



## CASE REPORT

**Rare case of hereditary aplastic anemia [Fanconi anemia]**Agarkhedkar S. R.<sup>1</sup>, Vineeta Pande<sup>2</sup>, Sandeep Kuchi<sup>3\*</sup>, Yojana Sunkoj<sup>4</sup>, P. V. Raghavaiah<sup>5</sup>

Department of Paediatrics, Dr. D.Y.Patil Hospital, Pimpri, Pune, Maharashtra, India.

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**Abstract:** Fanconi anaemia is rare autosomal recessive disease characterized by pancytopenia, varied phenotypic abnormalities, hyperpigmentation and developmental delay<sup>1</sup>. It is diagnosed by Mitomycin C sensitive chromosomal fragility test of blood lymphocytes<sup>2</sup>. We are reporting a rare case of Fanconi anaemia in a 12-year-old child. She has grossly hyperpigmentation over face, tongue, neck, intertriginous area upper and lower limb. Elder sister also had hyperpigmentation all over the body. Peripheral smear revealed macrocytic hypochromic anaemia with few ovalocytes, leukopenia and thrombocytopenia with elevated red blood cell mean corpuscular volume. Fanconi anaemia was diagnosed by doing Mitomycin c stress cytogenetic test for Fanconis anaemia. Hematopoietic stem cell transplantation is the only curative therapy for the hematologic abnormalities in fanconi anaemia<sup>3</sup>.

**Key words:** Fanconi anaemia, Hyperpigmentation, Mitomycin C, Stem cell Transplantation.

**Introduction**

Fanconis anemia is a very rare autosomal recessive disorder, it is characterized by pancytopenia, varied phenotypic anomalies, hyperpigmentation and developmental delay. It is associated with physical developmental anomalies, the common identified anomalies are absent- hypo plastic thumbs, absent radius, microcephaly, Renal anomalies – aplasia, horse shoe kidney, short stature and abnormal skin pigmentations like café-au-lait and hyperpigmentation or occasionally hypo pigmented spots<sup>1</sup>.

Approximately 75% of patients are 3-14 yrs. of age at the time of diagnosis. Patients have abnormal chromosome fragility, which is seen in metaphase preparations of peripheral blood lymphocytes cultured with phytohemagglutinin and enhanced by adding clastogenic agents such as diepoxybutane (DEB) and Mitomycin C<sup>3</sup>. This is associated with an increased susceptibility to leukemia, myelodysplastic syndromes and other malignancies<sup>2</sup>.

**Case Study**

We are reporting a rare case of Fanconi anemia which has incidence of 1 in 3, 50,000. A 12 years old female child brought to our tertiary care center with complains of fever since 8 days, cold and cough since 6 days. Fever was of high grade, intermittent in nature not associated with chills and rigors and subsides after taking medication. Cough was not associated expectoration. Child was hospitalized 4 yrs. ago with complains of fever and not gaining height. Child was then treated symptomatically and discharged. Family history was not significant. Birth history was normal. Child was developmentally normally.

On admission child was having temperature of 101<sup>0</sup>F in right axilla, Pulse rate- 118 b/min, Resp rate- 18 cycles/min, BP- 106/62 mm of hg, SpO<sub>2</sub>- 100%. On examination child was having pallor,

**\*Corresponding Author:**

**Dr. Sandeep Kuchi,**  
Department of paediatrics,  
Dr. D. Y. Patil medical college,  
Pimpri, Pune-411018, Maharastra, India.

Angular stomatitis, Hyperpigmentation of face, tongue, neck, intertriginous area, upper and lower limbs. Hypoplasia of B/L thumbs was present. Elder sister also had complaints of hyperpigmentation all over body. Child was also short for her age. Her intelligence was normal. There were no urinary abnormalities.



Systemic examination-Abdomen was soft & Liver was palpable 3 cm below right coastal margin, liver span-12cm, systolic murmur in pulmonary and tricuspid area. CNS and respiratory system examination didn't reveal any abnormality.

**Lab investigations**

Haemogram showed Hb-5.5gm%, TLC- 2000cells/mm<sup>3</sup>, DLC- P4L90E4M2, ESR-18, platelet- 40,000 cells/mm<sup>3</sup>, reticulocyte count 0.6%, MCV-121.4, MCH-37.9, MCHC-31.3, Peripheral smear- Moderate anisopoikilocytosis, macrocytic Hypochromic anaemia, occasional ovalocytes, tear drop cells and pencil cells. Widal test was negative, Vitamin B12- 254 pg/ml, Sr Ferritin- 199.3, Folic acid >24ng/ml. Sickling and Hb electrophoresis were normal. Ultrasound examination of the abdomen was normal. 2d echo revealed a 5mm ostium secundum with left to right shunt with mild tricuspid regurgitation.

On the basis of pancytopenia and pigmentation all over body and other anomalies of thumb & other investigations turning out to be normal Fanconis anemia was suspected. Bone marrow aspiration showed hypo cellular marrow with fatty infiltration. Bone marrow aspirate was sent for Mitomycin c stress cytogenetic test for Fanconis anemia. In this test results were sensitive to Mitomycin c which was diagnostic of Fanconis Anemia.

### Management

Patient was treated with IV Fluids, Broad spectrum antibiotics covering bacterial, Viral and Fungal organisms. She was given two packed cell transfusions, and 2 platelet transfusions during her hospital stay. Danazol (Androgen) is given for 10 days. She was advised for hematopoietic stem cell transplantation. At the time of discharge her Hemoglobin was 7.2, TLC-2000/mm<sup>3</sup>, Platelet count- 20,000/mm<sup>3</sup>. Patient was admitted twice later with severe pallor she was given two more packed cell transfusion in a span of two months.

### Discussion

Fanconis anemia is a very rare genetic disease with incidence in 1 per 3, 50,000. Absence of radii and thumbs that are hypo plastic, supernumerary, bifid, or absent thumb are common. Anomalies of the feet, congenital hip dislocation, and leg abnormalities are seen<sup>3</sup>.

The diagnosis of Fanconis anemia is made by typical cutaneous, hematological findings and Mitomycin c stress cytogenetic test<sup>2</sup>. Cutaneous manifestations include abnormal skin pigmentation that is café-au-lait and hyperpigmentation or occasionally hypo pigmented spots<sup>1</sup>. The present case had hyperpigmentation over face, neck, and intertriginous area, upper and lower limbs. Hematological manifestations with peripheral smear suggestive of macrocytic hypochromic anemia with leukopenia and thrombocytopenia was seen. The child had short stature and hypoplasia of thumbs. Hence the official diagnosis of Fanconis anemia was made and treated accordingly. Malformation of kidneys in the form of aplasia or horse shoe kidney were described no such findings were found on ultrasound of abdomen. Intelligence is affected in 10% of Fanconi anemia patients. Intelligence in our patient was normal.

A major feature of the phenotype of Fanconi Anaemia is the propensity for cancer. The most frequent solid tumors are squamous cell carcinomas of the head, neck, and upper esophagus, followed by carcinomas of the vulva

and/or anus, cervix, and lower esophagus. Human papilloma virus is suspected in the pathogenesis. As a result of the large number of FANC genes, genetic diagnosis has traditionally been commenced with complementation testing<sup>2</sup>.

Hematopoietic stem cell transplantation is the only curative therapy for the hematologic abnormalities. Patients <10 yrs. old with FA who undergo transplantation using a human leukocyte antigen (HLA)-identical sibling donor have a survival rate >80%. Survival rates are lower for patients >10 yr. old who are undergoing the procedure. Androgens produce a response in 50% of patients, heralded by Reticulocytosis and a rise in hemoglobin within 1-2 months<sup>3</sup>.

For prenatal diagnosis, abnormal chromosome breakage analysis and genetic testing can be performed in amniotic fluid cells or in tissue from a chorionic villus biopsy. Blood counts should be performed every 1-3 months, bone marrow aspiration and biopsy are indicated annually for leukemia and MDS surveillance by means of morphology and cytogenetics<sup>3</sup>.

### Conclusion

FA is a genetic condition that strongly predisposes patients to aplasia, MDS and Acute Myeloid leukemia. Follow-up of FA patients requires a specialized multidisciplinary clinical and biological expertise. To optimize treatment, it is of critical importance to understand the step-wise molecular and cellular mechanisms of the Bone marrow failure and clonal evolution. Hematopoietic stem cell transplantation is the only curative therapy for the hematologic abnormalities.

### References

1. Mahapatra Manoranjan. "Pancytopenia; Fanconi anaemia" de Gruchy's Clinical Haematology in medical practice. 1.6(2013): 116-117. CBS Publishers.
2. Blanche. P *et al.*, "Fanconis anaemia; investigations" guidelines for diagnosis and management of Fanconi anaemia. 1.3(2008):13-14.
3. Yigal Dror and Melvin H. Freedman. "The Inherited Pancytopenia's" Nelson textbook of Paediatrics. 2.20 (2015): 2362-2364. Elseiver Publishers.

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