

Fanconi Anaemia associated with café au lait spots: A rare case report

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Abstract

Fanconi Anaemia is an autosomal recessive disorder, which is characterised by progressive pancytopenia, café au lait spots (>50%), bruising, petechiae, recurrent infections, short height (50%), and thumb and radial bone anomalies (40%). Herein, is presented a case of a lean emaciated female child, who presented with the chief complaints of fever, loose stools and decreased appetite for one month reported at Sindh Government General Hospital, Karachi, on February, 1, 2023. She had cutaneous findings of hyperpigmentation and café au lait spots and a tri-phalangeal thumb. On investigation, pancytopenia and a low reticulocyte count of 0.7% was also observed. Karyotype and chromosomal breakage test induced by Diepoxybutane confirmed her as a case of Fanconi Anaemia.

Keywords: Fanconi Anaemia, Complete Blood Count, Diepoxybutane, Frontal-Occipital Circumference, National Institute of Blood Disease and Bone Marrow Transplantation.

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Introduction

Fanconi Anaemia (FA) is an autosomal recessive disorder dictated by mutations in numerous genes involved in the Fanconi Anaemia pathway.¹ This results in a progressive pancytopenic state, heightened cellular sensitivity to DNA-cross-linking agents, congenital anomalies, and an elevated susceptibility to acute myeloid leukaemia and various other malignancies.² As, these genes are responsible for DNA repair during DNA replication, their mutation results in genomic instability. A combination of a variety in genetic and clinical presentations and a prevalence of one in five million, make the diagnosis of FA a challenge.³ Clinical presentation of FA varies from the most common cutaneous manifestations such as café au lait spots (>50%),

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haematological symptoms such as bruising, petechiae, recurrent infections,⁴ short height (50%), thumb and radial bone anomalies (40%) to fewer common manifestations such as auditory, gonadal and renal defects as well as microcephaly and low birth weight.⁵ People born with FA may or may not show signs or symptoms of the condition at birth. For this reason, FA is not always diagnosed at birth. In fact, the median age at diagnosis is seven years.⁶ The tests used to diagnose FA depend on a person's age and symptoms. In all cases, medical and family history is an important diagnosing tool of FA. However, as FA has many of the same signs and symptoms as other diseases, only genetic testing can confirm its diagnosis. The aim of this case report of this potentially fatal genetic disorder is to shed light on the diagnostic approach and management, that requires prenatal screening and genetic counselling of parents.

Case Report

A five-year-old female, weighing 8kg came through OPD to the Paediatrics Ward at Sindh Government General Hospital, Karachi, on February 1, 2023, with the chief complaints of fever, loose stools and decreased appetite for one month. Fever was undocumented, intermittent, and in association with cough, and was unrelieved even on taking antipyretics. There was no history of vomiting and fits. She had five to six episodes of loose stools per day which were watery in consistency, yellowish in colour, and contained no blood or mucus. History of decreased appetite for one month was also reported. She had visited the OPD multiple times due to similar complaints and was prescribed antibiotics and multivitamins. Birth history was unremarkable; she was born via normal vaginal delivery at term with normal birth weight and history of immediate cry. She was a product of non-consanguineous marriage and has three siblings, all of whom are healthy; there is no chronic illness running in the family. Even she had achieved all developmental milestones at appropriate times. She was breastfed up to 2.5 years of age but weaning was started inappropriately from one year of age with tea and biscuits only. Her current diet comprised biscuits, tea, rice, and vegetables only with no egg, fish, or meat in her meals.

Examination showed a thin lean emaciated female child with severe pallor and irritability. Her vitals on arrival were

reported as heart rate: 112 beats/minute, respiratory rate: 40 breaths/minute, temperature 98°F, blood pressure 88/62 mmHg at the (50th centile), and random blood glucose 110mg/dl. Her recorded anthropometric measurements were: height 87cm that was <5th centile of height for her age, weight 8kg, that was <5th centile of weight for her age, frontal-occipital circumference (FOC) 47cm that was <3rd centile of FOC for her age, mid upper arm circumference 10cm that was <-3 standard deviation in WHO Weight-for-Height Reference card; thus, fulfilling the criteria of a severely malnourished child.⁷

Eye examination revealed a black spot present on the sclera of both eyes. She had hair thinning with recession of the hair line from the back, frontal bossing, and depressed nasal bridge without any dysmorphic features. No ulcers, sores, or lesions were present inside or around the mouth. Right anterior cervical lymph nodes were significantly enlarged and were about 2 cm in size, non-tender, mobile, rubbery, and not adherent to the underlying skin. Trachea was centrally placed with bilateral equal air entry and normal vesicular breathing. Heart sounds were normal, without any audible murmurs. Abdominal respiration was present and umbilicus was centrally placed and moving along with respiration. There was no hepatosplenomegaly. She had a Glasgow Coma Scale (GCS) of 15/15 with normal tone and power. Her family history was negative for such symptoms and manifestations. She also had cutaneous findings of prominent vertebral column and rib cage with rachitic rosary, tri-phalangeal thumb, hyperpigmentation over the neck and fingers with café au lait spots over the back and abdomen (Figures 1-2).

Investigations were ordered and on complete blood count (CBC) report, pancytopenia was revealed with haemoglobin- 3.7 g/dl (normal: 12-16g/dl), total leukocyte count $4,000 \times 10^9/L$ (normal: $4,500-11,000 \times 10^9/L$), platelet count $60,000/L$ (normal: $150,000-450,000/10^6/L$), neutrophils 55% (normal 40-60%), lymphocytes 35%

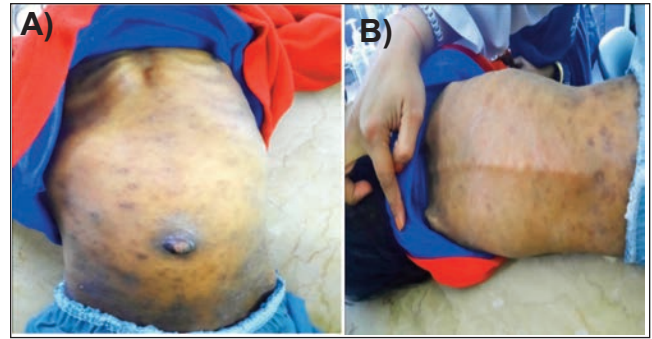


Figure-2: A and B: Prominent vertebral column and rib cage with rachitic rosary and Café Au Lait Spots over the back and abdominal region.

(normal: 20-40%), eosinophil 5% (normal: 1-4%), basophils 5% (normal: 0.5-1%), MCV-104 fl (normal 80-100fl), MCH 27 pg (normal 27-31 pg), MCHC 26 g/dl (normal 32-36 g/dl). A low reticulocyte count of 0.7% (normal 0.5-2.5%) was also observed. Renal function tests and liver enzymes were all normal. Nutritional profile was done and came out to be normal. Repeat CBC revealed a similar picture and she received packed red blood transfusions. Her abdominal and renal ultrasound imaging was normal and echocardiogram findings were unremarkable.

Differential diagnoses of Fanconi Anaemia including nutritional anaemia and acquired aplastic anaemia were made and treatment started with intravenous Ceftriaxone and Paracetamol, oral calcium, folic acid, and zinc. Packed red cells were also transfused. The patient remained in the hospital until her symptoms were resolved and investigations were normalised.

Later, she was referred to National Institute of Blood Diseases and Bone Marrow Transplantation (NIBD), where karyotype and chromosomal breakage test induced by diepoxybutane (DEB) confirmed her as a case of Fanconi Anaemia.



Figure-1: A, B and C: Tri-Phalangeal Thumb and Hyperpigmentation on Neck and Fingers.

Discussion

Fanconi Anaemia is an autosomal recessive disorder characterised by multiple gene mutations; loss of Fanconi Anaemia's pathway¹ leads to genomic instability. This causes progressive pancytopenia, cellular hypersensitivity to DNA-cross-linking agents, congenital abnormalities, propensity to acute myeloid leukaemia and other malignancies.² Infections and cutaneous lesions were common initial findings in multiple case reports by Sharma et al.,³ Qadri et al.,⁴ Alina et al.,⁸ and in our reported case. Consanguinity is considered a major factor in the prevalence of FA and studies^{9,10} have shown that 63-65% of the cases in Pakistan came from consanguineous marriages. However, unlike the case presented by Qadri et al.,⁴ our patient was the child of a non-consanguineous marriage and had no family history of similar clinical presentation or diagnosis but still showed typical symptoms of café au lait spots, short stature, and fifth metacarpal abnormality.⁴ Initial differentials based on laboratory investigations were nutritional deficiency anaemia, acquired aplastic anaemia, and Fanconi Anaemia. Because of such variable presentations of FA, a chromosomal breakage test is necessary for an accurate diagnosis,³ which was performed on the patient confirming FA. An early diagnosis is necessary not only for a better prognosis but to prevent an inappropriate immunosuppressive therapy used in aplastic anaemia, dangerous amounts of chemotherapy or radiotherapy in leukaemia or solid tumours and toxic types of preparation for stem cell transplantation.⁴

Conclusion

In conclusion, this case study highlights the importance of prompt diagnosis and management of rare genetic disorders such as Fanconi Anaemia, which was diagnosed in a five-year-old child presenting with malnourished anthropometric measurements and cutaneous manifestations. Despite the limited published literature on the treatment and course of such disorders, timely intervention is crucial to prevent life-threatening complications. Moreover, comprehensive evaluation and counselling of family members are vital to improve the patient's quality of life and that of their family. This case

serves as a valuable reminder of the significance of early detection and multidisciplinary care in managing rare genetic disorders.

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Author Contribution:

MQ: Concept, design, data acquisition, analysis and interpretation, drafting, critical revision, and final approval.

BAK, VK: Concept, design, data acquisition, analysis, interpretation, final approval.

MA, KA: Drafting, critical revision and final approval.

All authors agree to be accountable for all aspects of the work.