

Fanconi anemia: Case report on rare aplastic anemia

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Abstract

Fanconi anemia is a rare disease which is autosomal recessive in inheritance and characterized by congenital anomalies, defective hematopoiesis and increased risk of development of malignancies like acute myeloid leukemia and myelodysplastic syndrome. The diagnosis is based on the clinical findings of congenital anomalies, hematological abnormalities (pancytopenia, macrocytosis and bone marrow failure) along with genetic studies. Here we present a case of 6 years old girl with the complaints of bleeding from gums and petechiae. Physical and laboratory findings were consistent with fanconi anemia. Confirmation of diagnosis was done by positive Fanconi associated chromosomal breakage studies after culturing with Mitomycin C.

Keywords

anemia; fanconi anemia; acute myeloid leukemia; horseshoe kidney; pancytopenia; hematopoietic stem cells; mitomycin C

Case Report

A 6 years old female child presented to the pediatric department of a tertiary care hospital in Islamabad, Pakistan with the complaints of bleeding from gums and petechiae over the body. The patient was the first born child of a consanguineous marriage born via spontaneous vertex delivery at 37 weeks of gestation .

Physical Examination: On general physical examination child was conscious, alert and well oriented in time, place and person with patches of hyperpigmented areas on skin. She had absent thumbs of both hands (Figure1). Rest of the physical and systemic examination was unremarkable.

Laboratory Investigations:**Table 1:** Showing blood complete picture

Sr. No	Blood CP Parameters	Value	Normal Range
1	Hemoglobin	8.4g/dl	14-18 g/dl
2	Red Cell Count	2.31x10 ⁶ uL	4.1-6.1x10 ⁶ uL
3	White Cell Count	3.7x 10 ³ /uL	4.0-11.0x10 ³ /uL
4	Hematocrit	25.2%	30-40%
5	Platelet Count	72x1000/UL	150-450X1000/UL
6	MCV	109.1fl	70-86fl
7	RDW-CV	18.8%	11.5 -14.5 %
8	Reticulocyte count	1.3%	2-6 %

**Figure 1:** Absent thumb of both hands

Peripheral smear examination: Hypochromic macrocytic picture with mild anisocytosis a, few spherocytes, few codocytes (also known as target cells which are the red cells that have a dark center surrounded by a white ring and another dark outer second ring) and platelets were decreased on smear (Figure 2). Differential leukocyte count revealed 38% neutrophils, 56% lymphocytes, 03% monocytes, 02% myelocytes and 1% eosinophils.

Radiological findings: Ultrasound abdomen and pelvis showed horse shoe kidney with bilateral empty renal fossa (Figure 3).

Bone marrow examination: Bone marrow aspirate and trephine was taken from posterior superior iliac spine which showed hypocellular bone marrow fragments with increased fat spaces and depressed erythropoiesis, myelopoiesis and megakaryopoiesis (Figure 4 and 5).

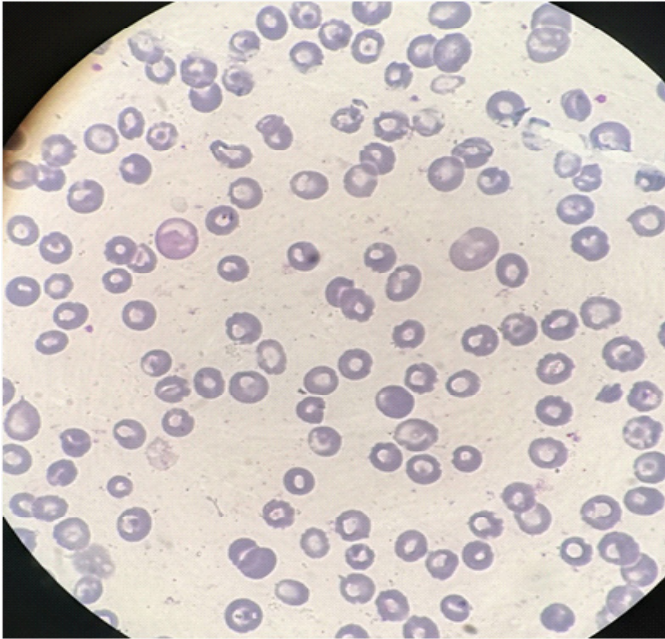


Figure 2: showing macrocytic hypochromic picture with target cells.



Figure 3: showing horse shoe kidney on ultrasound

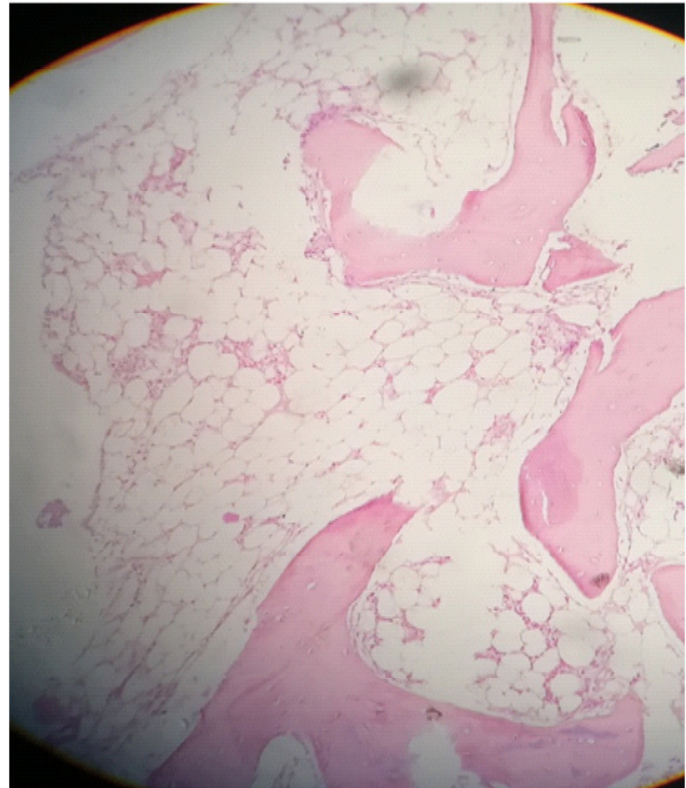
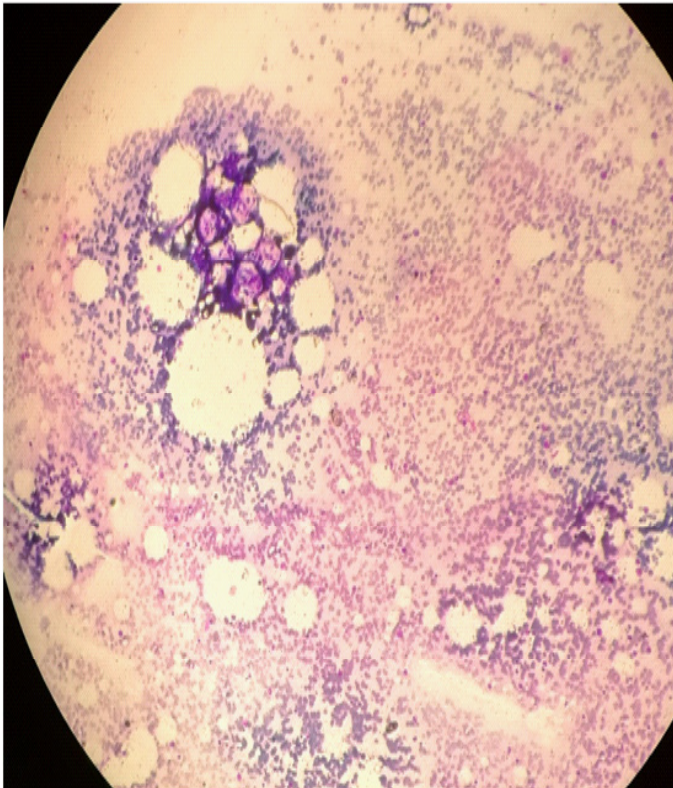


Figure 4 & 5: Bone marrow aspirate and trephine showing hypocellular marrow with increased fat spaces on 10X resolution

Keeping in view the characteristic physical, laboratory and bone marrow biopsy findings a provisional diagnosis of Fanconi anemia was made.

Cytogenetic studies: Cytogenetic studies were done to confirm the diagnosis which came out to be positive for Fanconi related chromosomal breakage by culturing with mitomycin –C.

Treatment: The child was referred to another tertiary care hospital for hematopoietic stem cell transplantation.

Discussion

Fanconi anemia is a form of hereditary aplastic anemia which is autosomal recessive in inheritance. It was first identified in 1927 by a Swiss pediatrician, Guido Fanconi [1]. It is a rare disease with an annual incidence of 1 in 129,000 live births with a male to female ratio of 1:1 and median age of onset is 7 years and average life expectancy of 25 years [2,3]. Mutations in at least 16 genetic subgroups have been identified as the cause of fanconi anemia. These genes have been designated as FANC A,B,C,D1,D2,E,F,G,I,J,L,M,N,O,P and Q and are responsible for DNA repair [4]. The disturbed mutant gene products impose damaging effects on sensitive tissues resulting in DNA instability characterized by congenital anomalies, bone marrow failure and increased predisposition to development of malignancies [2,5]. Clinically fanconi anemia is characterized by growth retardation, skeletal abnormalities like absent thumbs, dysplastic radii, hip abnormalities, heart defects, absent or fused kidneys, vaginal or uterus aplasia, infertility in females and hypospermia in males. Microcephaly and mental retardation may be present. In many cases there is abnormal skin pigmentation and presence of café au lait spots on skin [6,7]. The patients of Fanconi anemia gradually develop bone marrow failure usually evident towards the end of first decade of life. Bone marrow failure manifests as anemia, leukopenia and thrombocytopenia. The symptoms include easy fatigability, pallor, dyspnea, weakness, bleeding from mucosal surfaces and increased susceptibility to infections. There is pancytopenia with macrocytic red blood cells on peripheral blood examination along with a hypoplastic bone marrow aspirate and trephine. There are numerous chromatid breaks in myeloid and lymphocytic series cells. This chromosomal damage becomes intensified after exposure to DNA crosslinking agents like mitomycin and diepoxybutane. This forms the basis of the chromosomal breakage studies performed to confirm the diagnosis of Fanconi anemia [8]. Genetic studies can also be done to specify the gene mutation responsible for Fanconi anemia. About 20% of fanconi anemia patients develop various kinds of cancers out of which acute myeloid leukemia, myelodysplastic syndrome, head and neck squamous cell carcinoma and gynaecological squamous cell carcinomas are most common [1,9]. Allogenic hematopoietic stem cell transplantation is the only available treatment available for the restoration of hematopoiesis [10]. The prognosis of fanconi anemia is not good with most of the patients dying before the age of 10 years owing to bone marrow aplasia [11]. In our case report a 6 years old girl presented with short history of petechiae over body and bleeding gums. She had absent thumbs of both hands and horseshoe kidney. Bone marrow biopsy was markedly hypocellular and chromosomal breakage studies were positive after exposure to DNA crosslinking agent mitomycin C.

Conclusion

Fanconi anemia is a rare disease with a diverse spectrum of clinical presentation so it should be kept in mind while dealing with patients who have specific clinical findings. Genetic studies for identification of gene mutation should be carried out if possible in all the patients, siblings and parents. This helps in choosing the treatment plan along with suitable donors for hematopoietic stem cell transplantation and genetic counselling.

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