CASE REPORT

Clinical Case of Perinatal Diagnosis of Bourneville-Pringle Disease

NATALIYA PETROVNA PAVLOVA, ELENA ANATOLYEVNAMAKSIMTSEVA, NINA MIKHAILOVNAARTEMOVA, OLEG MIKHAILOVICHURYASIEV, VADIMANATOLEVICHLUNYAKOV, ALEXANDRA VICTOROVNASOLOVIEVA
Therapy Department, Ryazan State Medical University, Vysokovoltnaya str., 9, Ryazan, Russian Federation.
Correspondence to NataliyaPetrovnaPavlova, natusikryazan@gmail.com, +7-906-545-14-57, Vysokovoltnaya str., 9, Ryazan, Russian Federation

ABSTRACT

The article highlights the relevance of early diagnosis, dynamic observation and the possibility of pharmacological correction of polysystem manifestations of genetic disease. A clinical example of prenatal diagnosis of tuberous sclerosis, genetically confirmed, with multi-organ and polysystem lesions is presented.
Keywords: prenatal diagnosis, tuberous sclerosis, heart rhabdomyoma, hamartoma

INTRODUCTION

Bourneville-Pringle disease, tuberous sclerosis, is a genetically determined disease characterized by hyperplasia of meso-, ectoderm derivatives with the formation of benign tumors (hamartomas) of the brain, eyes, skin and internal organs[1]. The disease has an autosomal dominant mode of transmission, along with this,there are de novo mutations in the genes TSC1 and TSC2[2,3].

The basic and additional criteria of diagnostics, methods of genetic analysis are well known, protocols of management and treatment of this pathology, including preventive, are offered. All this allows timely diagnosis and control of such a rare disabling disease with a progressive course. It is known that tuberous sclerosis type 2, caused by a mutation of the TSC2 gene, is characterized by early clinical manifestation and severe progressive course. Clinical cases of early and late onset tuberous sclerosis are presented in the medical literature[4,5].

In infants and children the pathology often manifests with heart damage, is often accompanied by affection of the nervous system and subsequently dominates. The appointment of preventive antiepileptic therapy in the detection of tubers in the brain contributes to the reduction of epileptiform activity and the prevention of intellectual disturbances[6]. In half of the cases of tuberous sclerosis, heart rhabdomyomas are detected, while among all rhabdomyomas, tuberous sclerosis is the cause in 86% of cases[7]. Often, cardiac arrhythmia may be the first and one of the few manifestations of Bourneville-Pringle disease[8].

A clinical case of prenatal diagnosis of orphan disease, genetically confirmed, with multi-organ and polysystem lesions is presented.

CASE REPORT

Clinical observation began with the intrauterine period of the patient's development, after the detection of multiple rhabdomyomas of the heart at 20 weeks of pregnancy. Perinatal history is burdened by the threat of termination of pregnancy at 32-33 weeks, a long anhydrous period, urgent Caesarean section. At birth, the child's weight was 3810 grams, body length 53 cm, Apgar score 7/8 points, gray hair was on a nape. On the 10th day, anmagnetic resonance imaging (MRI) of the brain was performed, nodular hamartomas of the retina of both eyes were revealed, and the diagnosis of Tuberous sclerosis was made. No productive symptoms were observed. With months of age there were areas of hypopigmentation of the skin the subsequent with a tendency to progression. Electroencephalographic examination at the age of 1 month revealed no changes. At the age of 5 months during electroencephalographic video monitoring daytime sleep (March, 2018) epileptiform activity was revealed in the form of sharp waves left central-parietal, central and frontal areas.Anticonvulsant therapy was started: vigabatrin 500 mg per day with gradual dose up to 1000 mg per day.

MRI of the brain with contrast showedsigns of tuberous sclerosis with the presence of cortical, subcortical multiple tubers in both hemispheres with the formation of cysts in some of them, subependimal nodes in the lateral walls of the lateral ventricles of the brain.

Electrocardiography (ECG) data were migration of supraventricular rhythm driver, single supraventricular polytopeextrasystoles, incomplete right bundle branch block, early ventricular repolarization syndrome.

Ultrasound examination of the heart revealed hyperechogenic formations not associated with blood flow (rhabdomyomas) in the cavity of the left ventricle 13.1×9.7 mm and 3.1×4.1 mm, in the cavity of the right ventricle 3.4×3mm and 3.5×3.4 mm without signs of obstruction of the outflow tract. There were signs of apatentforamen ovale(diameter 2.7 mm)with hemodynamically insignificant left-to-rightshunting. The heart chambers are not dilated. Systolic and diastolic functions of ventricles are not impaired.

Conclusion of daily ECG monitoring at the age of 6 months: average heart rate during the day 150 beats per minute, average heart rate at night 116 beats per minute, average heart rate per day 134 beats per minute, supraventricular extrasystoles - 14898 per day, 7 sinus pauses at night period with maximum duration up to 1188 ms. Genetic analysis revealed a mutation in the TSC2 gene.

Postnatal examination has allowed to confirm the diagnosis of tuberous sclerosis, symptomatic multifocal epilepsy, multiple rhabdomyomas of both heart ventricles, patentforamen ovale, supraventricular extrasystoles.

Three months later at the age of 7 months(June, 2018) the onset of focal seizures was in the form of bout of fading on respiratory viral infection with febrile fever. The dose of vigabatrin has been increased up to 2500 mg per day since July 2018, two additional anticonvulsants (valproic acid 200mg per day, levetiracetanum 300 mg/day)

were prescribed.Positive dynamics in the form of reduction of seizures was noted. From 1 year of life (October, 2018) the attacks in the form of fading eyes, torso tilt forward followed by paresis in the right hand lasting up to 1 minute The number of attacks decreased after the withdrawal of valproic acid.

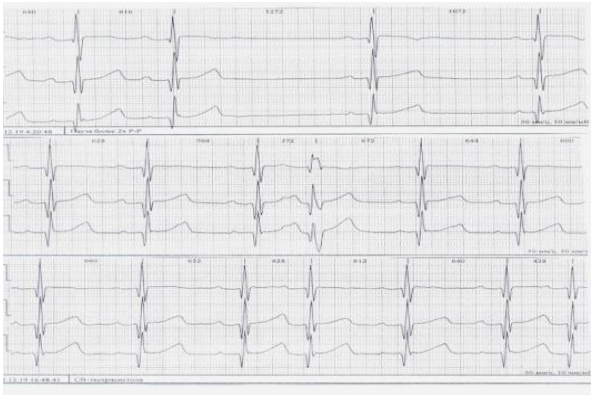
There is a mixed circadian rhythm profile, a decreased amount of extrasystoles against the background of increased heart rate, supraventricular extrasystoles-7857 per day (up to 618 per hour of observation), 1473supraventricular extrasystoles with aberrant conduction, 29 sinus pauses at night with maximum duration up to 1200 ms during daily ECG monitoring at the age of 1 year 5 months.

During daily ECG monitoring at the age of 2 years 2 months there were episodes of sinus arrhythmia, supraventricular extrasystoles 3417 per day (up to 505 per hour of observation), 1815supraventricular extrasystoles with aberrant conduction, 9 sinus pausesat night with maximum duration up to 1272 ms.

Ultrasound examination of abdominal cavity revealed: angiomyolipomas, primary kidney cysts, hepatosplenomegaly, enlarged lymph nodes in the portal fissure, abnormality of shape and enlargement of the gallbladder. Mutations were not revealed duringmolecular genetic study of the family members.

Despite the detection of multiple rhabdomyomas of both ventricles, the absence of outflow obstruction, as well as signs of pronounced intramural tumor growth was the reason for the choice of conservative tactics of patient management. In the future, MRI of the heart is appropriate to determine the degree of myocardial invasion by the tumor. Heart disorder is accompanied by rhythm disorders with supraventricular arrhythmia, migration of supraventricular pacemaker, pauses of heart rhythm, which significant for children of this age, as well as a violation of the conductivity type of incomplete right bundle branch block(Fig.1).

Figure 1.Fragment of daily ECG monitoring with registration of 1272ms sinus rhythm pause, supraventricular extrasystole, 03.12-04.12.2019.



In dynamic observation, there is some regression in the number of supraventricular extrasystoles on the background of metabolic therapy.

The child is under the dynamic supervision of a neurologist, cardiologist, pediatrician with regular control studies, which allows timely correction of treatment.

DISCUSSIONAND & CONCLUSION

The diagnosis of tuberous sclerosis is undoubted already in the presence of two main or one main and two additional criteria (2012 TSC Clinical Consensus Conference). The patient for a short period of observation were identified five main signs of the disease: hypopigmental spots, multiple retinal hamartomas, cortical tubers of the brain, rhabdomyomas of the heart, kidney angiolipomas and two additional criteria-kidney cysts and gray hair on the head. Genetic analysis revealed a mutation in the TSC2 gene.

The described clinical case will contribute to the accumulation of data on prenatal manifestations of multi-organ lesions of neurodegenerative disease Bourneville-Pringle. Early detection of the disease will allow to adjust the tactics of pregnancy, to provide adequate medical and genetic counseling of the family, which helps to reduce the frequency of birth of children with severe forms of tuberous sclerosis.

Declaration of author's competing interests: The authors declare no conflict of interest.

REFERENCES

1. Dorofeeva M.YU., Belousova E.D., Pivovarova A.M. Recommendations for diagnosis and treatment of tuberous sclerosis.Journal of neurology and psychiatry 2014; 114(3):58-74.
2. Rosset C., Netto C.B., Ashton-Prolla P. TSC1 and TSC2 gene mutations and their implications for treatment in Tuberous Sclerosis Complex: a review. Genet Mol Biol. 2017; 40 (1): 69-79.doi: 10.24411/2074-1995-2019-10008.
3. Janus G.A., Suspitsyn E.N., DorofeevaM.Yu., et al. Molecular diagnosis of tuberous sclerosis. Pediatrician 2013;4(1):3-8.
4. Zobikova O.L., Pribushenya O.V., Buchel Y.Y. Prenatal diagnosis of tuberous sclerosis in the third trimester of gestation. Prenatal Diagnosis. 2017; 16 (4): 347-51.
5. Mullahmetova O.A., Zykov S.Y., Trushnikova R.V. Pringle-Bourneville disease. radiology case report in a pregnant woman. REJR. 2016; 6 (4):144-149. doi:10.21569/2222-7415-2016-6-4-144-149.
6. Grigoryeva A.V., DorofeevaM.Yu., Gorchkhanova Z.K., et al. Preventive antiepileptic therapy in patients with tuberous sclerosis. Russian journal of pediatric neurology 2017;12(2):34-39. doi: 10.17650/2073-8803-2017-12-2-08-20
7. Belozerov Yu. M., Leontieva I. V., Bregel L. V., Subbotin V. M. Tumors of the heart in children. Ulyanovsk: Zebra, 2016. - 107 p.
8. Sharykin A.S., Shilykovskaya E.V., Popova N.E. Successful elimination of supraventricular rhythm disorders in an infant with cardiac rhabdomyoma. Bulletin of the National medical and surgical Center. N. I. Pirogova 2011; 6(4):132-135.