A RARE CONGENITAL ANAEMIA

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ABSTRACT: Anemia in children may arise from a wide variety of pathogenetic mechanisms that include congenital and acquired disorders. Often the diagnostic considerations include disorders that are not seen commonly in adults and lifelong disorders that arise in children and persist throughout life. Consideration of diverse causes of anemia such as red cell membrane disorders, red cell enzymopathies, congenital dyserythropoietic anemias, congenital sideroblastic anemias, and hereditary pure red cell aplasia (Diamond-Blackfan anemia), as well as infectious causes such as parvovirus B19 infection, often is required when diagnosing anemia in an infant or young child. Knowledge of these entities that are important causes of anemia in the pediatric population, including clinical manifestations and laboratory workup, will aid in recognition of the specific disease entities and effective workup of pediatric red cell disorders. Inherited and acquired red cell disorders in children include a diverse group of disorders that include red cell enzyme disorders, red cell membrane disorders, congenital dyserythropoietic anemia, sideroblastic anemia, hemoglobinopathies, and red cell aplasias. Most of these disorders are manifested in the child by anemia with hypoproliferative or hemolytic mechanisms underpinning the development of anemia. Hypoproliferative anemia arises secondary to decreased overall RBC precursors or ineffective erythropoiesis, suggesting an abnormality in bone marrow production or erythroid precursors. Conversely, the anemia may be hemolytic in nature, reflecting abnormalities in RBC structure or biologic function that affect RBC life span and are associated with normal to increased erythropoiesis. Clinical manifestations, RBC characteristics, specific laboratory testing, and bone marrow findings are all useful in trying to classify the cause of the anemia and define a specific disease process.

INTRODUCTION: Pure red cell aplasia (PRCA) is an uncommon disorder in which maturation arrest occurs in the formation of erythrocytes. Erythroblasts are virtually absent in bone marrow; however, WBC and platelet production is normal. The anemia due to PRCA is usually normocytic but can be macrocytic. In 1922, Kaznelson recognized that this condition was a different entity from aplastic anaemia, which presents with pancytopenia. The characteristics of PRCA include a severe anemia, a reticulocyte count of less than 1%, and the presence of less than 0.5% mature erythroblasts in the bone marrow. The bone marrow is usually normocellular. The etiology of PRCA is heterogeneous. A congenital form of PRCA was initially described by Joseph in 1936 and by Diamond and Blackfan in 1938. Congenital PRCA is a lifelong disorder and is associated with physical abnormalities.

PRCA can be transient and reversible. Transient erythroblastopenia of childhood (TEC) can occur after viral infections. PRCA due to medications is also often reversible when these medications are discontinued. PRCA due to infections is often reversible. In adults, most cases of chronic PRCA are idiopathic, and a cause cannot be established. Secondary PRCA occurs in patients with conditions such as autoimmune disorders, thymomas, hematologic malignancies,

and solid tumors. The life expectancy of patients with idiopathic PRCA is about 1-2 decades. The survival of patients with congenital PRCA is limited. The lifespan of patients with secondary PRCA depends on the course of the underlying disorder.

Most cases are sporadic, although dominant or recessive patterns of inheritance are indicated by familial occurrence in ≈15% of patients. The primary defects are in the erythroid progenitor cells, where there is an intrinsic defect that results in increased apoptosis (programmed cell death). High levels of erythropoietin (EPO) are present in serum and urine, although a search for mutations in the EPO receptor gene has been negative.

In about 25% of sporadic and inherited cases mutations are seen in a gene (DBA1) for a ribosomal protein S19, mapped to chromosome 19q13. A second gene for Diamond-Blackfan anemia has been linked to chromosome 8p, and most likely other genetic abnormalities will be identified.

CASE STUDY: A 2 yr old male child was admitted with c/o severe pallor & breathlessness since 45 days of life .Investigation showed severe anaemia with neutropenia & was transfused twice with 2 months interval. Currently had come with increased pallor & breathlessness since past one month & facial puffiness since past 8 days.

h/o repeated lower respiratory tract infections.
No h/o petechiae/purpura/rash.
No h/o joints pain / swelling.
No h/o yellowish discoloration of sclera or urine.
Birth/Family History:
Full term LSCS at hospital in view of breech presentation
Cried immediately after birth
Birth wt-2.25 kg
No h/o NICU stay.
Development History: Normal for age & sex.
Immunization: BCG, OPV-all doses, DPT-all doses given.
Growth: Length-62 cms (3rd – 5th centile),
Wt- 6.2 kg (3rd-50th centile),
HC- 40 cms (3rd centile)
ON examination: Unconscious, lethargic, altered sensorium, febrile
HR- 146 b/m
BP- 60/35 mm of Hg , RR-36 cpm
CRT-> 3 sec
AF- closed
Pallor- (++)
No icterus/petechiae/ purpura, No knuckle pigmentation.
Dysmorphic Features: Large ears, depressed nasal bridge
No neurocutaneous markers.
S/E- Liver 5 cms, below Rt costal margin, soft, non tender.
Intervention - cardioprotective resuscitation was done.

Immediately IV volume expanders like NS bolus was given, epinephrine (1: 10,000) – 0.1 ml/kg was given, until the heart rate was stabilized. IV Sod. bicarb 2 mEq/ kg was given to prevent acidosis. Child was put on ventilator for respiratory support.

After stabilization child was transfused whole blood at a volume of 20 ml/kg after giving 1 mg /kg of furosemide.

Child has been transfused 8 times till now & receiving oral prednisolone 5 mg BD.

BLOOD REPORTS:

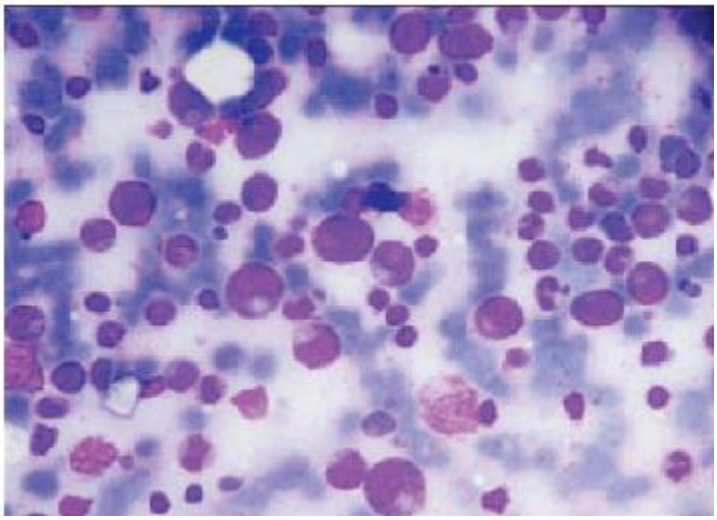
CBC done at subsequent intervals

WBC Count (Cells /cu mm)	2900	4100	6200	10700	8800	8700
RBC Count (Millions/cu mm)		2.96	2.54			1.55
HGB (Gr %)	5.10	8.9	7.3	8.6	2.34	4.8
HCT (%)		25.2	22.8	24.0	22.8	15
MCV (fl)	79	85.2	90.1	78.9	97.4	97
MCH (pg)	27	30.0	28.7	28.3	32.1	31
MCHC (g/dl)	34	35.3	32.0	35.8	32.9	31
Platelet count (Lacs)	2.7	1.54	3.98	3.95	3.97	4.23
Diff.count (WBC)						
Neutrophils (%)	03	36	70	42	65	40
Lymphocytes (%)	96	59	26	52	24	51
Eosinophils (%)	00	05	04	02	05	04
Monocytes (%)	01	00	00	04	01	05
Basophils (%)	00	00	00	00	01	00

Blood group- B positive

PERIPHERAL SMEAR REPORT

Normocytic normochromic, mild anisocytosis, leucopenia, neutropenia with adequate platelets

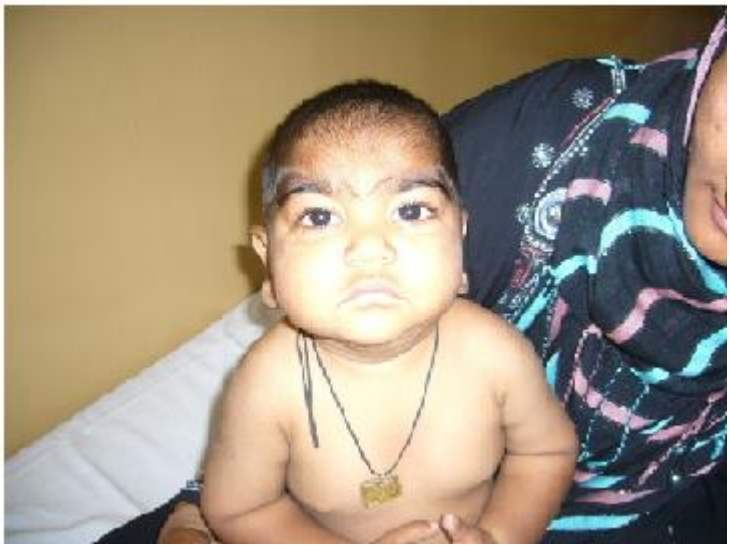


BONE MARROW STUDY:

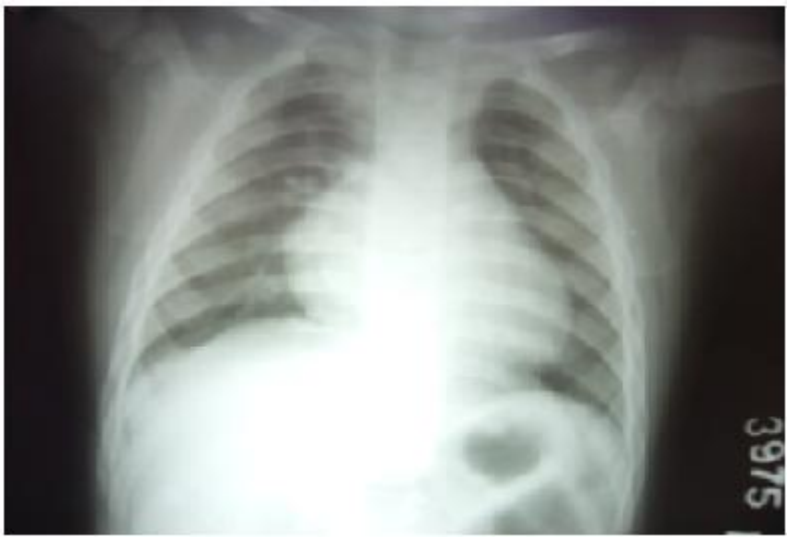
Cellularity	: Low cellularity
M: E ratio	: Increased 7:1
Erythroid Series	: Erythroid series hypoplasia, few colonies of normoblasts
Myeloid Series	: Few granulocytes, few myelocytes, few metamyelocytes.
Megakaryocytes	: Normal in distribution.
Impression	: Hypocellular marrow with erythroid hypoplasia, consistent With Red cell Aplasia.

OTHER TESTS:

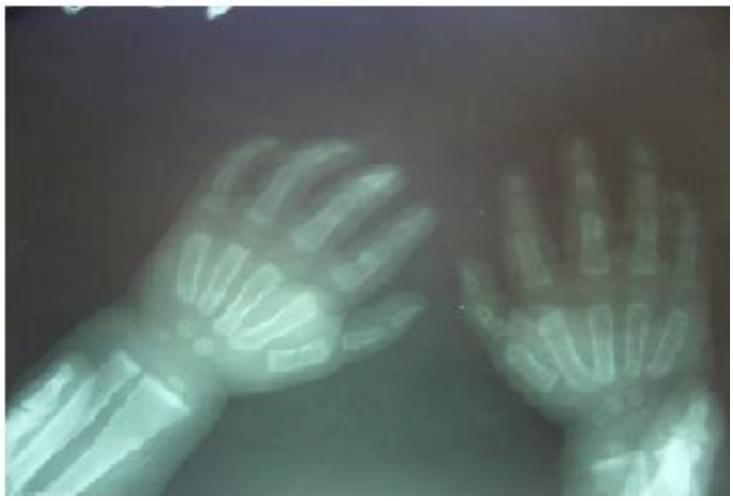
HIV- negative
HBsAg- negative
Hb electrophoresis- Increased Hbf.
Direct coombs test – negative.
Parvo virus B 19 – negative.
Blood culture- MRSA sensitive to erythromycin, vancomycin, teicoplanin, clindamycin, tetracycline, rifampicin, linezolid.
Sr.Iron –240 microgm/ dl (normal- 50 to 160 microgm/dl)
Sr.Folic Acid (Done by CLIA, Abbott) -- > 20 nanogm /ml (normal -2.52 to 17.56)
Sr.Vit B12- (Done by CLIA, Abbott) --109.00 pg/ml (normal- 198 to 883 pg/ml)
Child was transfused 8 times whole blood till now & receiving oral prednisolone 5 mg BD.



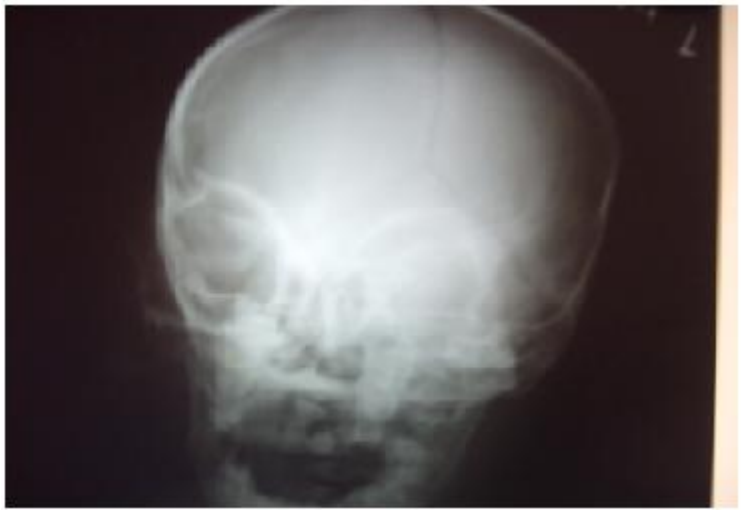
Large ears, depressed nasal Bridge with steroid faces.



CHEST X RAY PA VIEW



X RAY OF BOTH HANDS



X RAY SKULL

DISCUSSION: Diamond-Blackfan anemia is a disorder of the bone marrow. The major function of bone marrow is to produce new blood cells. In Diamond-Blackfan anemia, the bone marrow malfunctions and fails to make enough red blood cells, which carry oxygen to the body's tissues. The resulting shortage of red blood cells (anemia) usually becomes apparent during the first year of life. Symptoms of anemia include fatigue, weakness, and an abnormally pale appearance (pallor).

Although relatively uncommon, inherited red cell disorders must be considered as possible causes for anemia in a child or an infant. Also in the differential diagnostic considerations will be acquired causes of anemia that can be seen in adult and pediatric populations. Careful examination of RBC morphologic features, laboratory findings, and bone marrow morphologic features, as well a correlation with clinical features, often allows for a definitive diagnosis to be made.

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