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THROMBOCYTOPENIA AND ABSENT RADIUS (TAR) SYNDROME - CASE PRESENTATION

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Abstract

TAR Syndrome is congenital disease produced by a genetic mutation characterized by low platelet count and radial aplasia. We report the interesting case of non-identical twin sisters with TAR Syndrome, in evidence at the Bihor Regional Genetic Centre from "Gavriil Curteanu" Hospital. From clinical examination of the two girls we noted limb shortening as a consequence of radial aplasia and laboratory findings revealed thrombocytopenia. Both sisters had normal intelligence development and no other associated malformations. Differential diagnosis can be made with Fanconi anaemia but it`s unlikely because of the presence of normal red blood cells and white blood cells count.

Key words: congenital malformation, thrombocytopenia, absent radius

INTRODUCTION

TAR Syndrome is a rare genetic disease with an incidence of 0.42 cases per 100.000 live births. The main features that give the name of the syndrome include absence of the radial bone in both forearms and thrombocytopenia. Additional features include mental retardation, facial dimorphism, cardiovascular and genito-urinary anomalies. Thrombocytopenia appears in infancy and in some cases becomes less severe with time. Complications of the disease are haemorrhages, spontaneous or as a result of trauma, that can be severe especially when they appear in the brain or other organs. Children who survive the first two years of life have a normal life expectancy. Interestingly children affected by the syndrome have an increased risk of allergic reaction to consumption of cow`s milk.

MATERIAL AND METHOD

We present the case of non-identical twin sisters with TAR Syndrome, in evidence at the Bihor Regional Genetic Centre from "Gavriil Curteanu" Hospital. Both girls were examined clinically and paraclinically: laboratory findings, X-Ray and ecochardiography.

RESULTS AND DISCUSSIONS

PATIENTS HISTORY

Our patients are two twin sisters taken in evidence in the Genetics Department from the age of five months. They were the children of healthy, young, non-consanguineous parents. Family history was remarkable, they had a sibling who suffered from a congenital cardiac malformation, phocomelia, mental retardation and died at two months. The two girls were born prematurely, weighting approximatively 2250gr. each, with an Apgar score of 6/7. Physical exam revealed malformative syndrome concerning the upper limbs that presented forearm shortening in both girls.

CLINICAL AND PARACLINICAL EXAM

Clinical exam at presentation revealed grade I dystrophy with a Ponderal Index of 0,80 , pale skin, marmorated extremities, purpuric lesions and micropetechiae spread on the thorax and abdomen, limb anomalies the upper limbs being shortened because of forearm shortening, the radial bones were absent in both forearms, hand flexion on the forearm and thumb flexion on the hand, facial dimorphism with mandibular hypoplasia, ogivale palate, gross patterning of the external ear.

Preclinical exam revealed the following:

- Laboratory findings:
    - anaemia, regenerative type (RBC=3.200.000/mm^3, Hb=7,2g/dl in one of the girls and RBC=3.800.000/mm^3, Hb=9g/dl, reticulocytes= 32.000/mm^3)
    - thrombocytopenia (PLT=65.000/mm^3 respectively PLT=90.000/mm^3)
    - hyperplastic bone marrow on the erythrocytes and granulocytes series, hypoplasia of megakaryocyte series with athrombocytogenic megakaryocytes
- Radiological findings:
- Absent bilateral radius, curved cubitus, humerus hypoplasia

POSITIVE DIAGNOSIS

Based on the association of the fallowing, a diagnosis of TAR syndrome was made.

- Absent radius bilaterally in both girls
- Craniofacial dimorphism
- Thrombocytopenia
- Positive family history with previous birth of a sibling with malformative syndrome suggesting a genetic disease with hereditary inheritance

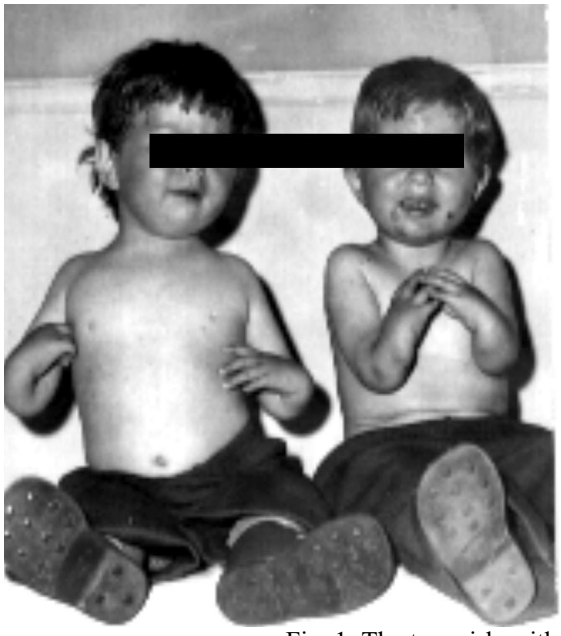

Fig. 1. The two girls with radial aplasia

DIFFERENTIAL DIAGNOSIS

The most likely differential is that of Fanconi Syndrome.

Findings consistent with this diagnosis are:

- radius absence
- thrombocytopenia

Findings against the diagnosis:

- absence of aplastic anaemia a major criteria of diagnosis in Fanconi Syndrome

MANAGEMENT AND TREATMENT. FOLLOW-UP PERIOD

- neurodevelopment evaluation considering the fact that some of the affected individuals present mental disability

- avoid consuming cow's milk for the first year of life because cow's milk allergy is associated with TAR
- equilibrate, normocaloric nutrition for prevention of dystrophy
- prevention of infectious diseases
- avoidance of trauma due to high risk of life-threatening bleeding episodes
- in the case of significant thrombocytopenia <80.000 PLT/mm^3 platelets transfusion
- prevention of platelet transfusion risks like infection, anaphylaxis, formation of antiplatelet antibodies, and haemolytic reactions
- splinting of the hands during infancy

During the follow-up period of over 20 years the two sisters presented persistent thrombocytopenia and minor bleeding events. Both of them had normal neurodevelopment with normal IQ.

TAR Syndrome is caused by a mutation of RBM8A gene. Individuals with TAR syndrome have a mutation in one copy of the RBM8A gene and a small deletion on chromosome 1 that includes the other copy of the RBM8A gene. TAR syndrome exists as a consequence of the deletion of a 200-kb region at chromosome band 1q21.1 and a second pathogenic variant of RBM8A on the other homologue chromosome. TAR Syndrome has an autosomal recessive inheritance pattern. In most cases the child inherits a 200kb deletion on 1q21.1 from one parent and a pathogenic variant of RBM8A from the other parent, in other cases the deletion on 1q21.1 appears de novo and the child inherits on the other homologue chromosome a pathogenic variant of RBM8A gene. In our presented cases the most probable mechanism is the first one, considering the fact that the couple had a child from the first pregnancy with clinical manifestation that were similar to the manifestation of TAR syndrome. The two girls have clinical and paraclinical manifestation that lead to the diagnosis of TAR Syndrome. They did not present cardiac malformations or mental retardation. The risk of recurrence of TAR Syndrome in a future pregnancy is 25%.

CONCLUSION

We presented the case of two twin non-identical sisters affected by TAR Syndrome. In the presence of bilateral radius agenesia and thrombocytopenia the physician should suspect TAR Syndrome, exclude other syndromes with similar characteristics, give the proper advice considering treatment and prevention of bleeding complications and direct

the parents to a geneticist for confirmation of the syndrome and genetic counselling.

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