All India Institute of Medical Sciences Rishikesh (AIIMSR)
Department of Paediatrics

Rishi Vansh

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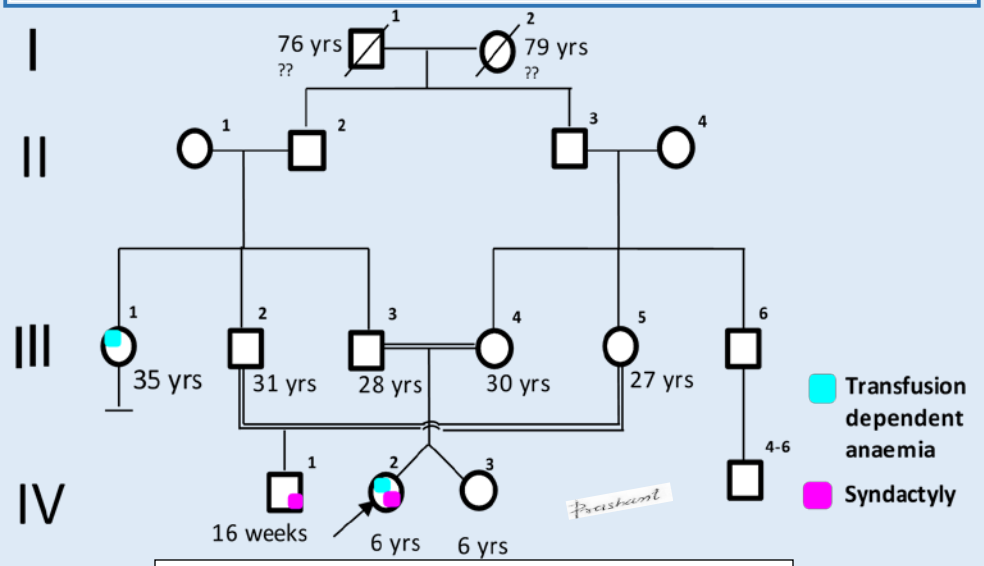
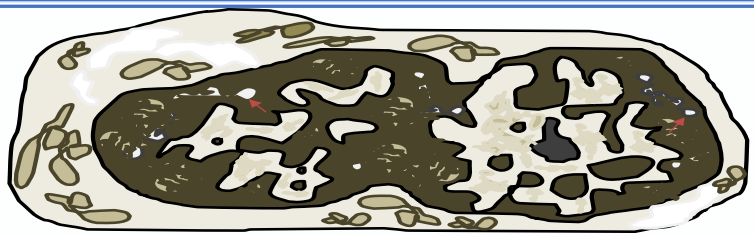
From the desk of Editor

The Department of Paediatrics is publishing a monthly newsletter for faculty and residents. The newsletter is related to genealogical parlance and deliberate attempt to enhance awareness for genetic disorders with recent updates.

Hereditary disorders of RBCs -IV: CONGENITAL DYSERYTHROPOIETIC ANAEMIA(CDA)



Pathognomonic finding in erythroblast of CDA-I



Electron microscopy view with magnification 9 4000

Binuclearity and 'Spongy' or 'Swiss Cheese' heterochromatin with *electron-lucent areas* (*marked with arrow*)

Insight:

1. When to suspect CDA?
2. How does the treatment of CDA differ from thalassemia? What is the role of α-interferon in the management of CDA?
3. What is the genetic heterogeneity of CDA?
4. What are the core differences between CDA type Ia and II?
5. What are the distinctive features in first session counseling for case IV.1?

Plausible tenets:

Genes related to CDA.

Gene	Location	CDA	MOI	Miscellaneous	Other Phenotypes	Functions
CDAN1	**15q15.2**	**Ia**	**AR**	Megaloblastic changes, dysmorphology present		Nuclear envelope integrity
CDIN1	**15q14**	**Ib**	**AR**			Differentiation of erythroid cell
SEC23B	**20p11.23**	**II**	**AR**	**Most common type CDA**, normocytic	**? Cowden syndrome 7**	Part of the coat protein complex II (COPII) for vesicle trafficking
CDAN3	**15q21**	**III**	**AD**	Erythroblastic multinuclearity (Gigantoblasts)		Not known
KLF1	**19p13.13**	**IV**	**AD**	Raised Hb F	**HPFH*, Blood group-Lutheran inhibitor**	Erythrocyte Transcription regulator and repressor

Clinical features:

- Manifest at varying ages, from intrauterine period (hydrops fetalis) to late childhood
- Variable severity of anaemia, jaundice, hepatosplenomegaly, secondary iron load
- 4-14 % of Type I CDA have **acrodysostosis**** (syndactyly, absence of nails, supernumerary toes)

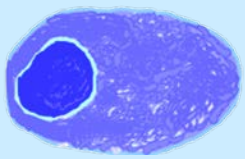
- **Should be a differential diagnosis** in any child with ineffective erythropoiesis & erythroblasts having morphologic evidence of dyserythropoiesis Or **undiagnosed anaemia despite routine workup**
- **Macrocytic anaemia (MCV >90 fl) to Normocytic anaemia with relatively low reticulocyte count for the degree of anaemia**
- **Peripheral smear** (anisocytosis and poikilocytosis), Pseudo-Gaucher cells in Bone marrow (CDA II).
- **Treatment:** Supportive (Blood transfusion), Alpha Interferon (**α-IFN**) to increase Hb & diminishing iron burden, splenectomy (specifically for some cases of CDA II), allogenic bone marrow transplantation (only for **resistant cases to IFN therapy**) & management of complications (Iron overload).

* **Hereditary persistence of fetal hemoglobin * *Acrodysostosis: bone abnormalities, especially in acral part of body (hands & feet)**

Feature	CDA I	CDA II
RBC size	Macrocytic	Normocytic
Severity of anaemia	Less	More
Serological feature*	Absent	Present
Splenectomy	Not indicated	Indicated in few cases
α-IFN response	Yes	No

* Serologic feature: lysis of RBCs with acidified serum. Used to screen for paroxysmal nocturnal hemoglobinuria (PNH)

Pseudo-Gaucher cells



Gaucher-like cells do not show diffuse iron staining & lack typical tubular cytoplasmic inclusions.
Causes: First reported with acute lymphoblastic leukemia, later found in other conditions such as Hodgkin's disease, thalassemia, & disseminated mycobacterial infection, multiple myeloma, myelodysplasia, chronic myeloid leukaemia etc**.**

Genetic Counselling for case IV.1 for diagnosis: presence of consanguinity, positive family history & acrodysostosis

- **Needs workup for inapparent features especially hematological & radiological.**
- **Review lab investigations of IV.2 and III.1 cases to find out the proband phenotype & diagnosis.**
- **Symptomatic management**
- **Routine care for neonate & awareness of warning signs.**

Thought Riveting:

- ***How encouraging is research based on -induced pluripotent stem cells (iPSCs), in comprehending the disease mechanism in vivo?***
- ***Can "hepcidin hormone therapy" be used to reduce iron absorption from gut?***
- ***Why Stem cell transplantation is not equally successful for CDA as is for thalassemia?***
- ***How useful can be "Selective histone chaperones" in purview of cancer therapy?***
- ***What are the possible functional interactions between the genes responsible for CDA?***
- ***How does Alpha Interferon (α-IFN) increase Hb in CDA I-thinkable molecular mechanism?***

Authros: Dr. Prashant Kumar Verma, Dr. Vinod Kumar
Reviewer: Dr. Raksha Ranjan