Fanconi’s Anemia—Rare Aplastic Anemia at Ten Year-Old Boy in Mogadishu-Somalia: Case Report

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Abstract

Fanconi’s anemia (FA) alson called Fanconi Pancytopenia is a rare, potentially life-threatening failure of haemopoiesis characterized by aplastic anemia that is associated with a variety of congenital abnormalities (Cafe-au-lait spots, abnormalities of fingers, hyperpigmentation of the skin, short stature, microcephaly, deformities of the ear, hypogenitalism, renal anomalies, etc.) and a high risk of developing of malignancy and chromosomal instability. FA is the first described in 1927 by Guido Funconi reported 3 brothers with pancytopenia and physical anomalies. The diagnosis is based on morphological abnormalities, hematologic abnormalities and genetic tests. The present case report describes a 10 years old Somali boy was diagnosed with a Fanconi anemia after recurrent blood transfusion. Though aplastic anaemia in children is an important haematological disorder, there is no study having been undertaken in Somalia and this is the first reported by the patient with Fanconi’s anemia in Somalia. We report this case to create awareness among clinicians the presence of this disease and have a consideration when it comes differerntial diagno-sis of recurrent blood transfusion patients with pancytopenia because it’s a rare genetic disease in Mogadishu and around the world.

Keywords

Androgens, Fanconi Anemia, Haematopoitic Growth Factors, Haematopoietic Stem Cell Transplantation

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1. Introduction

Fanconi aplastic anemia was discovered by Fanconi in 1927, where Fanconi described three brothers who had pancytopenia and birth defects [1]. 99% of the cases is autosomal recessive (patients are homozygous or double heterozygous for one or more mutations). X-linked transmission cases have been also described [2]. Its manifestation as congenital developmental anomalies, progressive pancytopenia and an increased risk of malignancy, chromosomes in Fanconi’s anemia are peculiarly susceptible to DNA cross-linking agents. Patients with Fanconi’s anemia typically have short stature, café-au-lait spots, and anomalies involving the thumb, radius, and genitourinary tract. At least 12 different genetic defects (all but one with an identified gene) have been defined; the most common, type A Fanconi’s anemia, is due to a mutation in FANCA. Most of the Fanconi’s anemia gene products form a protein complex that activates FANCD2 by monoubiquitination to play a role in the cellular response to DNA damage and especially interstrand cross-linking [3].

It is usually diagnosed at children aged between 5 and 15 years, sex ratio is approximately equal to M/F = 1.3/1. At birth, the blood count is usually normal and macrocytosis is often the first detected abnormality, followed by thrombocytopenia and neutropenia. Patients with FA have immune deficiencies before bone marrow failure. Pancytopenia typically appears between the ages of 5 and 10, the median age of onset being 7 years old [3]. So approximately 10% were diagnosed in the neonatal period and 75% in the second decade of life [2]. Fanconi anemia has been found in all ethnic groups. Its frequency has been estimated to be 1/350,000 births with a higher frequency in Ashkenazi Jews and Afrikaners in South Africa [3].

The most common anomaly is hyperpigmentation of the trunk, neck, and intertriginous areas, as well as café-au-lait spots and vitiligo, alone or in combination. Most patients have short stature. Growth failure may be associated with abnormal growth hormone secretion, or with hypothyroidism. Absent radii and hypoplastic, supernumerary, bifid, or absent thumbs are common. Anomalies of the feet, congenital hip dislocation, and leg abnormalities are seen. Males may have an underdeveloped penis; undescended, atrophic, or absent testes; and hypospadias or phimosis. Females can have malformations of the vagina, uterus, and ovary. Many patients have a Fanconi “facies,” including microcephaly, small eyes, epicanthal folds, and abnormal shape, size, or positioning of the ears (see Figure 2). Approximately 10% of patients are mentally retarded. Ectopic, pelvic, or horseshoe kidneys are detected by imaging, as well as duplicated, hypoplastic, dysplastic, or absent organs [4]. Although this highly variable phenotype makes accurate diagnosis on the basis of clinical manifestations which are difficult in some patients, laboratory study of chromosomal breakage induced by diepoxybutane (DEB) or other crosslinking agents provides a unique cellular marker for the diagnosis of the disorder either prenatally or postnatally. Diagnosis based on abnormal response to DNA crosslinking agents can be used to identify the pre-anemia patient as well as patients with aplastic anemia or leukemia who may or may not have the physical stigmata associated with the syndrome [5].

2. Case Report

We report the case of 10 years old male hospitalized in the Children’s Hospital of Mogadishu-Somalia (SOS Hospital), for the following reasons: fever, early fatigue, loss of appetite for last 6 months. In initially he stated to refuse food after that followed by fatigue and fever after a week, his parents said that their child is not growing well and also said there is no hospitalized before for anemia and he has no other medical conditions. During the hospital he gets three times of blood transfusion and he doesn’t get for any improvement.

On Clinical Examinations indicated a temperature of 38˚C, pulse 102/min and respiratory rate 24/min, severe general conditions, pale in conjunctiva, ringworm lesions on the face, a broad nasal base, small eyes, epicanthal folds (Figure 1), and café-au-lait spots on trunk (Figure 2) and thumbs attached by a thread (Figure 3).

On abdominal examination its impalpable liver and spleen.

Laboratory investigations revealed: pancytopenia (Leucocytes = 2.4 × 10⁹/L, Hemoglobin = 6.0 g/dl, Thrombocytes = 37 × 10⁹/L).

Unfortunately we don’t have a well equipped hematological center in our setup that capable to investigate bone marrow and in genetic testing in order to confirm the diagnosis of the disease.

By correlating clinical and laboratory data the positive diagnosis is based on the following criteria:

1) Clinical history

2) Physical abnormalities (pale in conjunctiva, a broad nasal base, small eyes, epicanthal folds and café-au-lait spotson trunk and thumbs attached by a threads)
3) **Hematology test** (pancytopenia)

The management of the disease is considered in corticosteroids treatments for three weeks to improve his hemoglobin but unfavorable evolution for the treatment given and we also considered in antibiotic therapy due to fever in neutropenia, anti-fungal (Ketoconazole cream) for tenia and micronutrients as supportive management. Lastly we recommended the case to go aboard for confirmation and comprehensive management.

3. Discussion

This syndrome is inherited in an autosomal recessive manner in almost every case; it occurs in all racial and ethnic groups. It is characterized by progressive bone marrow failure leading to death of many patients in their childhood while development of cancer at later stages of life in some. At presentation, patients may have: 1) typical physical anomalies, but normal hematologic findings; 2) normal physical features, but abnormal hematologic findings; or 3) physical anomalies and abnormal hematologic findings, the classic phenotype (39% of cases) [4].

![Figure 1. Close-up of the patient’s face, showing the characteristic of ringworm lesions on the face (arrows) and pale conjunctiva with epicanthal folds.](image1)

![Figure 2. Café-au-lait spots in anterior trunk (arrow).](image2)
Early diagnosis of FA permits the exclusion of other diseases and precludes inappropriate management of hematologic disease (aplastic anemia [AA], myelodysplastic syndrome [MDS], acute myeloid leukemia [AML]), and permits appropriate consideration of stem cell transplant, androgens, hematopoietic growth factors or supportive care. Surgical intervention for orthopedic, renal or other anomalies is also optimized if the diagnosis of FA is known [6].

Diagnosis of Fanconi anemia is made by abnormal hematologic findings and characteristic physical anomalies suggest the diagnosis, which is confirmed with a chromosomal breakage study using DEB. No other constitutional pancytopenia is associated with an abnormal chromosomal breakage study [4].

The diagnosis is usually performed only after the onset of symptoms of hematologic dysfunction, which usually start at around 7 years of age, ranging from birth to 31 years [7].

Our diagnosis based on both physical anomalies and abnormal hematological findings of our patient as shown in (Table 1) and other pictures above.

The treatment of FA is still a medical challenge. Current treatments of Fanconi anemia include androgen administration, blood transfusions, hematopoietic growth factors administration and hematopoietic stem cell transplantation (HSCT) [8]. Allogeneic hematopoietic cell transplantation (HCT) remains the only treatment that can correct the haematological manifestations in patients with Fanconi anaemia [9].

Although the treatment of this disease still on a research the available options which have some limitation, for example, androgens are not a permanent cure, but only prolong the life of patients.

Patients’ response to androgens only if the treatment is started at early stage. Though 70% of the patients respond to androgens, the response is slow, drug dependent and incomplete. Other limitations include several side effects such as masculinisation, acne, growth spurt and premature closing of epiphysis and risk to liver tumours [8].

Patients who receive multiple transfusions of red blood cells are at risk for accumulating toxic levels of iron. The liver, heart, and endocrine organs are primary sites of iron accumulation, and end-organ damage may result (e.g. hepatic cirrhosis, heart failure, endocrine dysfunction) [6].

4. Conclusion and Recommendations

The disease is a heterogeneous condition that can present with a variety of congenital defects. The main causes of morbidity and mortality are aplastic anemia, myelodysplasia, acute myeloid leukaemia, and solid tumours at older ages. We recommend to all healthcare professionals to be aware of this disease especially to include their differential diagnosis at recurrent blood transfusion case with pancytopenia.
### Table 1. Complete blood count report.

<table>
<thead>
<tr>
<th>Blood Component</th>
<th>Results</th>
<th>Units</th>
<th>Reference Interval</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>2.4</td>
<td>×10⁹/L</td>
<td>4.0 - 10.0</td>
<td>LOW</td>
</tr>
<tr>
<td>Lymph#</td>
<td>1.4</td>
<td>×10⁹/L</td>
<td>0.8 - 4.0</td>
<td>Normal</td>
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<tr>
<td>Mid#</td>
<td>0.3</td>
<td>×10⁹/L</td>
<td>0.1 - 1.2</td>
<td>Normal</td>
</tr>
<tr>
<td>Gran#</td>
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<td>×10⁹/L</td>
<td>2.0 - 7.0</td>
<td>Low</td>
</tr>
<tr>
<td>Lymph %</td>
<td>57.7</td>
<td>%</td>
<td>20.0 - 40.0</td>
<td>High</td>
</tr>
<tr>
<td>Mid%</td>
<td>14.6</td>
<td>%</td>
<td>3.0 - 14.0</td>
<td>High</td>
</tr>
<tr>
<td>Gran%:</td>
<td>27.7</td>
<td>%</td>
<td>50.0 - 70.0</td>
<td>Low</td>
</tr>
<tr>
<td>HB</td>
<td>6</td>
<td>g/dl</td>
<td>11.0 - 16.0</td>
<td>Low</td>
</tr>
<tr>
<td>RBC</td>
<td>2.73</td>
<td>×10¹²/L</td>
<td>3.50 - 5.50</td>
<td>Low</td>
</tr>
<tr>
<td>HCT</td>
<td>13.0</td>
<td>%</td>
<td>37.0 - 54.0</td>
<td>Low</td>
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<tr>
<td>MCV</td>
<td>55.1</td>
<td>ft</td>
<td>80.0 - 100.0</td>
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</tr>
<tr>
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<td>pg</td>
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<tr>
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<td>g/dl</td>
<td>32.0 - 36.0</td>
<td>High</td>
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<tr>
<td>Platelet</td>
<td>37</td>
<td>×10⁹/L</td>
<td>100 - 300</td>
<td>Low</td>
</tr>
</tbody>
</table>

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### References


