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CASE REPORT

Pearson Syndrome, A Medical Diagnosis Difficult to Sustain Without Genetic Testing

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SUMMARY

Background: **The detection of sideroblastic anemia in a newborn may suggest developing Pearson syndrome. The prognosis of these patients is severe and death occurs in the first 3 years of life, so it is important to find new ways of diagnosis.**
Case Presentation: **In the case of our patient the diagnosis was supported only at the age of 5 months, highlighting the difficulties of diagnosis at this age.**
Conclusions: **The diagnosis of Pearson syndrome with neonatal onset is difficult to sustain or even impossible at that age. This diagnosis can be confirmed and supported during disease progression.**
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KEY WORDS

newborn, sideroblastic anemia, pancytopenia, pancreatic insufficiency newborn, sideroblastic anemia, pancytopenia, pancreatic insufficiency

INTRODUCTION

Pearson syndrome is a mitochondrial disease characterized by sideroblastic anemia, vacuolization of hematopoietic precursors and exocrine pancreatic insufficiency [1]. The mechanism of this syndrome is a deletion in mitochondrial DNA. The severity of this disease depends on the number of mutant mitochondrial DNA molecule present in the cells. Pearson syndrome is transmitted by maternal inheritance [2]. The causes are known to be rare and it is manifested as a multisystemic disease and mitochondrial cytopathy with anemia, neutropenia, and thrombocytopenia as well as variable hepatic, renal, and endocrine failure and early death, usually in infancy. Pearson syndrome is very rare, less than a hundred cases have been reported in medical literature worldwide [3,4].
The hematological symptoms begin during infancy, but only a few of newborns with hematological symptoms

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have been described. Pearson syndrome is actually a marrow failure characterized by neutropenia and thrombocytopenia. The patients usually have a macrocytic sideroblastic anemia and require transfusion. The marrow examination highlights a normal or increased number of erythroid precursors with characteristic vacuolization of hematopoietic precursors and ringed sideroblasts [5,6].

Patients also have an exocrine pancreatic insufficiency secondary to fibrosis with malabsorption and diarrhea or a defect of oxidative phosphorylation with lactic acidosis. Other organs may be affected simultaneously or in the course of the disease. Patients may develop kidney disease such as tubulopathy and aminoaciduria. They can also present with liver injury along with hepatomegaly, cytolysis, and cholestasis. Pearson syndrome may also have endocrine and neuromuscular disorders. Patients can develop cardiac or splenic disease [5,7-9]. The main cause of this syndrome is linked to mitochondrial DNA deletions. Distribution of the mitochondrial DNA during cell division is responsible for the common presence of normal and mutant DNA within a cell. This coexistence called heteroplasmy explains the great variability of clinical expression [2,8]. A specific treatment of Pearson syndrome does not exist. Death often occurs before the age of three. Causes of death are sepsis, lactic acidosis, and liver failure [10].

CASE PRESENTATION

We present the case of a male patient, who was diagnosed with Pearson Syndrome in the Pediatric II Clinic in Cluj Napoca.

The child comes from a family with healthy parents. He also has a 7-year-old healthy brother. The pregnancy had a physiological evolution with vaginally birth at term and breast milk nutrition until the age of five months. The disease onset occurred soon after birth. Lab investigations had indicated that the value of hemoglobin was 11.6 mg/dL at just one week after birth. Clinically the child presented pallor but simultaneously he had a yellowing of the mucous membranes because of the physiological jaundice with a high level of indirect bilirubin. Evaluation of the hematological parameters at the age of 3 weeks showed the level of hemoglobin as 8.6 mg/dL and normal number of leukocytes and thrombocytes. At the age of 1 month the child was sent to the Pediatric II Clinic where the results showed the level of hemoglobin at 6.9 mg/dL, MCV = 102.7 fL, 7,600/μL leukocytes and 162,000/μL thrombocytes. Liver samples were normal. The sideremia was 89 μg/dL and ferritin blood level was 499.1 ng/mL, which is an increased level. Direct and indirect Coombs tests were negative.

The patient presented in our medical service with important pallor, tachycardia with a heart rate of 170 beats per minute, and hypotonia. Taking into account the clinical signs associated with a hemoglobin level of 6.9 mg/dL, the child received a blood transfusion after which the hemoglobin rose to 11.2 mg/dL.

One month after transfusion parents were back to our service because their child again presented intense pallor, weakness, difficulty eating, and tachycardia. The hematological parameters indicated a hemoglobin level of 7.6 mg/dL and MCV = 77 fL. Liver samples are normal, sideremia was 182 μg/dL, and ferritin was 952 ng/mL. Considering these values, a bone marrow aspiration was done and the smear analysis showed the presence of sideroblasts with 90% in Pearls coloration. These parameters made us think of Pearson syndrome or myelodysplastic syndrome. Based on these conditions the case was transferred to Pediatric Oncology Hematology, which confirmed the diagnosis of myelodysplastic syndrome. Substitution treatment with red blood cells was recommended and a return at the age of 1 year for a bone marrow transplant.

We mentioned that the fecal elastase determination was negative at 2 months after onset and the amylase level was normal. Blood pH showed no lactic acidosis. The patient returned to our services for monthly substitution treatment with red blood cells because the level of hemoglobin oscillated between 5 and 7 mg/dL.

At the age of 5 months, on the background of an upper respiratory tract infection with significant changes of clinical status, we detected the presence of fecal elastase and lactic acidosis. At the same time, the liver samples became abnormal and for the first time the leukocytes and thrombocytes decreased below the normal values (leukocytes = 3,200/μL, thrombocytes = 62,000/μL). At the age of five months, Pearson syndrome fully supported by ringed sideroblasts anemia, exocrine pancreatic insufficiency, hepatocytolysis syndrome, and pancytopenia appearance. The patient continued to receive monthly red blood cell transfusions, maintaining pancytopenia, and pancreatic insufficiency, validated by a stagnant weight, voluminous stools, liver damage. At the age of 1 year, the patient weighed 7.4 Kg. Iron and ferritin continued to increase. Through hematological degradation, the patient developed mycosis in the upper digestive tract (oral cavity, esophagus, and stomach) evidenced by upper digestive endoscopy, because the child vomited and refused food. Following treatment with Fluconazol intravenous 1 ampule per day for one week, the fungal lesions disappeared.

At the age of 1 year and 2 months the patient presented the signs of hemorrhagic syndrome validated by petechiae and ecchymosis on the trunk, nosebleeds, bleeding gums and through the digestive tract (hematemesis and rectal bleeding). At this time the level of thrombocytes was 8,000/μL. He required administration of platelets and Factor VII. After 3 days of substitution, the level of thrombocytes reached 60,000/μL, the bleeding stopped and the petechiae and ecchymosis followed its evolution course. For a therapeutic opinion for eventual bone marrow transplant the case was directed to Oncology-Hematology department of Children's Hospital Timisoara where possibilities of bone marrow trans-

plant exist. Investigation of the case in this service confirmed the diagnosis of Pearson syndrome but did not recommend bone marrow transplantation. The case returned to our service and continued substitution therapy but because ferritin reached high levels (up to 4,000 ng/mL), the administration of iron chelators - deferasirox in dose of one tablet/day was started.

The child's clinical condition continued to deteriorate. Live failure started including low ceruloplasmin and transaminases over 200 U/L. The weight curve remained stationary, but the hematological parameters such as leukocytes reached 1,200/µL and thrombocytes 29,000/µL. Due to this clinical and biological altered state, the child developed hepatic failure, a hematological syndrome with digestive bleeding, and sepsis at the age of 1 year and 7 months. Resuscitation in the intensive care remained without result.

DISCUSSION

Pearson syndrome with neonatal onset is an entity where diagnosis is difficult from the beginning. In the case of our patient, anemia started immediately after birth [4]. At admission to our service we found a significant anemia with hemoglobin lower than 7 mg/dL. We excluded hemolytic anemia by performing direct and indirect Coombs tests that were negative. Others hematological parameters were normal as well as liver and kidney test. The first signs of Pearson syndrome occurred at 2 months of age when biological markers of bone marrow aspirate indicated the presence of sideroblasts by 90% in Pearls coloration.

To support Pearson syndrome diagnosis, we needed the presence of pancreatic insufficiency and the involvement of other organs and systems in the pathological process. To highlight the pancreatic insufficiency, we determined fecal elastase, which was negative, and the level of blood amylase, which was normal. Hematological parameters did not indicate leukopenia and thrombocytopenia, and blood pH did not reveal lactic acidosis. With these conditions, we thought of Myelodysplastic syndrome as a possible diagnosis. The latter would have more chances of success with therapy than Pearson syndrome. Only at five months old, pancreatic insufficiency was determined. At this age liver tests started to change and for the first time leukocytes and platelets dropped below the normal level for the age. The serial determinations of blood pH revealed lactic acidosis. So, at 5 months after disease onset, we confirmed the diagnosis of Pearson syndrome.

References about treatment options of Pearson syndrome are disappointing. Currently there is no treatment to stop the progression of disease [10]. We considered a bone marrow transplantation of pluripotent stem cells might be capable of producing healthy marrow precursors leading to better results and supporting organ function that may be affected in the evolution of the syndrome could also be beneficial.

CONCLUSION

The diagnosis of Pearson syndrome with neonatal onset is difficult to confirm or even impossible at that age. This diagnosis can be confirmed and supported during disease progression.

Declaration of Interest:
The authors have declared that no conflict of interest exists.
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