



## Case Report

# Pancytopenia with Hyperpigmentation – Fanconi Anaemia : A Case Report

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### Abstract

Fanconi Anemia (FA) is a rare autosomal recessive disorder associated with pancytopenia, spontaneous chromosomal instability and a variety of congenital anomalies. A variable phenotype and age of onset of anemia makes the diagnosis difficult in some cases. We report a case of Fanconi anemia who had triangular facies, hyperpigmentation, a few café-au-lait spots, microcephaly and short stature. Peripheral blood film showed pancytopenia, bone marrow study revealed aplasia and the patient had history of sibling (elder brother) death from same problem consistent with Fanconi anaemia.

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### Introduction

Fanconi anaemia is an autosomal recessive disease characterized by defective haemopoiesis, congenital abnormalities and a high risk of developing acute myeloid leukaemia and certain solid tumours<sup>1</sup>

It is the commonest type of inherited bone marrow failure syndrome and the incidence of Aplastic anaemia, MDS and AML are all greatly increased in homozygotes. At birth the blood count is usually normal. Pancytopenia typically presents between the ages of 3-14 years. (mean age 8-9 years, range 0-48 years.)<sup>2</sup>

Clinically the patients are presented with Hyperpigmentation of the trunk, neck and intertriginous areas, as well as Café-au-lait spots

and vitiligo, alone or in combination. The affected patients have a Fanconi facies including triangular face microcephaly, small eyes, epicanthic folds and abnormal shape, size or positioning of the ears.

Of the skeletal abnormalities, radial ray defects such as hypoplasia of thumb and radius are most common. Besides these, supernumerary or bifid thumb, congenital hip dislocation, anomalies of feet and leg are also present. Most patients are short statured. LBW is common and median height of Fanconi anaemia patient lies around 5th centile and there may be association of abnormal growth hormone secretion or with hypothyroidism.<sup>3</sup>

Renal abnormalities are present in approximately one third of patient and include unilateral renal aplasia, renal hypoplasia, horse-shoe kidneys or

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double ureters. In males there is a high incidence of genital abnormalities such as hypogenitalia, undescended testis and hypospadias. Females may also have underdeveloped genitalia and uterine anomalies.<sup>4,5</sup> Conductive deafness is also a feature of Fanconi anaemia which can be mild and may or may not be associated with external ear malformations.

We report a case of a short statured child with pancytopenia and hyperpigmentation with positive family history.

### Case report

Rifat, 8 years old boy, 3rd issue of a non-consanguineous parent from Godaghari, Rajshahi admitted in ward-10, RMCH on 28-08-13 with fever for 1 month and generalized weakness and progressive pallor for last 20 days. Fever was intermittent in nature and associated with occasional cough and loose motion. The mother noticed that for the last 20 days the child became easily fatigue after running and walking for 10-15 minutes and gradually unable to perform his daily activities. He has no history of any bleeding episode or bodyache and no history exposure to radiation.

The child was born at term by NVD at home with normal birth weight. He has uneventful antenatal, natal or postnatal history, was exclusively breastfed and immunized according to EPI schedule. His milestones of development were age appropriated. He comes from a middle class socioeconomic condition with healthy parents and a sister. But his elder brother died at 10 years of age due to the same complaints. His mother states that her elder son suffered from progressive pallor and had history of 4 episodes of blood transfusion within 3 months before death. He also had small facies and double thumb on right hand.

On examination, the child was severely pale with hyperpigmentation over face and extremities. He has microphthalmia, low set ears, pulse rate was 120/ minute, blood pressure 100/60 mmHg, temperature 101°F, respiratory rate 20/ minute. On skin survey, there were few Café-au-lait spots over chin, forehead and left leg.

There was no jaundice, oedema, dehydration, palpable lymph nodes, organomegaly or bony deformity. No abnormality was found on systematic and ENT examination.

Anthropometric measurement reveals, weight 18 kg which is below 3rd centile of CDC chart; height 116.5 cm which lies at 3rd centile of CDC chart; OFC 46 cm, weight for age -2.67 SD, height for age - 1.9 SD and weight for height -2.5 SD.

Laboratory investigation showed Haemoglobin 44.2 gm/ L, ESR 30 mm in the 1st hour, Total count of WBC  $3.8 \times 10^9$ / L, polymorph 23%, lymphocyte 68%, monocyte 4%, eosinophil 3% and basophil 2%, total platelet count  $100 \times 10^9$ / L. Peripheral blood film showed features of pancytopenia. Bone marrow study revealed hypocellular marrow, all cell lines diminished with normal myeloid: erythroid ratio. Urine routine microscopy, chest radiograph and abdominal ultrasonogram revealed normal findings.

Although confirmatory test based on chromosomal breakage study using DEB (Diepoxybutane) or MMC (Mitomycin C) could not be performed due to the patient's financial constrains, history, clinical examination and laboratory investigation findings all suggest the patient to be a case of Fanconi anaemia.

After provisional diagnosis, the patient was treated with broad spectrum antibiotic (Inj. ceftriaxone) and 3 episodes of blood transfusion (20 ml/ kg body weight) under coverage of Inj. frusemide at 2 days interval. He was given oral prednisolone (1 mg/ kg/ day) and followed up at 15 days interval. He was improved on follow up evidenced by FBC (Haemoglobin 110 gm/ L, ESR 20 mm in 1st hour, TC  $9 \times 10^9$ / L, TPC  $150 \times 10^9$ / L).

### Discussion

Fanconi anaemia was first described by the Swiss paediatrician Guido Fanconi who described a familial form of aplastic anaemia in three brothers with short stature, hypogonadism and skin pigmentation. Since then, over 900 cases have been reported.<sup>6,7</sup>

The mainstay of diagnosis is based on abnormal haematological findings with characteristic

physical anomaly confirmed by chromosomal breakage study using DEB. No other constitutional pancytopenia is associated with an abnormal chromosomal breakage study.<sup>8</sup>

Our patient has Fanconi face with multiple Café'-au-lait spots and pancytopenia on haematological profile. His height for age is – 1.9 SD. His elder brother died with same type of illness with double thumb. Radial ray defect, endocrine abnormalities and renal complications are absent in this case.

Management depends on the age of presentation and presence or absence of haematological abnormalities. All patients should have haematological assessment, hearing test, ophthalmological assessment, endocrinological assessment in case of growth failure and orthopaedic intervention in skeletal deformity. The family should be referred to a clinical geneticist and other sibs should be examined offering DEB testing.<sup>1AA</sup> progression of marrow failure. Androgens, usually oral oxymethalone once a week, are often used resulting in response in 50% of patients heralded by reticulocytosis and a rise in haemoglobin level within 1-2 months. Low dose oral prednisolone every 2nd day may be added to counteract androgen-induced growth retardation and to prevent thrombocytopenic bleeding by promoting vascular stability.<sup>2,9</sup> The main long-term complication is propensity for cancer and 15% patients may have acute leukaemia or MDS in later life.<sup>10</sup>

### Conclusion

Fanconi anaemia is a highly heterogenous syndrome, homozygotes can present at birth with congenital abnormalities or during childhood with haemopoietic abnormalities. The main causes of morbidity and mortality are aplastic anaemia, myelodysplasia, acute myeloid leukaemia and solid tumours at older ages in those surviving the childhood haematological malignancies.

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