Development of Acute Leukemia in a Known Case of Fanconi Anemia (Aplastic Anemia)

Asst. Prof.*, Asso. Prof.**, Resident***, Professor****, Prof & HOD*****. Department Of Pathology,
Smt. NHL Municipal Medical College Ahmedabad.

ABSTRACT:
Fanconi anemia is an autosomal recessive disease associated with an abnormal DNA damage. Although Fanconi anemia is well known for its association of aplastic anemia and characteristic birth defects, leukemia and solid tumors also occur at a high rate in this group of patients. A patient male / 20yrs, known case of Fanconi anemia presented with ulcer over right lower limb. On further evaluation, the patient was found to have pancytopenia and his peripheral smear revealed many atypical blast like cells. So bone marrow study was done which revealed it to be acute leukemia probably Acute Myeloid leukemia.

Key words: Fanconi Anemia (FA), Aplastic anemia, Acute Myeloid Leukemia

INTRODUCTION:
Fanconi Anaemia (FA) is an inherited chromosomal instability syndrome with a variable clinical presentation that includes congenital anomalies, progressive pancytopenia & cancer susceptibility. The mean age at diagnosis is generally reported between 7 and 9 yrs. Patient with FA have an estimated 15000 times greater risk than general population for developing Acute Myeloid Leukemia (AML). We report a rare case of Acute Myeloid Leukemia in a known case of FA (Aplastic anaemia).

CASE HISTORY:
A 20yrs/Male patient presented with a non-healing ulcer since two months on right big toe following a snake bite and was admitted to Vadilal Sarabhai General Hospital on 13-4-11.

Past history: Patient was diagnosed with FA at the age of 12 yrs in 2003 by a practicing Haematologist in Ahmedabad. He was hospitalized for the complaint of fever since 3 days, vomiting, continuous right temporal headache, and epistaxis on and off. Patient had pancytopenia, subarachnoid haemorrhage, malrotated fused horseshoe kidney, hypoplastic right thumb and hyperpigmented knuckles. Bone marrow aspiration report was suggestive of Aplastic Anaemia.

At present, hematological findings showed mild anaemia (11.6gm/dl), thrombocytopenia (36,500/cu mm), reduced total WBC count (2430/cu mm).Peripheral smear showed presence of 38% atypical leukemic blasts and bone marrow findings were suggestive of acute Leukemia probably Acute myeloid leukemia.

DISCUSSION:
Fanconi anaemia is one of the inherited bone marrow failure syndromes which is associated with Aplastic anaemia, congenital anomalies and susceptibility to malignancies. There are currently 13 known FA subtypes A,B, C,D1, D2, E, F, G, I, J, L, M, & N. With the exception of subtype B, which isX-linked recessive, all the other forms are autosomal recessive. Patients with FA are at a great risk of developing MDS, AML or solid tumors at young age. In one study out of 41 patients 13 patients developed myelodysplastic syndrome and 3 patients

Fig: 1 Leukemic blasts in Bone Marrow Aspiration
developed leukemia. In another study out of 145 patients 18 patients developed solid tumors. There are multiple gene defects & chromosomal breakage that give rise to FA and affect distinct but functionally related protein that regulate cell cycle progression and DNA repair.

![Image](76x386 to 264x675)

Fig: 2 Leukemic blasts in bone marrow trephine biopsy

![Image](264x675 to 595x841)

Fig: 3 Chromosomal breakage with mitomycin-C

The mutation results in hypersensitivity to genotoxic agents such a Mitomycin CorDiepoybutane & chromosomal instability. Somatic mutations in several of FA genes have also been observed in AML outside the setting of FA thus further strengthening the link of these genes with predisposition for AML.

In present case, patient is a known case of Fanconi Anaemia associated with Aplastic Anaemia diagnosed at the age of 12yrs, treated appropriately along with regular CBC monitoring. Recently at the age of 20 yrs he developed non healing raw area at the site of snake bite in right great toe. Hematological investigations and bone marrow study in VSGH revealed the development of Acute myeloid leukemia. 48% of all nucleated cells in marrow were leukemic blasts with 2-3 nucleioli and scant agranular cytoplasm.

REFERENCES: