

Fanconi's anemia

Sir,

Fanconi described a fatal disorder in three brothers, that was characterized by pancytopenia, bone marrow hypoplasia and congenital anomalies.^[1] Although rare, the disorder is sufficiently common that an international study group has been established to register clinical experience.^[2] The disorder is characterized by a variable clinical picture consisting of pancytopenia, skeletal abnormalities, neurological and endocrine disorders, chromosomal instability, and an increased risk of leukemia and other tumors.

A seven year-old female child born to nonconsanguineous parents was brought to our out patient department for three year-old pigmentary changes on the trunk and limbs. There was no similar history in the family. General examination revealed gross pallor, while cutaneous examination revealed hypo- and hypopigmented macules 0.1–1 cm in size, distributed on the neck, trunk, and the dorsae of the hands and feet. Axillae, groins and palms and soles were also involved. A single café-au-lait macule was present on the chest. The left thumb showed syndactyly. Hemoglobin (Hb) was 3.5 g%; sickling test was negative while Hb electrophoresis showed the presence of HbA and HbF (15.7%). An X-ray of the left hand showed syndactyly of the left thumb. Ultrasonography of the abdomen showed a mild echogenic center in the liver. Bone marrow biopsy revealed a hypoplastic marrow of moderate degree. Histopathological examination of the skin showed a mild

hyperkeratosis, vacuolation of the basal layer with melanin pigment incontinence. Cytogenetic study of peripheral blood confirmed the diagnosis of Fanconi's anemia which showed a spontaneous chromosomal breakage of 1.37% and mitomycin stress induced chromosomal breakage of 4.52%. The cytogenetic study was done at the Centre for DNA Fingerprinting and Diagnostics, Hyderabad.

Fanconi's anemia is a rare autosomal recessive disorder. Cells from Fanconi's anemia patients are uniquely hypersensitive to the damaging effects of DNA-modifying agents such as diepoxybutane and cyclophosphamide.^[3] Currently, there are 11 known Fanconi's anemia genes.^[4] The usual age of detection of the disease is about seven years but it may also be apparent at birth or the diagnosis may not be established until the 3rd or 4th decade of life. Cutaneous and hematological abnormalities may be the presenting manifestations. There is a generalized dusky or olive brown pigmentation, often most intense in the lower trunk, flexures and on the neck. Raindrop-like, depigmented macules are scattered over the dusky areas of pigmentation;^[5] rarely, café-au-lait macules may be seen. Our case has most of the classical clinical features of Fanconi's anemia such as pigmentary changes, syndactyly and anemia. Affected children are usually slenderly built with short, broad hands and tapering fingers

A constant feature of Fanconi's anemia is progressive hypoplastic anemia with neutropenia and thrombocytopenia. Malformations of various organs are observed. Renal anomalies are seen in 28% of patients of Fanconi's anemia, which include renal aplasia and horseshoe kidney. Microcephaly, mental retardation and hypogonadism are frequent. Some (21%) patients have ocular abnormalities such as strabismus and microphthalmia. Hypogonadism is seen in 20% of all patients. Giampietro *et al*, have also reported four cases of Fanconi's anemia with pigmentary and digital anomalies.^[6] Patients with Fanconi's anemia have a higher incidence of hematological malignancies, particularly nonlymphatic leukemia.

The course is often progressively downhill with death from infection, hemorrhage, or neoplasia. Most patients of Fanconi's anemia respond to corticosteroid therapy. The neutrophil count increases in most patients but the platelet response is less consistent. Patients with Fanconi's anemia need continuous maintenance androgen therapy. Hemopoietic stem cell gene therapy to reintroduce wild type cDNA, is a new concept in the treatment of hereditary diseases and may be applicable in Fanconi's anemia as this disorder can be successfully treated by allogenic stem cell

transplantation. Umbilical cord blood cell transfusion can be an alternative source of hemopoietic stem cells for allogenic transplantation. Morimoto *et al*, have treated a five year-old girl suffering from Fanconi's anemia with umbilical cord blood cell transfusion.^[7]

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