
CASE REPORT

Acute Lymphoblastic Leukemia in a Child with Fanconi's Anaemia

Naureen Mushtaq1, Rabia Wali2, Zehra Fadoo1 and Ali Faisal Saleem1

ABSTRACT

Fanconi anaemia (FA) is an autosomal recessive inherited disorder with progressive bone marrow failure, associated congenital malformation and solid and haematological malignancies. Acute myeloid leukemia is the commonest haematological malignancy followed by myelodysplastic syndrome in children with FA. FA transformed into acute lymphoblastic leukemia (ALL) is a rare phenomenon and one of the rarest haematological malignancies associated with this disorder. We are reporting a 13 years old girl with FA and positive chromosomal breakage. She required regular blood product transfusion. She was planned for haematopoietic stem cell transplantation (HSCT) but the sibling-matched donor was found to have chromosomal breaks as well. Later on, her peripheral smear showed blast cell. Bone marrow showed pre-B ALL. She was started on chemotherapy but died shortly due to complications of the treatment. For this rare condition conservative management is indeed essential, however, safe and appropriate chemotherapy regimen is needed.

Key words: Fanconi anaemia. Acute lymphoblastic leukemia. Bone marrow failure.

INTRODUCTION

Fanconi anaemia (FA) is a constitutional pancytopenia of childhood with mostly autosomal recessive inheritance with diverse clinical heterogeneity including congenital malformations, progressive bone marrow failure and high propensity for cancer in long-term, mostly solid tumours and carcinoma of head, neck and upper oesophagus followed by carcinoma of vulva and/or anus and lower oesophagus; however, it is also associated with acute leukemia with marked predisposition with acute myeloid leukemia (AML) and rarely acute lymphoblastic leukemia (ALL).1,2 Myelodysplastic syndromes may follow clinically overt aplastic anaemia or develop without a detectable antecedent.3 The incidence of AML or myelodysplastic syndrome in FA is approximately 15%.4 All patients have underlying abnormal chromosome fragility seen in metaphase preparations which was enhanced by adding clastogenic agents such as diepoxybutane.4,5 Growth hormone (GH) therapy for FA can also lead to ALL.6 Sensitivity to DNA damaging agents limits therapy in patients with FA; however, severe toxicity and marrow aplasia without haematological recovery has also been described in the literature.7

FA transformation into ALL is a rare phenomenon. There are very few case reports in the literature. Here we present this rare entity of FA with ALL.

CASE REPORT

The patient was a 13 years old girl at presentation to the haematology and oncology clinic with prolonged history of blood transfusion since last 6 years. She had no previous records available. However, she was on regular once fortnightly packed cell transfusion and weekly platelet transfusion. On examination, she was short statured with microcephaly, having triangular facies and areas of hyperpigmentation. There was no organomegaly or lymphadenopathy. She had six siblings and they were healthy when she presented to us.

Because of FA suspicion her laboratory workup was done. Her complete blood count showed pancytopenia, with < 20% cellularity of bone marrow on trephine biopsy and chromosomal breaks was positive. She was kept on supportive management and planned for haematopoietic stem cell transplantation (HSCT). Her human leukocyte antigen (HLA) typing along with her siblings was also done. Unfortunately, the patient's HLA matched donor was also positive for chromosomal breaks.

Two months later she presented in emergency with jaundice, abdominal pain, swelling of feet and abdominal distension. Her laboratory work-up was positive for Hepatitis B virus active infection and with the consultation with infectious diseases expert she was started on anti-hepatitis B therapy. Her general condition improved.

After 2 months she again presented to the emergency room with intermittent fever and worsening pallor. Her examination showed marked hepatosplenomegaly. Laboratory work-up revealed pancytopenia with 63% blast cells; Bone marrow flow-cytometry was consistent with Pre-B ALL.

Her clinical status deteriorated rapidly and she became vitally unstable. She was planned for four-drug induction

1 Department of Paediatrics and Child Health, Aga Khan University Hospital, Karachi.
2 Department of Paediatrics, Shaukat Khanum Cancer and Research Hospital, Lahore.

Correspondence: Dr. Naureen Mushtaq, C-87 Block 4, Gulshan-e-Iqbal, Karachi.
E-mail: naureen.mushtaq@aku.edu

Received October 29, 2011; accepted February 17, 2012.

1458
therapy (vincristine, L-asparaginase, prednisolone and daunorubicin) as per ALL protocol, but because of her severe diastolic dysfunction daunorubicin was omitted from the chemotherapy. She succumbed to infection and died on the 7th day of induction therapy with septicemia; however, none of her cultures were positive.

**DISCUSSION**

Fanconi anaemia (FA) is a genetic disorder characterized by congenital abnormalities, cancer predisposition, and progressive pancytopenia. The cellular phenotype of FA is characterized by increased sensitivity to DNA cross-linking or alkylating agents that block DNA replication and RNA transcription.\(^2\)

FA children typically present in the first decade of life on recognition of aplastic anaemia.\(^1\) The classic features of FA consist of thumb and radial absence malformations; less obvious features include a deeper cleft between the first two digits. The gold standard for FA quantify chromosomal breakage in cells exposed to cross-linking agents to which FA cells are hypersensitive.\(^2\)

FA patients have a very high risk of developing progressive bone marrow failure along with an increased risk of future long-term malignancies. The most frequent malignancy in FA is acute myeloid leukemia (AML) with a cumulative incidence of 33% by 40 years of age.\(^8\)

This patient developed ALL which is rare, but possible acute leukemia in FA. The FA-related leukemias differ from leukemia in the general population in several important ways.\(^9\) In FA patients, 94% of the acute leukemias are myeloid and only 6% are lymphoid compared with 84% of the acute leukemias being lymphoid in general paediatric population. The age distribution for acute leukemia in FA was normally distributed around a mode of 14 years; however, in the general population in which the incidence of AML is higher in infants, it was declined to around age 10, and then rises slightly in the late teens.\(^2\) The age of this patient was 13 years when she diagnosed as ALL.

Cancer risk assessment was done for FA. Table I showed the three studies with their haematological frequency of malignancies. First was a literature review of 1300 reported cases of FA from 1927 to 2001;\(^10\) second was of 754 FA patients from the International Fanconi Anaemia Registry (IFAR) ascertainment from 1982 to 2001,\(^8\) while the third was a cross-sectional study of 145 North American patients during 2000.\(^11\) It was seen that the cumulative incidence of ALL in FA was 0.5% (12/2200 patients).

<table>
<thead>
<tr>
<th>Studies</th>
<th>Total cases of Fanconi anaemia</th>
<th>Haematological malignancies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AML</td>
<td>MDS</td>
</tr>
<tr>
<td>Alter BP (2003) (10)</td>
<td>1301</td>
<td>109</td>
</tr>
<tr>
<td>Kutler DI (2003) (8)</td>
<td>754</td>
<td>60</td>
</tr>
<tr>
<td>Total cases</td>
<td>2200</td>
<td>–</td>
</tr>
</tbody>
</table>

**REFERENCES**


