“ A rare thing may be just like any other but it is also paradoxically nothing like any of them.”

A RARE ANEMIA WHERE THERE IS PAUCITY AMIDST PLENTY.

Dr.Rena,
DNB Pediatrics Resident,
Dr.Mehta's Children Hospital.

CLINICAL PRESENTATION

HISTORY

- Master V.
- 7month old male infant.
- 2nd born to non-consanguineous parents.

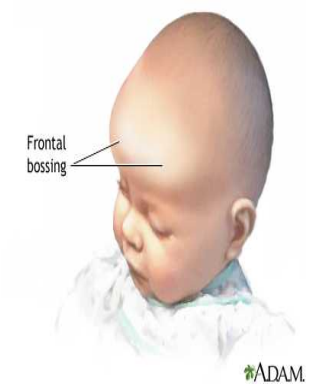
HISTORY(contd..)

H/O progressive pallor and increased pre-cordial activity noted by the mother for the past one month.

No H/O

- Jaundice
- Fever
- Bleeding episodes
- Blood transfusions
- Family history

EXAMINATION

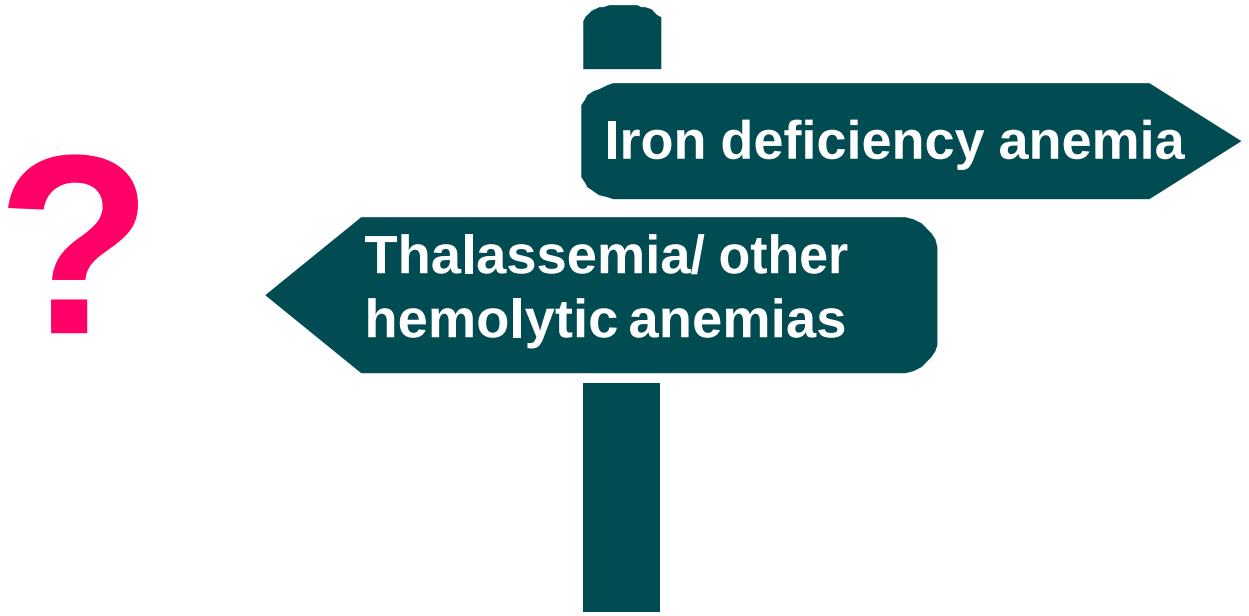


✓ Severe pallor
✓ Frontal bossing
✓ Liver- 3cm below right costal margin, spleen tipped.

NO
Icterus
Cyanosis
Lymphadenopathy

Milestones normal for age
CVS,RS – Normal.

A 7-month old boy + Anemia



Hb (g/dl)	6.3
Total leucocyte count (cells/cumm)	14000
Platelet count (lakh/cumm)	3.41
PCV (%)	21.1
MCV(fl)	55
MCH (pg)	16.3
MCHC (g/dl)	29.7
Reticulocyte count (%)	2.3
Serum iron (ug/dl)	24
Serum ferritin (ng/ml)	1391
TIBC (ug/dl)	299

Anemia

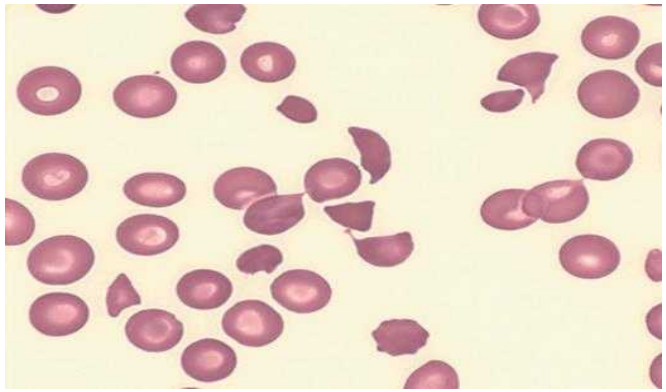
+

Normal serum Iron

Normal TIBC

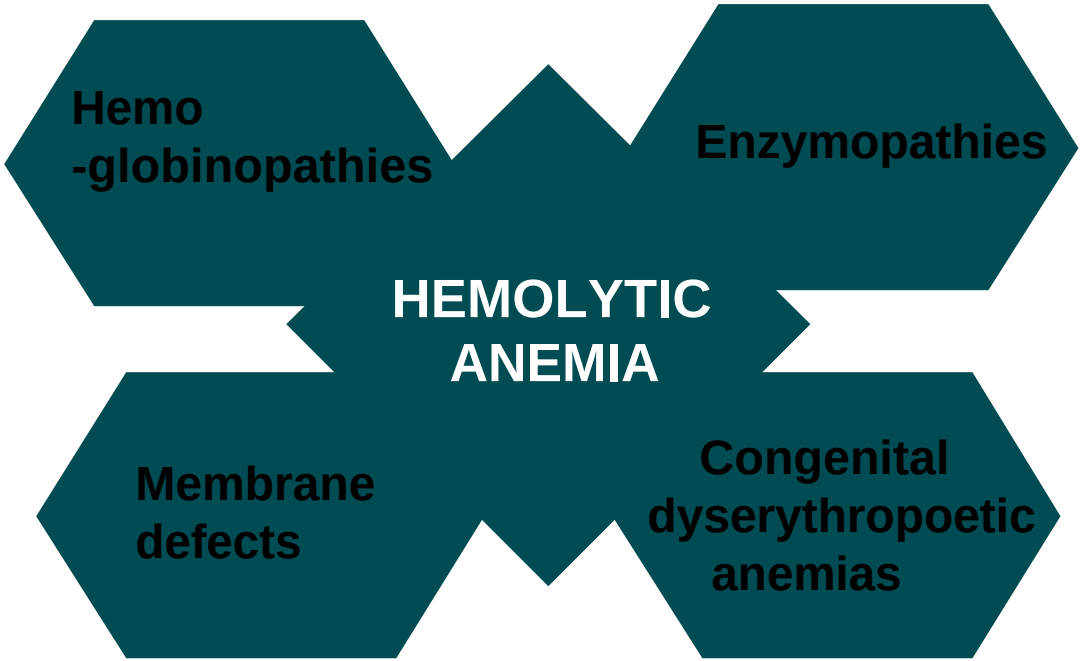
IRON DEFICIENCY ANEMIA

PERIPHERAL SMEAR



- Hypochromic, microcytic RBCs.
- Anisopoikilocytosis, polychromasia.
- Occasional normoblasts.
- Target cells, schistocytes.
- Lymphocytic response.
- Mild thrombocytosis.

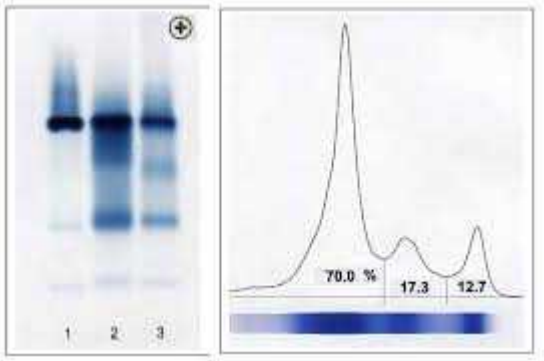
HEMOLYSIS



Lanzkowsky's Manual of Pediatric Hematology and Oncology, 4th edition.

Hb electrophoresis

NORMAL



Thalassemia ickle-cell anemia

OTHER POSSIBILITIES

Other hemolytic anemias:

- Membrane defects.
- ? Enzymopathies.
- ? Congenital dyserythropoetic anemia.

WHAT NEXT?

Hb (g/dl)	6.3
Total leucocyte count (cells/cumm)	14000
Platelet count (lakh/cumm)	3.41
PCV (%)	21.1
MCV(fl)	55
MCH (pg)	16.3
MCHC (g/dl)	29.7
Reticulocyte count (%)	2.3
Serum iron (ug/dl)	24
Serum ferritin (ng/ml)	**1391**
TIBC (ug/dl)	299

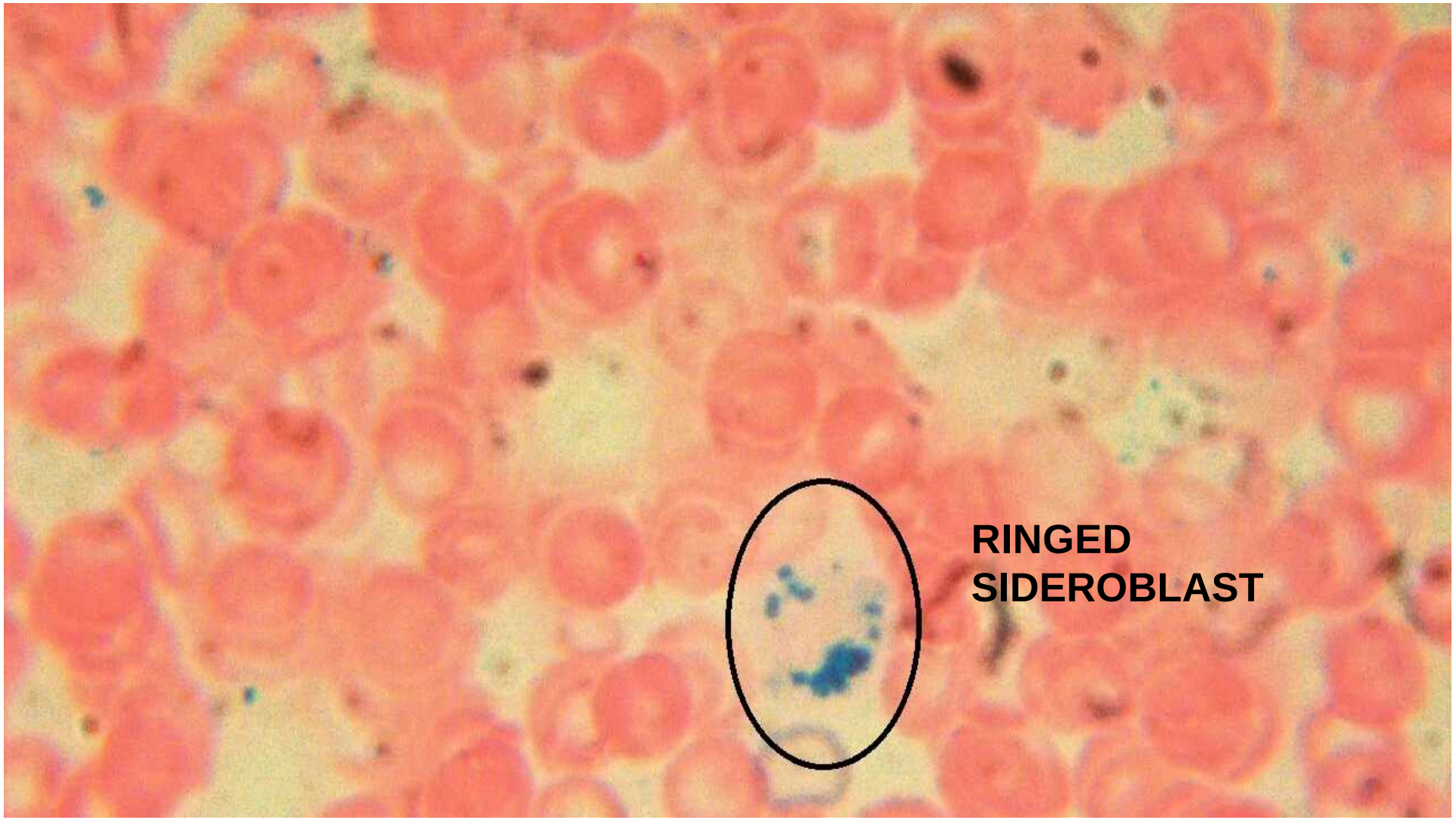
Anemia + Hemolysis + Hyperferritinemia 

? SIDEROBLASTIC ANEMIA

BONE MARROW EXAMINATION

- Normal cellularity.
- M:E ratio = 1:1
- Normoblastic erythroid maturation
- No significant dyserythropoesis.
- Myeloid and megakaryocytic series within normal limits.

Prussian blue staining
- Increased iron stores.
- Presence of ringed sideroblasts in 10% of erythroid precursors.


RINGED
SIDEROBLAST

- A molecular analysis or enzyme levels could not be done.

- A final diagnosis of congenital sideroblastic anemia was suggested.

- Child was started on 50mg oral pyridoxine per day.

FOLLOW UP

	On admission	On follow-up
Hb (g/dl)	**6.2**	**7.8**

There was rise in hemoglobin in the first three weeks of treatment and child is still under follow-up.

DISCUSSION

WHEN TO SUSPECT SIDEROBLASTIC ANEMIA??

- a microcytic, hypochromic anemia with a large RDW and erythrocyte dimorphism.
- mild to moderate hemolysis due to peripheral RBC destruction of unknown etiology.
- ineffective erythropoiesis(i.e,erythroid hyperplasia in bone marrow despite anemia).
- an abundance of ringed sideroblasts, especially in late erythroid precursors (at least 10%).
- a clinical response to high doses of pyridoxine.

- *Nathan and Oski's Hematology and Oncology of Infancy and Childhood,8th edition.*
- *Lanzkowsky's Manual of Pediatric Hematology and Oncology, 4th edition.*

SIDEROBLASTIC ANEMIA

Congenital

Acquired

- Toxins
- Drugs
- Nutritional
- Neoplastic

Nathan and Oski's Hematology and Oncology of Infancy and Childhood,8th edition.

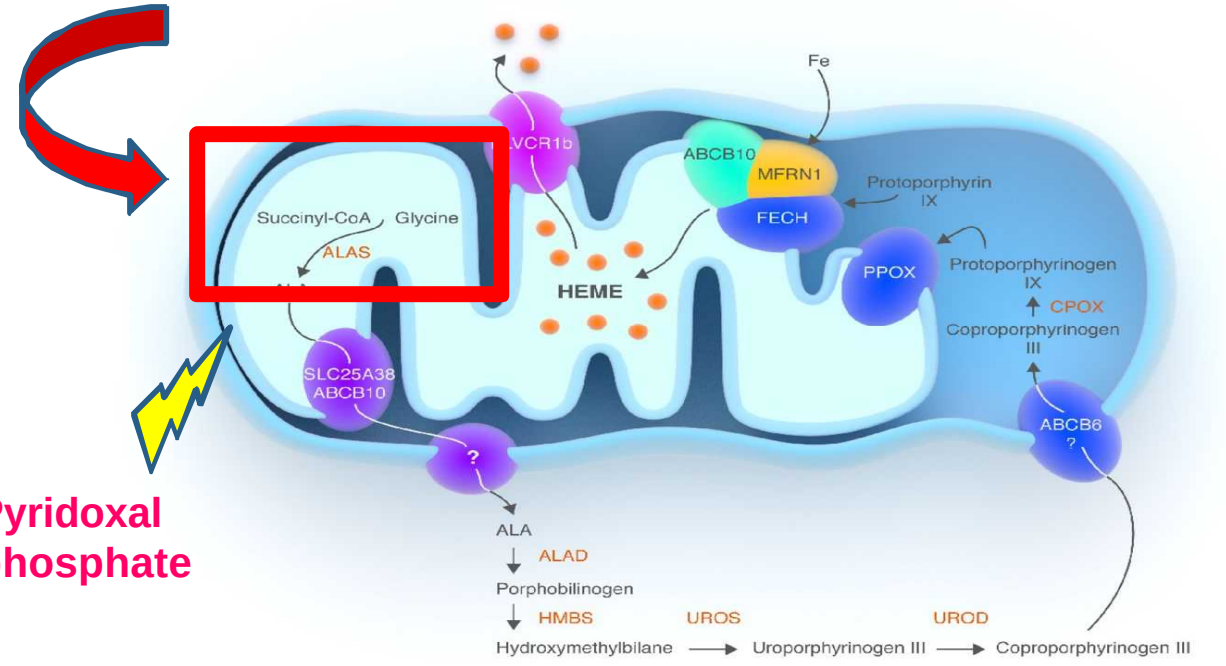
CONGENITAL SIDEROBLASTIC ANEMIA

X-LINKED	AUTOSOMAL RECESSIVE	MATERNAL INHERITANCE
• X-linked sideroblastic anemia. • X-linked sideroblastic anemia with ataxia. **PROTOTYPE**	• Thiamine-responsive Megaloblastic anemia. • Mitochondrial myopathy with lactic acidosis and Sideroblastic anemia-PUS1, YARS2. • SLC25A38. • GLRX5. • SIFD.	• Pearson Marrow-Pancreas Syndrome

▪ *Nathan and Oski's Hematology and Oncology of Infancy and Childhood,8th edition.*
▪ *Mark D.Fleming. Congenital Sideroblastic Anemias : Iron and Heme Lost in Mitochondrial Translation. Hematol 2011; 525-531.*

X-LINKED SIDEROBLASTIC ANEMIA

Erythroid –specific isoform of the enzyme delta-aminolevulinic acid synthase (ALAS2) catalyses the first and regulatory step of heme synthesis in erythroid precursors.



Pyridoxal phosphate

X-LINKED SIDEROBLASTIC ANEMIA(contd..)

- Impaired heme production due to ALAS2 deficiency results in variable degrees of microcytic hypochromic anemia and excess mitochondrial iron manifests as ringed sideroblasts.

- The excess non-heme iron deposited in the cell may act as a toxin resulting in ineffective erythropoiesis.

- Local mitochondrial iron overload is present in all sideroblastic anemias, whereas systemic iron overload occurs only in primary or secondary deficiency of ALAS2.

Gupta SK, Rao S, Kar R, Tyagi S, Pati HP. Congenital sideroblastic anemia: A report of two cases. Indian J Pathol Microbiol 2009; 52(3) : 424-426.

X-LINKED SIDEROBLASTIC ANEMIA(contd..)

Treatment:

- Standard treatment: Pyridoxine 50-100 mg/d with use of higher doses occasionally.

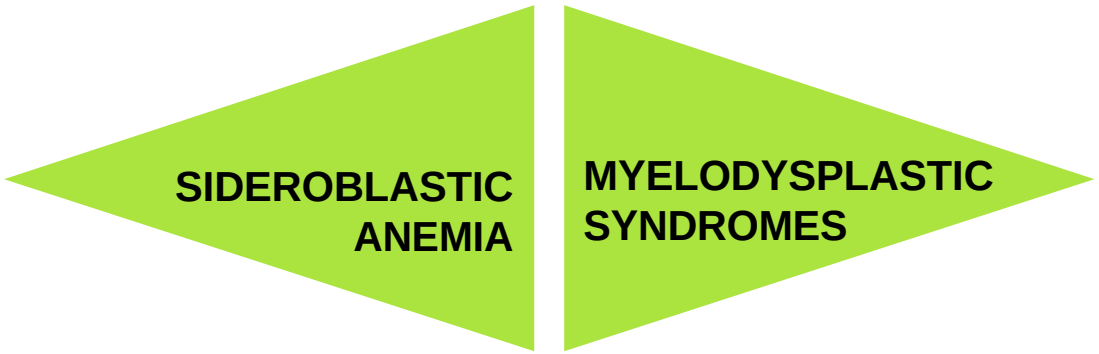
- Maintenance therapy with low dose pyridoxine is advocated for the responders to maintain an adequate pool of pyridoxal phosphate and prevent recurrence of anemia.

- Regular blood transfusion – partial response or not responding.

- Bone marrow transplantation – tried in few cases of severe sideroblastic anemia in children not responding to pyridoxine.

Gupta SK, Rao S, Kar R, Tyagi S, Pati HP. Congenital sideroblastic anemia: A report of two cases. Indian J Pathol Microbiol 2009; 52(3) : 424-426.

RINGED SIDEROBLASTS

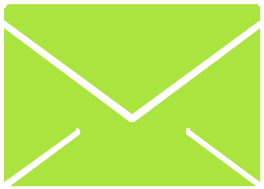


- Porphyrin ring synthesis is unaffected.
- Possible mechanism: mitochondrial respiratory chain defect.
- Unlikely to respond to pyridoxine therapy.

- *Gupta SK, Rao S, Kar R, Tyagi S, Pati HP. Congenital sideroblastic anemia: A report of two cases. Indian J Pathol Microbiol 2009; 52(3) : 424-426.*
- *Cazzola M, Invernizzi R. Ringed sideroblasts and sideroblastic anemias. Haematol 2011; 96(6) : 789-792.*

TAKE HOME MESSAGE

Microcytic hypochromic anemia + non-contributory Hb electrophoresis, serum iron studies, bone marrow examination.



- **Bone marrow for iron stain.**
- **Screening for ringed sideroblasts.**

The early detection of these cases may lead to early institution of pyridoxine which may be therapeutic in many cases and prevent long-term complications of anemia.

CASE REPORTS

Case Report

Congenital sideroblastic anemia: A report of two cases

Sanjeev Kumar Gupta, Seema Rao, Rakhee Kar, Seema Tyagi, Hara Prasad Pati

Department of Hematology, IRCH, All India Institute of Medical Sciences, Ansari Nagar, New Delhi -110 029, India

Address for correspondence:
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Indian Pediatrics

Case Reports

Indian Pediatrics 1999;36: 1158-1161

Congenital Sideroblastic Anemia

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- Dr.Thulasi Raman,Consultant Pathologist, KKCTH.
- Dr.Gnanabalan,Consultant Pediatrician,Dr.Mehta's Children Hospital.

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- Bone Marrow Failure.In : Manual of Pediatric Hematology and Oncology, 4th Edn, Eds, Philip Lanzkowsky , Elsevier Saunders, Philadelphia, 2005; pp 126- 129.

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- Das R, Trehan A, Neelam, Marwaha RK. Congenital Sideroblastic Anemia. Indian Pediatr 1999; 36: 1158-1161.

- Mark D.Fleming. Congenital Sideroblastic Anemias : Iron and Heme Lost in Mitochondrial Translation. Hematol 2011; 525-531.

- Cazzola M, Invernizzi R. Ringed sideroblasts and sideroblastic anemias. Haematol 2011; 96(6) : 789-792.


THANK YOU !