CASE PRESENTATION

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PERSONAL PROFILE

NAME : Sumairra

AGE : 12yrs

SEX : Female

ADDRESS : Azad Kashmir

DATE OF ADMISSION : 28TH Feb 2007
PRESENTING COMPLAINTS

1. Progressive pallor ................ 3 months
2. Bruises .................................. 1 week
3. Epistaxis.......................... 1 day
HISTORY OF PRESENT ILLNESS

Perfectly well 3 months back

- Progressive Pallor ............... 3 months
- Bruises over arms & legs... 1 week
- Epistaxis..... 1 day
- No h/o bleeding from any other site
SYSTEMIC REVIEW

• **Respiratory System**: No wheezing, sore throat, recurrent chest infections.

• **GIT**: No history of abdominal pain, diarrhea, constipation, abdominal distention, jaundice, hematemesis, malena.

• **CVS**: No dyspnea, or edema feet.

• **CNS**: No history of fits, paresis or paralysis
PAST HISTORY & TREATMENT HISTORY

➢ No past H/O any significant illness

➢ No significant treatment history
BIRTH & DEVELOPMENTAL HISTORY:

- SVD / Home Delivered / No perinatal complications.
- Developmentally Normal
IMMUNIZATION HISTORY

• Vaccinated
• BCG scar present
FAMILY HISTORY

- Product of consanguineous marriage

- No history of contact with TB
SOCIOECONOMIC HISTORY

• Low socioeconomic group
EXAMINATION

- A young girl, markedly pale, conscious & cooperative, in no obvious cardiopulmonary distress

- Vitals
  - H/R ............ 90 / min
  - R/R ............ 23 / min
  - Temp .......... 98 F
  - B.P ................. 100 / 60 mmHg(50\textsuperscript{TH} centile)
• Anthropometric measures:
  - **Height**.....146cm (25\textsuperscript{th} centile)
  - **Weight**....32 kg (10\textsuperscript{th} centile)
  - **Head Circumference**.... 53cm (50\textsuperscript{th} centile)
- Multiple petechiae & bruises over arms & legs
- Hyperpigmented tongue & lips
- No jaundice, clubbing, cervical & axillary lymphadenopathy, pedal / sacral edema
SYSTEMIC EXAMINATION
• **GIT**: Soft abdomen, no hepatosplenomegaly

• **RESPIRATORY SYSTEM**: B/L vesicular breathing with no added sound

• **CVS**: S1 + S2 + no added sound

• **CNS**: Intact
SUMMARY:

Sumaira, 12 yrs old FC, a product of consanguineous marriage, developmentally normal & vaccinated, admitted with 3 months H/O progressive pallor, 1 wk H/O bruises over arms & legs & 1 day H/O epistaxis. Has 2 siblings with similar complaints. O/E markedly pale having multiple petechiae & bruises over arms & legs. There were hyperpigmented lips & tongue. Rest of the systemic examination was normal.
DIFFERENTIAL DIAGNOSIS

- Constitutional pancytopenias
- Acquired aplastic anemia
- Acute leukemia
- ITP
INVESTIGATIONS

• **BLOOD COMPLETE PICTURE:**
  - Hb .......... 3.5 gm / dl
  - RBC Count.........0.98X10^9 / L
  - TLC....... 2.1 X10^9 / L
  - Platelets ......12 x 10^9 / L
  - Retics..........0.5%
  - MCV.......................100.6fL
  - MCH........................30.6pg

• **RBC MORPHOLOGY:**
  - Macrocytosis+
  - Poikilocytosis+
  - Anisocytosis+
  - Occasional target cells
• **PT/APTT:** Normal

• **RFTS:**
  - Urea ....................... 2mg/dl
  - Creatinine .......... 0.9mg/dl
  - Uric acid .......... 2.1mg/dl

• **LFTS:**
  - Total bilirubin ........ 0.8mg/dl
  - ALT ......................... 41U/L
  - Alk. phosphatase ....... 477u/l

• **ELECTROLYTES:**
  - Na ................. 135 meq / L
  - K ................. 3.9 meq / L
• **BONE MARROW BIOPSY:**
  
  Hypocellular marrow

• **BONE MARROW TREPHINE BIOPSY:**

  ▪ Hypocellular marrow
  ▪ Markedly decreased Megakaryocytes
  ▪ Depressed Erythropoisis & Myelopoisis
  ▪ Prominent plasma cells, lymphocytes & histiocytes
  ▪ Unremarkable fibrosis

**OPINION:**

▪ Findings consistent with Aplastic Anemia
**CYTOGENETIC STUDIES:**

- Blood cultures were subjected to clastogenic stress by Mitomycin C.

- In 60% of metaphases chromosomal aberrations such as chromatid breaks & exchanges were detected.

**Opinion:**

Female karyotype positive for Fanconi’s anemia
• **X-RAY HAND & ARM:**
  - Radius present
  - No evidence of hypoplastic thumb

• **USG ABDOMEN:**
  Normal study

• **EYE EXAMINATION:**
  No cataract/Blephritis/Nystagmus

• **HB-ELECTROPHORESIS:**
  - HbA1............96.3%
  - HbF.............1.1%
  - HbA2............2.6%
FINAL DIAGNOSIS

FANCONI ANEMIA
HOSPITAL STAY:

- Admitted for last 3 months
- Received injectable antibiotics for intercurrent respiratory tract infections
- Repeated blood & platelet transfusions
- Vaccinated for HBV
- Androgens (Tab Oxymethalone) started in consultation with pediatric oncologist
- Discontinued after 4 weeks with no response
- Now receiving Tab Cyclosporin for last 1 ½ months as advised by pediatric oncologist
CURRENT PROBLEMS & FURTHER PLAN:

• No response to cyclosporin

• Paediatric oncologist consultation regarding further management

• Option of bone marrow transplantation
PANCYTOPENIAS
Pancytopenias can result from

- failure of production of hematopoietic progenitors,

- their destruction or

- replacement of bone marrow by tumor or fibrosis

leading to varying degrees of anemia, leucopenia, & thrombocytopenia
TYPES OF PANCYTOPENIAS

• Constitutional Pancytopenia

• Acquired pancytopenia
CONSTITUTIONAL PANCYTOPENIA

• DEFINITION:

Pancytopenias arising as a consequence of inherited genetic defects affecting the hematopoietic progenitors.
Constitutional Pancytopenias include:

- Fanconi Anemia
- Dyskeratosis Congenita
- Shwachman-Diamond Syndrome
- Amegakaryocytic Thrombocytopenia
A genetic predisposition to bone marrow failure should be considered in all cases of aplastic anemia in children.
Swiss pediatrician Guido Fanconi, MD, first identified Fanconi anemia in 1927.
EPIDEMIOLOGY:

- A rare heterogeneous disorder;
- can present from birth to 35 yrs of age
- Mean age at presentation 7 ½ yrs
- About 1000 cases described so far
- Male : Female Ratio 1 : 3
INHERITANCE:

- Autosomal Recessive
PATHOPHYSIOLOGY

• Spontaneous / Clastogen induced chromosomal breaks

• Lymphoid, hematopoietic & fibroblast cells demonstrate:
  ▪ Defective DNA Repair
  ▪ Increased susceptibility to oxidative stress
  ▪ Decreased cell survival

• Depressed levels of:
  ▪ GM-CSF
  ▪ Stem Cell Factor
  ▪ Interleukin - 6
TYPES:

- 8 types
- Known as complementation group A to H
CLINICAL PRESENTATION

Most common presentation with

- pancytopenia
- aplastic bone marrow
• Physical abnormalities in 80%

• **SKIN CHANGES (55%):**
  - Hyperpigmentation
  - Cafe’-au-lait Spots

• **SHORT STATURE (51%)**
• **UPPER LIMB ABNORMALITIES (48%)**:  
  - Absent radius or absent or hypoplastic thumbs
• **EYES (23%):**
  - Microphthalmia, strabismus, cataracts, nystagmus

• **RENAL (21%):**
  - **KIDNEY:** Horseshoe, pelvic, hypoplastic
  - **COLLECTING SYSTEM:** Hydronephrosis, hydrourreter, VUR
  - **VASCULATURE:** Abnormal artery

• **GENITALIA (32% males & 3% females):**
  - **MALES:** Undescended testes, delayed puberty, azoospermia
  - **FEMALES:** Hypoplastic vulva, bicornuate uterus, ovarian atresia
• **GIT & CARDIOPULMONARY (11%)**:  
  - Esophageal, duodenal & jejunal atresia, tracheoesophageal fistula, imperforate anus  
  - In heart—structural defects, cardiomyopathy

• **EAR ABNORMALITIES (9%)**:  
  - Structural abnormalities  
  - Hearing loss

• **LOWER LIMBS (8%)**:  
  - Toe syndactyly, abnormal toes, CDH
• OTHER ABNORMALITIES:
  - High arched palate, microcephaly, micrognathia
  - Hydrocephalus, vertebral abnormalities
  - Mental retardation (25%)
• NONE (25%)
• 14 – 25 % patients with cytogenetic abnormalities of fanconi anemia lack the major physical stigmata of disease, the condition referred to as

ESTREN DAMASHEK SYNDROME
DIAGNOSIS:

- Pancytopenia
- Macrocytosis
- Raised Hb F
- Increased expression of I antigen
- Chromosomal fragility in metaphase
PRENATAL DIAGNOSIS:

- The only method of prevention
- Identifies fetus at risk for FA
- If fetus is unaffected, it provides HLA matching for an affected sibling
- Chromosomal Breaks
- Identification of FAC
CHROMOSOMAL BREAKAGE STUDIES:

Metaphase spread from a Fanconi Anemia patient exhibiting multiple chromosomal breaks.

Partial metaphase from a Fanconi Anemia patient showing radial formations when exposed to MMC-stress test.
TREATMENT:

- **SUPPORTIVE:**
  - Blood / platelet transfusions
  - Antibiotics for superadded infections

- **SPECIFIC:**
  - Androgens
    - Oxymethalone
    - Nandrolone
  - Steroids
    - Transient response in 50% cases
    - Relapse common

- Allogenic bone marrow transplant (curative)
Bone marrow transplant

A. Bone marrow

B. Red blood cell
   White blood cell
   Platelets
   Bone marrow is harvested from the iliac crest

C. Bone marrow is filtered

D. Donor marrow
   Transplantation
TREATMENT:

- CLINICAL TRIALS:
  1. Growth Factor Therapy (GM-CSF & G-CSF)
  2. Gene Therapy
  3. Human umbilical cord blood transplantation
COMPLICATIONS

• **Leukemia** (Usually Myeloid) ........ 12%

• **Liver Disease** ........ 4%

• **Other Cancers** ........ 5%

(eg. head & neck, esophageal, GIT, vulvar & anal)
PROGNOSIS

• Poor

• Spontaneous Remission very rare

• Mean survival age 30 yrs
THANK YOU