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Case Report

Fanconi Anaemia - A Rare Case Report with Review of Literature

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ABSTRACT

Fanconi anemia (FA) is rare & most common form of inherited constitutional aplastic anemia. There are currently 15 subtypes, all autosomal recessive except one which is X linked recessive. Incidence of FA is 1 in 350000 births with few cases reported in India. An 8 yr-old female born of consanguineous parents presented with generalized weakness, breathlessness, and fever and physical abnormalities. Patient had short stature, generalized hyperpigmentation with café au lait spots, flat thenar eminence, absent right thumb and rudimentary left thumb, triangular face, microcephaly, hypertelorism, abnormal pinna, low set ears with narrow ear canal, developmental delay, learning disability and wide 1st web space of both feet. Peripheral smear showed pancytopenia, bone marrow aspiration and biopsy showed features of hypoplastic marrow. FA is rare disorder diagnosed with physical abnormalities as detailed above, pancytopenia, bone marrow showing aplastic anemia with history of consanguinity. This case was diagnosed on history, clinical features and haematological findings.

Key words: fanconi, café au lait, aplastic anemia, pancytopenia, consanguinity.

INTRODUCTION

Fanconi Anemia (FA) is rare & most common form of inherited constitutional aplastic anemia. It was initially described in three brothers by Swiss Paediatrician Guido Fanconi in 1927. There are currently 15 known complementation groups, defined by somatic cell hybridization. FA subtypes are - A, B, C, D1, D2, E, F, G, I, J, L, M, N, O and P. All FA subtypes follow an autosomal recessive pattern of inheritance, except subtype B which is X-linked recessive. The mean age at diagnosis is generally reported to be between 7 and 9 years. Fanconi anemia has been reported in all races with global incidence of 1 in 1,60,000 births [1] to 1 in 3,50,000. [2] It is commonly seen among Ashkenazi Jews, South Afrikaners, Sub-Saharan blacks and Spanish gypsies. It is a very rare disease in India with few cases reported.

CASE REPORT

An 8 yr old female child presented with generalized weakness, breathlessness, and fever and physical abnormalities. She was first full term born of consanguineous healthy parents. Antenatally, mother had no specific complaints and was uneventful. Past history of epistaxis and easy bruising was present. Physical examination revealed patient had short stature as Height for Age (H/A) was below 10th percentile as per Indian Association of Pediatrics growth chart. She also had triangular face, microcephaly, hypertelorism, abnormal

pinna, low set ears with narrow ear canal (Figure 1 a,b,c).

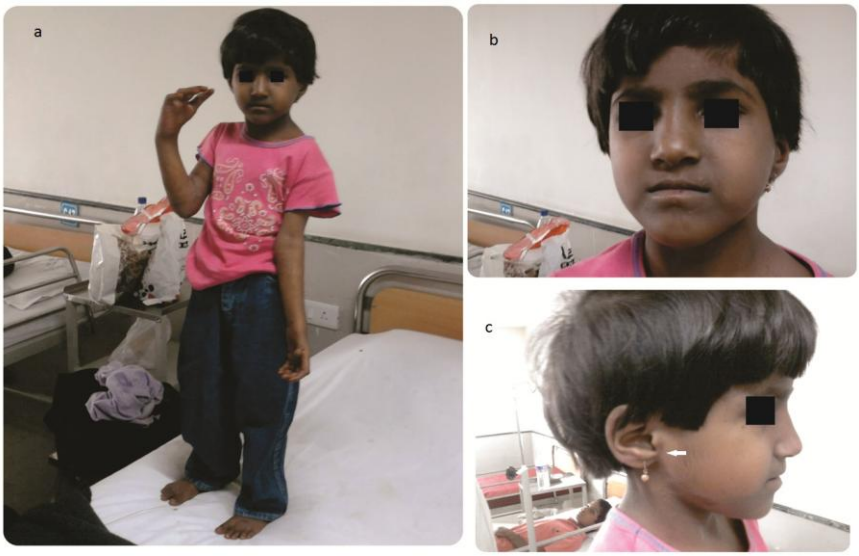

Figure 1 a,b,c - shows patient with short stature, triangular face, microcephaly, hypertelorism, abnormal pinna with low set ears and narrow ear canal.

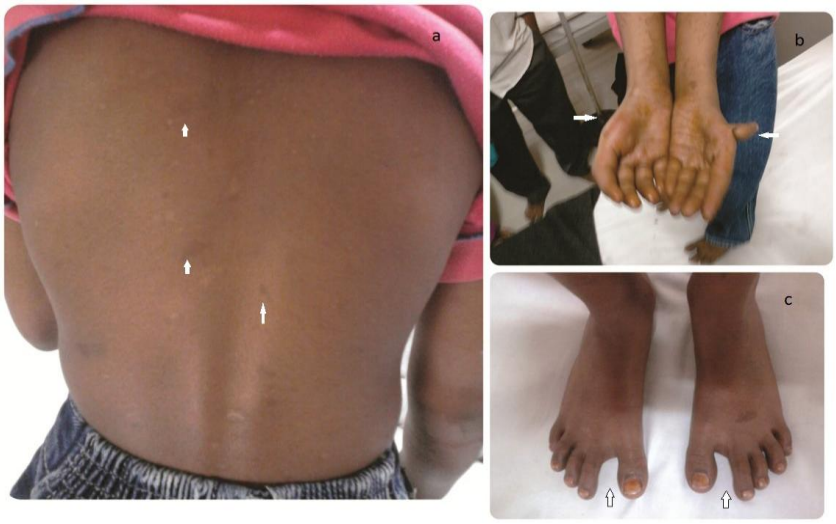

Figure 2 a,b,c - shows generalized hyperpigmentation with café au lait spots, flat thenar eminence, absent right thumb and rudimentary left thumb and wide 1st webspace of both feet.

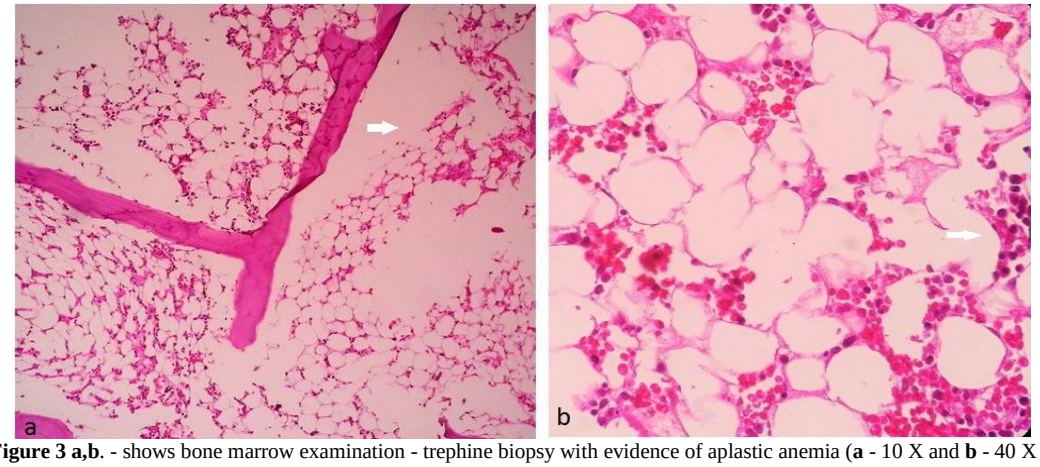

Figure 3 a,b. - shows bone marrow examination - trephine biopsy with evidence of aplastic anemia (**a** - 10 X and **b** - 40 X).

Patient also had generalised hyperpigmentation with café au lait spots, flat thenar eminence, absent right thumb and rudimentary left thumb and wide 1st webspace of both feet (Figure 2 a,b,c).

Patient also had developmental delay and learning disability. Investigations revealed hemoglobin - 5.5 gm%, PCV - 15%, RBC Count - 1.4 million/cumm, Total WBC count- 2400/cumm, Platelet count - 34200/cumm. Liver and renal function tests were within normal limits. Peripheral smear showed pancytopenia. Bone marrow aspiration and marrow biopsy showed hypocellularity with reduced erythroid, myeloid and megakaryocyte series cells suggestive of aplastic anemia. (Figure 3 a,b).

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 is done after culture with a DNA interstrand cross-linking agent such as Diepoxybutane (DEB) or Mitomycin C (MMC). The other tests are cell cycle arrest studies by flow cytometric assessment of G2 arrest, determination of complementation groups based on somatic cell fusion studies and molecular genetic testing to confirm /establish the diagnosis in a proband. [3] Future diagnostic modalities include determining the specific gene mutation which confirms the diagnosis and identifies the genotype.

The differential diagnosis of FA based on clinical and laboratory evaluation includes Dyskeratosis congenita, Shwachman-Diamond syndrome, Myelocerebellar disorder, Congenital amegakaryocytic thrombocytopenia, DNA ligase IV deficiency, Dubowitz syndrome, Nijmegen breakage syndrome, Reticular dysgenesis, Bloom syndrome, Seckel syndrome, VACTERL association and WT syndrome. [4]

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.

The conservative treatment given is packed red blood cells at frequent intervals. 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. [3] The 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. The Department of Health Research, New Delhi (India) in its XII Plan Document (2012-17) has emphasized that studies on genetic diseases would find a priority in new areas like cytogenetic and molecular studies, establishment of national database for genetic disorders, pre-implantation genetic diagnostic facility for intervention, research, genomic and proteomic studies in Fanconi anemia and other diseases. [5]

CONCLUSION

Fanconi anemia is rare disorder in India. Our case was diagnosed based on physical abnormalities as detailed above, pancytopenia on peripheral smear, bone marrow studies showing aplastic anemia with supporting history of consanguinity which is common in South Indian states

like Karnataka, Tamil Nadu and Andhra Pradesh. It was differentiated from other similar diseases based on clinical examination and laboratory evaluation. It is concluded that genetic study should be done if possible in all the cases of suspected FA. Adequate preventive measures must be taken to avoid the risk of FA. It will help us to plan appropriate treatment and also to select suitable donor for hematopoietic stem cell transplantation and to plan for genetic counseling. Registry of Fanconi Anemia in India (REFAIN) maintains the complete details of diagnosed cases of FA in India. General awareness about such organization needs to established and government should take initiatives to support the patients.

ACKNOWLEDGMENT

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