Asplenia in a patient with Fanconi's anemia-like congenital aplastic anemia

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Fanconi's anemia (FA) is an autosomal recessive disease manifested by pancytopenia resulting from bone marrow failure, variable physical anomalies and cancer susceptibility. A seven-year-old girl with Fanconi's anemia-like congenital aplastic anemia and concurrent asplenia without the congenital heart defects or the abdominal heterotaxia is reported. Asplenia was indicated using denatured red cells labelled with^{51} Cr, abdominal ultrasonography and computerized tomography. Immunological studies showed immunoglobulins (IgG, IgA, IgM), C_3 and C_4 levels within normal limits and the percentage of CD_3, and C_4 cells and the CD_4/CD_8 ratio decreased. The patient had not been exposed to recurrent pneumococcal infections. We think that isolated asplenia may occur in patients with Fanconi's anemia-like congenital aplastic anemia without the congenital heart diseases or abdominal heterotaxia.

Key words: asplenia, Fanconi's anemia-like congenital aplastic anemia.

Fanconi's anemia (FA) is an autosomal recessive disease that presents with pancytopenia, bone marrow failure, growth retardation, microcephaly, microphthalmia, hypogonadism, renal anomalies, café-au-lait spots and various skeletal anomalies[1].

Congenital absence of the spleen is rare. Congenital asplenia is usually associated with a characteristic group of anomalies of the cardiovascular and the gastrointestinal systems (asplenia syndrome)[2]. Deficiency or absence of splenic activity in congenital asplenia encompasses complex immunological defects, which in turn result in an increased susceptibility to severe bacteremia[3].

Here we report a Fanconi's anemia-like congenital aplastic anemia patient with asplenia without congenital heart diseases or abdominal heterotaxia; to our knowledge this has not been previously reported.

Case Report

A seven-year-old girl was admitted to our clinic with complaints of paleness and weakness for the previous two years. On physical examination, growth retardation (less than 3rd percentile for weight and height), microcephaly, microphthalmia, café-au-lait spots, and clinodactyly were noted. She had not been exposed to recurrent life-threatening infections related to pneumococci in the past. Her parents had first-degree consanguinity. Laboratory examination revealed hemoglobin 4.6 g/dl, leukocytes $4.1x10^9$/L, platelets $14x10^9$/L, mean corpuscular volume (MCV) 107 fl and reticulopenia (< 1%). Peripheral smear showed relative lymphocytosis, hypochromic-macrocytic erythrocyte morphology and Howell-Jolly body (Fig. 1). Fetal hemoglobin was 14 percent. Bone marrow aspiration showed hypocellularity in all trilineage series. Immunological analyses showed IgG as 980 mg/dl, IgA 84 mg/dl, IgM 155 mg/dl, C_3 45 mg/dl, C_4 110 mg/dl, CD_3 45%, CD4 38%, and the CD_4/CD_8 ratio 0.9 Abdominal computerized tomography (CT scan) didnot show the spleen. Functional spleen tissue was not determined using the denaturated red cells labelled with ^{51}Cr (Fig. 2). Telecardiography, electrocardiography and echocardiography were normal.

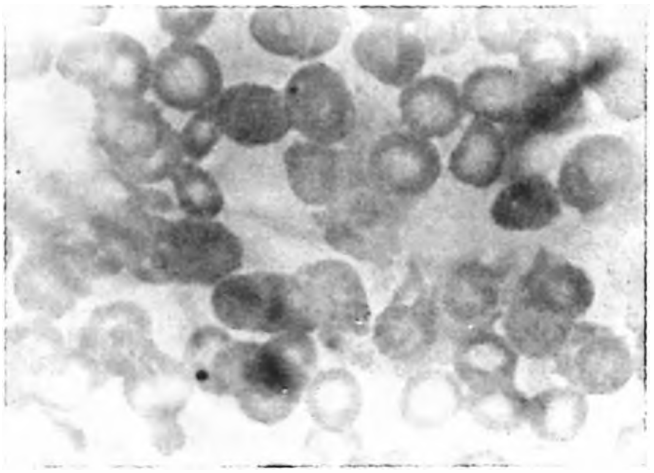

Fig. 1. Peripheral blood smear showing hypochromic-macrocytic erythrocytes and Howell-Jolly bodies (Wright's stain X 100).

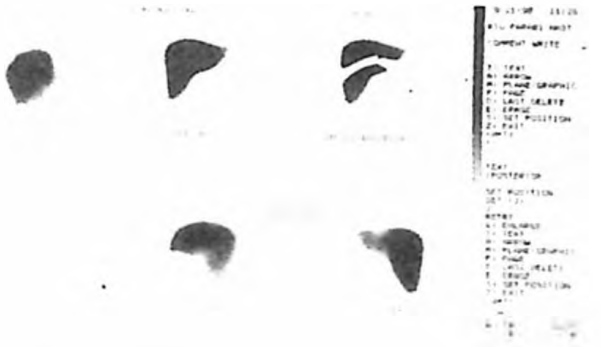

Fig. 2. Functional spleen tissue could not be shown by spleen scintigraphy.

Discussion

Fanconi's anemia is a heterogenous disorder, and the usual age of onset is five to 10 years[4]. It is a rare, autosomal recessive disease characterized by multiple congenital abnormalities, bone marrow failure, and cancer susceptibility[5]. Eight complementation groups of FA (FA-A through FA-H) have been described so far[6]. Complementation groups in FA are likely to represent distinct disease genes, three of which have been cloned (FACA on chromosome 16q24.3, FACC on chromosome 9q22.3 and FACD on chromosome 3p)[7-9]. Some evidence exists that a step in DNA repair is defective[10].

Asplenia syndrome is characterized by complex congenital heart defects and abdominal heterotaxia[2]. The most common congenital heart defects are atrial septal defect, common atrioventricular canal and conotruncal anomalies. With use of current information on timing of normal development, it was hypothesized that most defects originate at Streeter Horizon XIII; patients averaged 3.2 Horizon XIII defects, more than at any other stage. Extracardiac anomalies also exhibited a developmental spectrum. Because the normal spleen develops by Horizon XIII, asplenia originated then or earlier. Abnormal pulmonary lobation has occurred in 80 percent of cases; pulmonary branching asymmetry also originated at or before Horizon XIII. Abdominal heterotaxia has occurred in 72 percent of cases, but the timing of origin is unclear. Anomalies of genitourinary, musculoskeletal, endocrine, and nervous systems develop later (typically XV to XXIII)[11]. Two father-son pairs with isolated nonsyndromal asplenia were also reported. It was suggested that this may represent autosomal dominant inheritance of a mutation in a gene involved with spleen development and that screening for asplenia in first-degree relatives of individuals with asplenia should be considered[12].

The spleen was not determined by spleen scintigraphy, abdominal USG or CT scan in our patient. Therefore atrophy of the spleen, which is common in FA, was excluded. We think that asplenia originated after Horizon XIII in this patient because she had no pulmonary branching asymmetry, which originates at or before Horizon XIII. It is not clear to us why the congenital heart defects and abdominal heterotaxia were not seen in our patient.

It is suggested that IgG, IgA, IgM and C_3 and C_4 values are within normal limits and that the percentages of CD_3 and CD_4 cell and the CD_4/CD_8 ratio are decreased; in FA; therefore, profoundly decreased T cell function might account for the life-threatening infections frequently seen in patients with congenital asplenia[13]. Immunoglobulins, C_3 and C_4 were normal for age and the percentages of CD_4 and CD_8 cells and the CD_4/CD_8 ratio were lower than normal in our patient. It is interesting that the history of recurrent pneumococcal infections did not exist in our patient. Our case shows that isolated asplenia may occur in patients with Fanconi's anemia-like congenital aplastic anemia without the congenital heart defects or the abdominal heterotaxia.

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