



## Fanconi Anemia - A Rare Case Report

Deepak Sharma\* and Rakesh Sharma

Department of Pediatrics, Maharishi Markandeshwar Medical College and Hospital, India

### Abstract

**Background:** Fanconi Anemia, though rare, is the most common form of constitutional aplastic anemia with an autosomal recessive (except one x linkage) inheritance that results from defects in genes with 16 complementation groups that modulate the stability of the DNA characterized by diverse congenital malformations, progressive pancytopenia, and predisposition to both hematological malignancy and solid tumors. Congenital malformation varies from patient to patient and may affect the skeletal system as well as organ systems. With an incidence of 1 to 5 per million, a highly variable phenotypic presentation with clinical manifestations makes difficult for diagnosis in some cases and Chromosomal Breakage Study induced by MMC (Mitomycin-C)/DEB (Diepoxybutane) provide a unique cellular marker for diagnosis.

**Case Presentation:** In this case report, a 4 year old Asian male child presented with tachypnea, progressive pallor, intermittent fever and non productive cough. He was found to be short stature, underweight for his age and had microcephaly. Café au lait spots were present with absent thumb on the right hand.

**Conclusion:** Peripheral smear showed pancytopenia, bone aspiration was inconclusive due to insufficient particulate matter. X-Ray showed absent radius on right side and USG revealed right sided renal agenesis. Chromosomal Breakage Study was positive.

### Introduction

FA was first described in 1927 by the Swiss Pediatrician, Guido Fanconi. It is a rare, genetically inherited autosomal recessive disorder characterized by congenital malformations, progressive pancytopenia, cellular hypersensitivity to DNA-cross-linking agents, predisposition to Acute Myelogenous Leukemia (AML) and other malignancies [1]. The developmental and physical abnormalities may include hyperpigmentation, short stature, malformations of the thumb and forearms, skeletal anomalies, small head or eyes, renal problems, hearing defect, heart disease, gastrointestinal difficulties and hypogonadism [2,3].

### Case Presentation

A 4 year old Asian male child presented in pediatric emergency with complaints of tachypnea, progressive pallor, intermittent fever and non productive and non paroxysmal cough. He was born of 9 months of intrauterine life and delivered normally. After birth, the developmental milestones are delayed. Antenatally, mother had no specific complaints and was uneventful. He is the only child of his parents. Physical examination revealed patient had short stature as Height for Age (H/A) was below 3<sup>rd</sup> percentile or 2 Standard Deviations. His Weight for Age (W/A) and Head Circumference was also below 3<sup>rd</sup> percentile. He also had a triangular head, flat thenar eminence on the right hand with absent thumb on the same (Figure 1).

Further abdominal USG revealed absence of right kidney. Abdomen also showed outward projection of umbilicus which was not a herniation. Generalized hyperpigmentation with café au lait spots was present (Figure 2). Patient also had developmental delays along with learning disabilities. Peripheral smear revealed pancytopenia with anisocytosis. CBC revealed hemoglobin of 4 gm/dL. The platelet count was 20,000/ $\mu$ L which gradually improved on receiving PRBC and PC transfusions. ANC was decreased. Serum iron studies, B12 and Folic Acid levels were normal. Bone marrow was inconclusive due to hypoplasticity of the marrow. Echocardiography showed the presence of PDA (Figure 3). The blood and urine culture was sterile with normal thyroid profile. LFT and RFT were well within normal range. Patient also had very low oxygen saturation with a high respiratory rate. He was started on inhalation Oxygen.

Systemic examination of the respiratory system revealed crepitations in bilateral lung fields and diffuse rhonchi. X-Ray investigations of the chest showed bilateral infiltrates suggestive of

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#### \*Correspondence:

Deepak Sharma, Department of Pediatrics, Maharishi Markandeshwar Medical College and Hospital, Indira Gandhi Medical College, Himachal Pradesh, India,  
E-mail: [deepak3sharma2001@gmail.com](mailto:deepak3sharma2001@gmail.com)

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Figure 1: Position of right arm. Right hand shows Clinodactyly.



Figure 4: X-Ray of right arm showing hypophalangism with "radial club hand deformity".



Figure 2: Abdomen showing protuberance of umbilicus and Café au lait spots.



Figure 5: Cytogenic findings of a Chromosomal Breakage Study with DEB (Diepoxybutane).

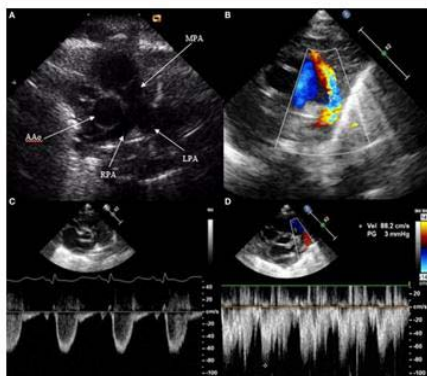


Figure 3: ECHO showing PDA.

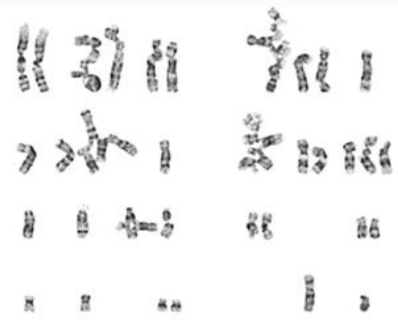


Figure 6: Cytogenic findings of a Chromosomal Breakage Study with MMC (Mitomycin-C).

pneumonia for which the patient was started on IV antibiotics which were soon stopped. Oxygen inhalation was gradually tapered off as respiratory distress improved. X-Ray of right arm showed absent radius bone along with bowing of ulna as well as Clinodactyly of the fingers (Figure 4). Absence of the right thumb is also evident. The left arm was normal. Karyotyping found normal male (46; XY) Cytogenic findings of Chromosomal Breakage Study with MMC and DEB which are DNA cross-linking agents confirmed the diagnosis of FA along with ruling out other differentials like Macrophage Activation Syndrome (Figure 5, 6). Autoimmune disorders were eventually ruled out.

### Discussion

Fanconi Anemia (FA) is a genetically heterogeneous rare autosomal recessive disorder characterized by congenital malformations, hematological problems and predisposition to malignancies.

This case was diagnosed based on physical abnormalities, blood investigations and bone marrow examination. Confirmatory tests are Chromosomal breakage studies where detection of chromosomal aberrations (breaks, rearrangements, radials, exchanges) in cells was done after culture with a DNA interstrand cross-linking agent such as DEB or MMC.

Differentials include:

- 1 Dyskeratosis congenita
- 2 Shwachman-Diamond Syndrome
- 3 Myelocerebellar Disorder
- 4 Congenital megakaryocytic thrombocytopenia
- 5 DNA ligase IV deficiency
- 6 Dubowitz Syndrome

- 7 Nijmegen breakage syndrome
- 8 Reticular dysgenesis
- 9 Bloom syndrome
- 10 Seckel Syndrome
- 11 VACTERL association
  - Vertebral defects
  - Anal atresia
  - Cardiac defects
  - Tracheo-esophageal fistula
  - Renal anomalies
  - Limb abnormalities
- 12 WT syndrome

The complications of fanconi anemia are bone marrow failure, acute myeloid leukemia, myelodysplastic syndromes and solid tumors of the head and neck, skin, gastrointestinal tract and genital tract. FA patients require transfusion red blood cells at frequent intervals [4-6]. Other therapies include androgens to raise the hemoglobin and platelet count, G-CSF and GM-CSF for neutropenia. Definitive treatment includes bone marrow transplant for marrow failure in FA patients. Preventive measures can be taken by prenatal testing and family planning. Prenatal testing includes fetal ultrasonography evaluation, molecular genetic testing by amniocentesis or chorionic villous sampling and chromosomal breakage studies with DEB/MMC. Family planning includes genetic counseling to young adults who are affected, carriers or at risk of being carriers [7].

## Conclusion

It is concluded that genetic study should be done if possible in all the cases of suspected FA, siblings, parents and close blood relatives. The screening of the FANCA gene for mutations supports the clinical diagnosis of FA. Further, it will help to plan appropriate treatment and also to select suitable donor for hematopoietic stem cell transplantation and to plan for genetic counseling. Future studies would clearly advance the current understanding of FANCA regulation and function.

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