

reported case so far which is showing presence of aneurysm in both peripheral and pulmonary artery. In our patient we found that he had aneurysm in both right common iliac artery along with right inter lobar pulmonary artery and he was a previously undiagnosed sporadic case without any positive family history of Marfan syndrome. There is a reported case of spontaneous rupture of dissecting aneurysm of left common iliac artery during playing in a forty years old male patient [4]. But in our case it was sudden and spontaneous rupture had occurred without any physical exertion. While lying down, he developed acute onset pain followed by sudden collapse with severe pallor and disappearance of swelling in the abdomen. The occurrence of such an aneurysm suggests that the inherent mural weakness in Marfan syndrome is more widespread in the arterial tree than is generally appreciated [3]. It is secondary to cystic medial necrosis in the aorta and in multiple visceral arteries with extensive mucoid degeneration of the media of arterial wall [4]. So, patients with Marfan syndrome should be followed for signs of weakness of the peripheral arterial system and sometimes even with minor straining aneurysmal arterial wall can rupture. The peculiarity in our case was that even during rest the aneurysm got ruptured and he died almost immediately before resuscitation. When we diagnosed this case, we had planned early endovascular treatment with covered stenting of right common iliac artery as per recent advancement [7], but due to financial constraint it was delayed. Even in the acute condition, if we could have diagnosed rupture of the aneurysm earlier, he could have been saved by

immediate closure of that artery by balloon dilatation just before the ruptured segment followed by immediate surgery with simple excision and end-to-end repair.

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Acute Lymphoblastic Leukemia with Treatment–Naïve Fanconi Anemia

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Fanconi anemia is known to have a predisposition to cancer, mostly associated with acute myeloid leukemia. We report an eight-year-old girl with treatment and naïve FA who developed acute-lymphoblastic-leukemia (ALL). She was initiated on chemotherapy but she failed to respond to treatment and died during induction phase of chemotherapy. While this association may be coincidental but possibility of transition of Fanconi anemia to ALL should be considered in view of high predisposition to cancer in this disorder.

Key words: Acute lymphoblastic leukemia; Aplastic anemia; Fanconi anemia; Malignancy.

Fanconi anemia is a genomic instability syndrome characterized by a wide array of congenital malformations, bone marrow failure, and a predisposition to cancer [1]. These

patients usually present with reduced numbers of progenitor cells, including myeloid, erythroid, and multipotent progenitors [2]. In addition, almost 25% of patients develop a neoplastic disorder including acute

myeloid leukemia (AML), myelodysplasia, and solid tumors, after a variable period of time [1-3]. The cumulative incidence of leukemia in Fanconi anemia is around 10% by 25 years of age, and the cumulative incidence of any hematological abnormality is up to 90% [1]. In this disorder 94% of leukemias are myeloid as compared to 84% of leukemia's being lymphoid in non-fanconi patients [3]. To date, only seven cases of acute lymphoblastic leukemia (ALL) with Fanconi anemia have been reported in literature [3]. We report a patient with treatment-naïve Fanconi anemia who developed acute lymphoblastic leukemia.

CASE REPORT

An 8-year-girl, presented with past medical history of physical anomalies (short stature and hypoplastic radial elements), and aplastic anemia. Laboratory examination was suggestive of pancytopenia. Bone marrow aspirate and biopsy revealed reduced marrow cellularity with increased chromosomal fragility as demonstrated by positive mitomycin C stress test. Based on these, she was diagnosed as Fanconi anemia and started treatment with red blood cell and platelet transfusions.

Six months later, she presented with multiple petechiae, purpurae, and features of raised intracranial pressure. Laboratory findings were as follows: hemoglobin=6.7g/dL, WBC=3.4×10⁹/L, and platelets=20×10⁹/L. CT scan of brain showed an intracranial bleed, with surrounding edema. She was managed with hyperosmolar therapy and blood component support. The child developed fever on day 3 of admission for which broad spectrum antibiotics were added. On day 9 of admission she developed leukocytosis with WBC count of 17×10⁹/L, with persistent anemia and thrombocytopenia. Peripheral blood smear revealed 10% blasts. Bone marrow examination revealed >30% blasts. The blasts were negative for myeloperoxidase stain and had lymphoblastic appearance. Flow cytometry confirmed CD10 positive acute lymphoblastic leukemia. The child was initiated on vincristine, L-asparaginase, prednisolone and daunorubicin based therapy. However, she had a rapidly deteriorating course and died during the induction phase of therapy.

DISCUSSION

Fanconi anemia is a member of at least two classes of cancer predisposition syndromes [3]. The first consists of autosomal recessive disorders of DNA repair and the second class comprises of inherited bone marrow failure syndromes [3]. Fanconi anemia patients with abnormal radii have a 5.5 times increased risk of developing bone

marrow failure compared with those cases with normal radii [4]. In children without the congenital abnormalities, the development of hematological abnormalities can be the presenting feature of this disorder [5].

The risks for developing myelodysplastic syndrome, leukemia or solid tumors for these patients are about 6%, 10%, and 10% respectively [6]. Biallelic mutations in any of the known thirteen FA genes leads to disruption of regular DNA double stranded break (DSB) repair by homologous recombination (HR), resulting in an increased rates of spontaneous DSBs. This disruption of HR mediated DSB repair may lead to activation of error prone end joining repair mechanisms resulting in misrepairs and further aggravating genetic instability and predisposing to leukemias and solid cancers [6].

In the past decade, three studies of leukemia in Fanconi anemia have been reported [1,3]. On the basis of these studies, the crude risk for leukemia in Fanconi anemia homozygotes is 5-10% [5]. Of the 1301 cases of Fanconi anemia, reported from 1927 through 2001, there were 116 reports of leukemia [3]. Among these patients with Fanconi anemia and leukemia, seven were ALL and the remainders were acute myeloid leukemia. This is in contrast to leukemias in general population wherein lymphoid leukemias predominant. Of the seven cases reported with Fanconi anemia and ALL in this disorder, all the seven cases had received pre-treatment (steroids and androgens, stem cell transplantation) before the leukemic transformation.

There were two intriguing aspects about our case. Firstly, our patient with Fanconi anemia developed ALL. While the occurrence may be a coincidence, but due to underlying genetic instability a predisposition to develop ALL in these patients must be considered. Secondly, though there have been seven cases reported before this, regarding development of ALL in patients of Fanconi anemia, but in all the instances, the patients had been pre-treated with androgens and steroids or had undergone stem cell transplantation. In our patient there was no exposure to any therapeutic intervention before the development of leukemia. This further underscores the fact that genetic instability secondary to DSB repair mechanism may be contributory to development of ALL through yet unknown pathway.

To the best of our knowledge, this is the first report of development of acute lymphoblastic leukemia in a treatment-naïve patient of Fanconi anemia. While this association may be coincidental, but the possibility of transition from Fanconi anemia to ALL must be contemplated in order to gain more insights on the role of

Fanconi anemia genes in leukemogenesis.

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Johanson-Blizzard Syndrome

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We present clinical features and genetic diagnosis in an Indian infant diagnosed with Johanson-Blizzard syndrome. This is a rare, autosomal recessive genetic condition with multi-system involvement and a characteristic facies. Molecular genetic testing is important to confirm the clinical diagnosis and offer prenatal diagnosis in future pregnancies.

Key words: Johanson-Blizzard syndrome, India.

Johanson-Blizzard syndrome (MIM2G3800) is a rare, autosomal recessive genetic condition with a characteristic 'diagnostic facies'. We present an Indian infant with this condition.

CASE REPORT

A 12-day-old female newborn was referred for Genetics consultation for her unusual facies and congenital heart defect. She was the first born to 3rd degree consanguineous parents without any family history of major medical or genetic disorders, except for well-controlled maternal hypothyroidism. She was born normally at term with a birthweight of 2.45 kg and suffered from a secondary apnea requiring resuscitation followed by feeding difficulties and poor weight gain.

On examination, on day 12, she weighed 2.3 kg, had head circumference of 32 cm and length of 50 cm. She had a striking facies (**Fig. 1**) with a small beak-like nose with hypoplastic alae nasi, long narrow upper lip, open mouth with protruding tongue, prominent eyes with palpebral fissures slanting upwards and epicanthic folds. She had a



FIG. 1 Patient at age of 12 days: Characteristic facies with beaked nose, hypoplastic alae nasi, long philtrum with thin upper lip and frontal hirsutism with upsweep of hair.