ALL	296		–	–	
NOPHO	ALL-2000	2002–2007	All	1023	1–15	79 (5)	89 (5)	Schmiegelow et al. [7]
			B-ALL	906		–	–	
			T-ALL	115		–	–	
COG	Various CCG,	2000–2005	All	7153	0–22	–	90.4 (5)	Hunger et al. [8]
	POG, and COG		B-ALL	5982		–	91.1 (5)	
	trials		T-ALL	459		–	81.6 (5)	
SJCRH	Total therapy	2000–2007	All	498	1–18	85.6 (5)	93.5 (5)	Pui et al. [9]
	XV		B-ALL	422		86.9 (5)	94.6 (5)	
			T-ALL	76		78.4 (5)	87.6 (5)	

Case 2

1-year-old Pakistani boy

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* Hemoglobin (Hgb) 8.5 L g/dL (11.1 - 14.1)
* Hematocrit (PCV) 27.40 L % (30 – 40)
* RBC Count 4.83 X10^6/uL (4.1 - 5.3)
* MCV 56.70 L fl (68 – 84)
* MCH 17.60 L pg (24 – 30)
* MCHC 31.00 g/dL (30 – 36)
* RDW 21.20 H % (11.6 – 14)
* Platelet Count 356.00 X10^3 / LL (200 – 550)
* WBC Count 6.28 X10^3 / LL (6 – 18)

Iron treatment given.

CBC result after iron treatment

* Iron, Serum 7.43 Lmol/L (4.7 - 19.7)
* Transferrin Saturation, Serum, Calculated 11.00 L % (20 – 50)
* Ferritin Serum 14.04 Lg/L (14 – 152)
* Unsaturated Iron Binding Capacity, (UIBC), serum 58.40 Lmol/L (22.3 - 61.7)

* Hemoglobin (Hgb) 8.8 L g/dL (11.1 - 14.1)
* Hematocrit (PCV) 29.10 L % (30 – 38)
* RBC Count 5.56 H X10^6/uL (3.9 - 5.1)
* MCV 52.30 L fl (72 – 84)
* MCH 15.80 L pg (25 – 29)
* MCHC 30.20 L g/dL (32 – 36)
* RDW 21.30 H % (11.6 – 14)
* Platelet Count 564.00 H x 10^9 /L (200 – 550)

* Hemoglobin A 88.6 L % (94.3 – 98)
* Hemoglobin A2 5.5 H % (1.5 - 3.5)
* Hemoglobin F 5.9 H % (0 – 2)
* Hemoglobin S 0.0 % (0 – 0)
* Hemoglobin D 0.0 % (0 – 0)
* Hemoglobin C 0.0 % (0 – 0)

Interpretation?

Hemoglobin pattern and concentrations are consistent

with BETA THALASSEMIA TRAIT.

MOLECULAR BIOLOGY

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BETA THALASSEMIA MUTATION DETECTION.

BETA THALASSEMIA codon 8/9 [+G] (c.27_28insG) heterozygous

Case 3

2 years old Filipino boy
2 courses of Iron treatment and history of iron treatment with mother

* Hemoglobin (Hgb) 10.1 L g/dL (11.1 - 14.1)
* Hematocrit (PCV) 34.80 % (30 – 38)
* RBC Count 5.56 H X10^6/uL (3.9 - 5.1
* MCV 62.60 L fl (72 – 84)
* MCH 19.40 L pg (25 – 29)
* MCHC 31.00 L g/dL (32 – 36)
* RDW 15.50 H % (11.6 – 14)
* Platelet Count 358.00 x 10^9 /L (200 – 550)
* WBC Count 10.98 X10^3 / LL (6 – 16)

* Iron, Serum 12.06 Lmol/L (5.2 - 16.3)
* Transferrin Saturation, Serum, Calculated 24 % (20 – 50)
* Ferritin Serum 49.84 Lg/L (6 – 67)
* Unsaturated Iron Binding Capacity, (UIBC), serum 38.80 Lmol/L (22.3 - 61.7)

* Hemoglobin A 95.6 % (94.3 – 98)
* Hemoglobin A2 2.6 % (1.5 - 3.5)
* Hemoglobin F 1.8 % (0 – 2)
* Hemoglobin S 0.0 % (0 – 0)
* Hemoglobin D 0.0 % (0 – 0)
* Hemoglobin C 0.0 % (0 – 0)

ALPHA THALASSEMIA PCR RESULT

ALPHA THALASSEMIA DNA PCR SHOWED HETEROZYGOUS ‘SEA’ DELETION DETECTED

Learning point?

* Microcytic hypochromic anemia is not always iron deficiency anemia in the context of UAE, but it could be a thalassemia carrier

Learning point?

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Case 4

14 years old boy
Severe tiredness for few months
Pallor progressive
No organomegaly
No bleeding episodes
No evidence of infections

What investigations you could do at this point?

*

What investigations could you do at this point?

* CBC and peripheral smear
* Reticulocyte
* DCT
* LDH
* LFT
* Iron profile
* Hb electrophoresis

- Hemoglobin (Hgb) 6.2 L g/dL 13 – 17
- Hematocrit (PCV) 24.00 L % 40 – 50
- RBC Count 4.08 L X10^6/uL 4.5 - 5.5
- MCV 58.80 L fl 81 – 99
- MCH 15.20 L pg 27 – 32
- MCHC 25.80 L g/dL 32 – 36
- RDW 28.30 H % 11.6 – 14
- Platelet Count 807.00 H x 10^9 /L 150 – 410
- WBC Count 8.30 X10^3 / LL 4 - 10.5
- WBC Differential normal

What other investigations

* Retic normal.
* DCT negative
* Iron, Serum 2.52 Lmol/L (4.7 - 19.7)
* Transferin Saturation, Serum, Calculated 7.00 L % (20 – 50)
* Ferritin Serum 2.87 L Lg/L (14 – 152)
* Unsaturated Iron Binding Capacity, (UIBC), serum 76.30 H Lmol/L (22.3 - 61.7)

Diagnosis?

* Severe Iron deficiency anemia

Management issues?

* Blood Transfusion?
* Iron Treatment? Oral or IV?

What I did in real scenario

* Oral iron but poor compliance
* Intravenous Iron administration

IV iron better than BT

Transfusion. 2016 Nov;56(11):2720-2726.

Ferric carboxymaltose reduces the number of red blood cell units transfused and allows transfusion independence to be obtained in patients with iron deficiency anemia secondary to gastrointestinal chronic blood loss.

Salvadori U[1], Sandri M[2], Melli C[3]

Author information

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2. Centre for Biomedicine, European Academy Bozen/Bolzano (EURAC), Bozen/Bolzano, Italy.
3. Transfusion Medicine Department, Udine University Hospital, Udine, Italy.

Follow up CBC after 6 weeks

- Hemoglobin (Hgb) 12.1 L g/dL (13 – 17)
- Hematocrit (PCV) 41.80 % (40 – 50)
- RBC Count 5.56 H X10^6/uL (4.5 - 5.5)
- MCV 75.20 L fl (81 – 99)
- MCH 21.80 L pg (27 – 32)
- MCHC 28.90 L g/dL (32 – 36)
- RDW 29.40 H % (11.6 – 14)
- Platelet Count 323.00 x 10^9 /L (150 – 410)
- WBC Count 6.56 X10^3 / LL (4 - 10.5)

Learning Points

* No need of blood transfusion in iron deficiency anemia.
* IV iron is very effective if oral is not tolerating

Case 4

One year old boy
Severe pallor developed in the last two days
Tachycardia
No trauma or no external bleeding

What pathological processes are happening here?

Acute hemolysis leading hemolytic anemia

What are the two differential diagnosis here?

What are the two differential diagnosis here?

1. G6PD deficiency anemia
2. Auto Immune Hemolytic Anemia (AIHA)

What questions you could ask in the history?

What investigations you could do?

What investigations you could do?

* CBC and Peripheral Smear.
* DCT.
* Reticulocyte, LDH, LFT.
* G6PD assay

Hemoglobin (Hgb) 4.0 L g/dL 11.1 - 14.1
Hematocrit (PCV) 12.5 L % 30 - 38
RBC Count 1.37 L X10^6/uL 3.9 - 5.1
MCV 91.2 H fl 72 - 84
MCH 29.2 H pg 25 - 29
MCHC 32.0 g/dL 32 - 36
RDW 16.3 H % 11.6 - 14
Platelet Count 368.00 x 10^9 /L 200 - 550
WBC Count 20.90 H X10^3 / LL 6 - 16

WBC Absolute Count
Neutrophils 11.64 H X10^3 / LL 1 - 7
Lymphocytes 7.04 X10^3 / LL 3.5 - 11
Monocytes 1.89 H X10^3 / LL 0.2 – 1

Direct Coombs Test, Negative

Bilirubin Total, serum 80.4 H Lmol/L 0 - 17
Lactate Dehydrogenase (LDH), Serum 675.0 H U/L 120 – 300

- RBCs are hypochromic microcytic with severe anisopoikilocytosis.
- Many bite cells and spherocytosis are seen on smear. Many polychromatic
  RBCs are seen. Few nucleated RBCs are seen on smear.
- WBCs : Leukocytosis with absolute neutrophilia. No toxic granulations, no left shift. No reactive or atypical cell seen. No premature cell seen.
- Platelets: Adequate on smear; normal morphology.
- Hemoparasite: Not seen.

INTERPRETATION:

Leukocytosis with absolute neutrophilia .
Many bite cells and spherocytosis are seen on smear. Many polychromatic RBCs are seen. Few nucleated RBCs are seen on smear.
Smear findings are suggestive of G6PD deficiency.
Qualitative and quantitative estimation of G6PD is suggested.

G6PD Quantitative, Blood 1.6 L U/gHb
Normal : 6.1 - 20.5
INTERMEDIATE: 2.5 - 6.0
DEFICIENT: < 2.5

Hemoglobin A 95.6 % 94.3 - 98
Hemoglobin A2 2.8 % 1.5 - 3.5
Hemoglobin F 1.6 % 0 - 2
Hemoglobin S 0.0 % 0 - 0
Hemoglobin D 0.0 % 0 - 0
Hemoglobin C 0.0 % 0 - 0

Treatment

Treatment

Blood Transfusion

Follow up investigaiton

Hemoglobin (Hgb) 10.4 L g/dL 11.1 - 14.1
Hematocrit (PCV) 30.40 % 30 - 38
RBC Count 3.53 L X10^6/uL 3.9 - 5.1
MCV 86.10 H fl 72 - 84
MCH 29.50 H pg 25 - 29
MCHC 34.20 g/dL 32 - 36
RDW 15.30 H % 11.6 - 14
Platelet Count 218.00 x 10^9 /L 200 - 550
WBC Count 15.08 X10^3 / LL 6 - 16

Learning point?

Differential diagnosis of severe anemia

Learning point?

Differential diagnosis of severe anemia

severe iron deficiency anemia
anemia due to G6PD deficiency
Autoimmune hemolytic anemia

Summary

- ALL is the most common cancer in children.
- In ALL, currently cure rate is reaching 90%.

* All hypochromic microcytic anemia are not IDA especially in UAE context.
* It could be beta thalassemia carrier
* If electrophoresis is normal, it could be alpha thalassemia carrier.
* Increased RBC is a clue for alpha thalassemia.
* But gene study is a confirmatory for alpha thalassemia.

* In iron deficiency anemia, even if it is very severe, we should avoid blood transfusion.
* IV iron injection is very effective.

* In acute, severe anemia, family history of G6PD and intake of fava beans need to ask.
* Do Direct Coombs test, if positive, it could be AIHA.
* It can be very difficult to manage.
* Discuss with hematologist.

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Thank you

Questions?