CASE REPORT

Thrombocytopenia Absent Radius (TAR) Syndrome

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**Aim:** The aim of the work was a presentation of one case with Thrombocytopenia absent radius (TAR) syndrome. **Methods:** Diagnosis of TAR syndrome has been established on the basis of pedigree, laboratory findings (hemogram, platelet count, peripheral smear), bone marrow biopsy, radiological examination and karyotype. **Results:** A patient was a two months old female child, hospitalized due petechial bleeding, upper limb anomalies and diarrhea. Laboratory findings: red blood cell count was 2.1 x 1012/L, hemoglobin value was 62 g/L, white blood cell count indicated the existence of leukemoid reaction (40.0 x 109/L), the eosinophil count at the leukocyte formula was increased (3%), bleeding time was prolonged (10'). The platelets at the peripheral blood smear were rarely present, whereas the megacaryocytes appeared in the bone marrow aspiration in the decreased number, or did not appear at all. At the radiological examination of the upper limbs, radius was absent in both shoulders. **Conclusion:** TAR syndrome is a rare hereditary disease. obligatory clinical manifestations are: thrombocytopenia and bilateral absence of the radius. Prenatal diagnosis can be established during the 16th week of gestation by ultrasound and if it is continued with the pregnancy it is preferred that the platelet transfusion be given intrauterine. The mortality rate depends on the age of the patient and the platelet count. **Key words:** TAR syndrome, thrombocytopenia, absent radius.

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1. **INTRODUCTION**

Thrombocytopenia absent radius (TAR) syndrome is a hereditary genopathy which is still unknown, but the hereditary model is extremely similar to the autosomal recessive heritance (1, 2, 3). However, the increase in the number of cases with TAR syndrome among marriages in blood relationship is not recorded, as it is the case with diseases that are inherited in an autosomal recessive manner. On the basis of the results of genetic researches of several authors (4, 5, 6, 7, 8, 9, 10, 11, 12) it has been proved that TAR syndrome is tied with microdeletion in 1q 21.1, but it is not sufficient to cause TAR syndrome. It is assumed that the patients with TAR syndrome suffered from two genetic changes: one microdeletion of the long arm chromosome has been identified and one rather frequent change of the genetic material or polymorphism of genetic material, which still has not been discovered. Region of the minimal deletion of chromosome 1 (1q 21.1) of 200 kb among patients with TAR syndrome includes at least 12 known genes: HFF2, LIX L, PIAS3, ANKRD35, ITGA10, RBMA8A, PEX11B, OLR3L, TXNIP, GNRRL1 and NUDT1. The biggest number of patients with TAR syndrome suffered from deletion of more that 55 kb which occupies the telomere of the long arm of chromosome 1, including also 5 genes of minimal deletion of 200 kb.

2. **AIM**

The aim of the work was a presentation of one case with TAR syndrome treated at the Pediatric Clinic.

3. **METHODS**

For the disease diagnosis, the following are used: anamnesis, physical examination, radiological examination, laboratory findings (hemogram, platelet count, peripheral smear), bone marrow aspiration, pedigree and karyotype (was done from peripheral blood lymphocytes).

4. **CASE PRESENTATION**

Patient (C. Q), 2 months old, weight 4450 g (50 percentile), height 54 cm (5-25 percentile), has been hospitalized at the Pediatric Clinic in Prishtina due to petechial bleeding, brusing in the forehead, upper limb anomalies and diarrhea (Figure 1). She has been a sixth child of the sixth pregnancy, three of which ended with abortion and two children died 6 days after the birth due to the intracranial bleeding, whereas the family did not admit the existence of hereditary disease (Figure 2).
Laboratory findings: red blood cell count has been 2.1 $\times 10^{12}$/L, hemoglobin value 62 g/L, white blood cells showed leukemoid reaction (40.0 $\times 10^{9}$/L), eosinophile count in the leucocyte formula has been increased (3%), bleeding time was prolonged (10’). Hypochromia, anulocytosis, anisocytosis, a great number of white blood cells have been noticed on the peripheral smear, whereas the platelets were absent (Figure 3).

At smear of the bone marrow aspiration, megacaryocytes were absent (Figure 4). Other laboratory tests showed referential values.

The radius was not present during the radiological examination of the upper limbs, radial deviation of hand is evident, humerus, metacarpal and phalangeal bones were present without changes (Figure 5). Other radiological changes on other bones of skeleton were not identified, as well as the other anomalies on organs.

Bacterial, viral and parasite examination of feces did not reveal the existence of bacteria, viruses and parasites. The patient was fed with the cow’s milk, which was pasteurized. Patient had persistent diarrhea due to cow’s milk allergy. The diarrhea was stopped after the patient was fed with the hypoallergenic milk formula.

Karyotype was normal 46.XX (Figure 6).

During a one month period of hospitalization, a patient went through the phases of exacerbation and remission of the thrombocytopenia and anemia. During the exacerbation, several platelet transfusions and concentrated red blood cell transfusions were given. After the treatment with platelet transfusions, the platelet count increased maximum to 54.0 $\times 10^{9}$/L (much lower than the referential value), red blood cell count increased up to 4.1 $\times 10^{12}$/L. However, after a short time period their number decreased again. White blood cell count was 40.4 $\times 10^{9}$/L, whereas the lowest count was 11.5 $\times 10^{9}$/L.

Despite the fact that the measure for treatment of a patient with TAR syndrome were taken, the patient’s health condition deteriorated after one month. The patient was somnolent, hypotonic, her breathing was not spontaneous, she was pale and the generalized seizures appeared. Computed tomography of the brain has been done and it showed the intracranial bleeding (Figure 7). The endotracheal intubation has been done accordingly. Despite the intensive medical care, the patient went in coma, and after two days she passed away.

5. DISCUSSION

Case presentation of TAR syndrome included the presentation of the main clinical manifestations and diagnostic criteria for the diagnosis of the TAR syndrome. Upper limbs anomalies were variable, whereas the bilateral absence of radius was a constant characteristic of all cases with TAR syndrome (4).
At our case karyotype was normal (46, XX). According to the findings of several authors (4, 12), two out of 16 of the patients with TAR syndrome had abnormal karyotype. One case was with karyotype 46, XY, dup (8) (p 23.1, p 23.1), whereas the other case had a karyotype with translocation de novo, 46, XY, t (1;7) (q 42; p15).

Other upper limb anomalies (aplasia and hypoplasia of ulna and humerus, hypoplasia of carpal bones, sindactyly, clinodactyly are rare (1, 2). Lower limb anomalies were not present in our case. However, the frequency of appearance of the lower limb anomalies (hips dysplasia, femoral and tibial torsion, pes equinovarus and equinovalgus and knee deformations) may be present in 47% cases (4, 6).

Our patient was on artificial food (she was fed with pasteurized cow’s milk), during the hospitalization she had diarrhea although the feces did not contain any bacteria, viruses, parasites and funges. Our patient suffered diarrhea due to allergy to cow’s milk. Combination of TAR syndrome with cow’s milk allergy appeared at 47% of cases (1, 4, 9).

Congenital heart anomalies (tetralogia Fallot, atrial and ventricular septum anomalies) appeared in 22-33% of the cases (1, 4), at our case it was not present. Urinary tract and genital anomalies appeared in among 3-23% of cases (1). Two cases lacked uterus, kidneys were in the form of horse shoe, ureter duplex, dilatation of pelvis etc. Face anomalies (micrognathia, face hamangiomia, hypertelorismus etc) were nor present in our case. On the other side, other authors (10) have encountered those in 53% of cases with TAR syndrome.

All changes of limbs and other organs of TAR syndrome that were here described can be present at the syndromes and other diseases (Holt-Oram syndrome, anemia Fanconi, Roberts syndrome, Aase syndrome, Blackfan-Diamond syndrome, embriopathy due to thalidomide etc.), which may be considered with the differential diagnosis with TAR syndrome.

TAR syndrome without thrombocytopenia does not exist, but the platelet count varies from case to case. In our case, the lowest count was 9.0 x 10^9/L. Other authors (4) recorded the platelet count from 7-92 x 10^9/L.

The most frequent cause of mortality among children with TAR syndrome was bleeding. The rate of mortality depends on the platelet count and other accompanied anomalies. According to the studies (2,10) out of the total number of patients with TAR syndrome (7), 20 patients died due to the platelet count (< 10 x 10^9/L).

The most frequent cause of death was due to the intracranial bleeding, especially during the first two years of life. If the thrombocytopenia is adequately treated, it shall subsequently appear to be weaker and rarer. And with surgical, orthopedic interventions and physical therapy, a child with TAR syndrome may live a normal life. Mental retardation was present in only 7% of children with TAR syndrome. It is believed that mental retardation is of secondary nature due to intracranial bleeding caused by the thrombocytopenia.

6. CONCLUSION

TAR syndrome is a rare hereditary disease. Bilateral aplasia of radius and hypo or amegakaryocytic thrombocytopenia are the obligatory manifestations of TAR syndrome.

Prenatal diagnosis can be established on the 16th week of the gestation by the ultrasound and cordocentesis (blood is taken for the analysis by which it is verified thrombocytopenia and karyotype is done), which is important for bringing decision on termination of pregnancy. If continued with the pregnancy, the platelets shall be intrauterine given, and the birth shall be done in a Cesarean manner (3, 7).

The mortality rate is tightly connected with the number of platelets and association with other anomalies on the other organs (4). The frequency of the episodes of the thrombocytopenia and...
the risk of the typical complications are the highest during the first two years of life. After this age the episodes of thrombocytopenia decreases and with the surgical interventions, orthopedic, physical therapy and the regular hematological examinations, the patient may lead a normal activities (5, 8).

REFERENCES