TEMPLE SYNDROME AND IN VITRO FERTILIZATION - CASE PRESENTATION -

MARIA ALEXANDRA ŞTEFAN[1]*, ALEXANDRA BUICĂ[2]

[1]Resident doctor in Child and Adolescent Psychiatry, "Prof. Dr. Alex. Obregia" Psychiatry Hospital, Child and Adolescent Psychiatry Department, Bucharest

[2]Assistant Prof., Child and Adolescent Psychiatry Department, University of Medicine and Pharmacy, Bucharest

ABSTRACT

Temple syndrome or maternal uniparental disomy of chromosome 14 (upd(14)mat) is a rare imprinting disorder caused by aberrations at the 14q32.2 imprinted region, characterized by low birth weight, growth failure, hypotonia and motor delay, feeding difficulties and early puberty. In vitro fertilization (IVF) with donor eggs is a laboratory technique consisting in fertilising previously harvested donor eggs with partner's sperm.

This paper presents the case of a one year and nine months patient admitted to the Child and Adolescent Psychiatry Department of the "Prof. Dr. Al. Obregia" Psychiatry Hospital from Bucharest. The main symptoms the patient presented were delay in expressive and receptive language development, feeding difficulties, growth failure and the inability to initiate and maintain social contact with other children. The data obtained from the family history, clinical examination, paraclinical investigations results, mental state evaluation and neurogenetic analysis suggested the diagnosis of Temple syndrome. In presenting this case, we are trying to highlight that enhanced comprehensive screening can exclude a significant number of candidates from an oocyte donor program and should be encouraged to assure optimal short-term and long-term outcomes for pregnancies achieved through oocyte donation.

INTRODUCTION

The human chromosome 14q32.2 region carries maternally and paternally expressed genes (PEGs and MEGs), together with the germ-line-derived DLK1-MEG3 intergenic differentially methylated region (MEG3/DLK1:IG-DMR) and the postfertilization-derived MEG3:TSS-DMR, function as imprinting control centers in the placenta and the body.

Since the first reports of Temple et al in 1991, a well characterised clinical phenotype has emerged for both maternal uniparental disomy of chromosome 14 (UPD14) [1]. Maternal uniparental disomy 14 (UPD(14)mat) results in a constellation of clinical features such as intrauterine growth retardation (IUGR), low birth weight, growth failure, hypotonia and motor delay, feeding difficulties in the neonatal period; and failure to thrive and developmental delay—particularly in relation to speech—in early childhood.

Premature puberty, with short stature and truncal obesity, but normal intelligence, were the key features in teenage years. Facial features include a broad forehead and short nose with a wide nasal tip, and the majority of patients have small hands and feet. However, many of the clinical features are non-specific, making diagnosis difficult [2].

Corresponding author: Maria Alexandra Stefan, MD, Resident in Child and Adolescent Psychiatry Department, "Prof. Dr. Al. Obregia" Psychiatry Hospital, Bucharest, Romania, Address: Berceni street, no. 10-12, 041914, sector 4, Bucharest, email: sm.alexandra21@yahoo.com.

To minimize the potential for harmful inheritable conditions, donors should be rigorously screened according to standard guidelines, yet such guidelines may not be sufficient to exclude egg donors with certain known inheritable conditions. The specific tests performed on egg donors include detection of Cystic fibrosis, Spinal muscular atrophy, Tay Sachs/Hexosaminidase A deficiency, Sickle cell anemia, Beta-thalassemia, Bloom syndrome, Gauchers disease, Canavan disease, Fanconi anemia Type C, Mucolipidosis Type IV, Niemann Pick disease Type A and Fragile X syndrome [3].

CASE PRESENTATION

We report the case of an one year and nine months old girl suffering from Temple Syndrome.

The patient B.M.A accompanied by his parents, refers to our clinic in January 2018, due to delays in expressive and receptive language development, growth failure, feeding difficulties and inability to socialize properly.

Family medical history

- the mother, age 48, diagnosed with depression and hypothyroidism;
- the father, age 49, healthy;
- brother, age 8, healthy;
- twin sister dies at three weeks old of intracranial hemorrhage.

Psychological personal history

Second child, twin pregnancy obtained through in vitro fertilization with donated eggs (there are no medical records that can prove preimplantational genetic testing of the oocytes) with pathological evolution, birth at 28 weeks (caesarean section-preeclampsia), birth weight: 940 g, birth length: 34 cm, cranial perimeter: 27 cm, Apgar Score 3/5/7/7, difficult adjustment to extrauterine life. Delayed psychomotor development in different stages of age: she lifts her head at 6 months, sits upright at 9 months, walks unassisted at the age of one year and a half, after kinetotherapy intervention. The patient has no ability to pronounce words or sentences.

Pathological personal history

1. Myopia of both eyes with correction
2. Gastroesophageal reflux disease
3. Iron deficiency anemia

Mental State Examination

At the examination, the patient is uncooperative, although she can establish eye contact with the examiner she cannot verbally respond when her name is called. She can't execute simple or complex commands; absence of expressive language - she doesn't use words with meaning (babbling). Cognitive: she can't recognize animals, colours, can't show objects around her, can't show hers or somebody else's body parts.

Presents difficulties with basic skills such as eating, undressing and using the potty. Socialization: she hardly accepts the presence of other people/children, hiding behind his father, she cannot initiate play with other children and she prefers to play alone. During the examination, we observed the absence of pointing or waving goodbye. Motor behaviour: hypokinetic behaviour, cries easily and for extended periods of time, often due to a lack of understanding.

Neurogenetical examination

No signs of meningeal irritation, masticatory deficiency, possible walking (postural with broader base of support), lack of balance, muscular hypotonia; clinical particularities, suggestive for Temple syndrome.

EEG line performed while the patient was awake - without pathological graphic elements.

Psychological assessment

The diagnosis was instrument by assessing the child's pathology with PORTAGE instrument, which revealed Mental Age = 11 months.

The positive first axis diagnosis was set to Temple syndrome and second axis: Global developmental delay. Parental Hyperprotection was set on the fourth axis.

The two imprinting syndromes Temple syndrome (TS14) and Prader–Willi syndrome (PWS) share many features in infancy and childhood. TS14 is an important, yet often neglected, differential diagnosis to PWS. Temple syndrome is presumably underdiagnosed, and should be considered when testing children for PWS [2]. Clinical characteristics excluded Prader-Willi syndrome diagnosis. The Global developmental delay should be differentiated from Autism spectrum disorder (non-significant ADOS instrument results, absence of stereotypes and the presence of mentally contact exclude such diagnosis), Landau-Kleffner syndrome (EEG-without pathological graphic elements) and sensory disturbances (deafness-normal audiogram; blindness). The practitioner could potentially diagnose Global developmental delay as a somatic or neurological disorder (cerebral palsy, hydrocephalus, severe cortical agenesis, genetic disorders like phenylketonuria or metabolism disorders - metachromatic leukodystrophy, tuberous sclerosis) but laboratory tests were within normal limits and excluded these diagnoses. [4]

Psychopharmacological treatment:

During hospital admission, the patient didn't receive neuropsychiatric treatment, only Omega-3 Fish Oil Supplements. During hospitalization, psychological intervention was based on teaching the parents several special educational techniques for cognitive stimulation therapy at home. They were encouraged to limit the time spent by the patient in front of the TV and other media devices. Discharge recommendations consisted in continuing neurotrophic supplements and kinetotherapy, applied behavioural therapy, speech therapy and cognitive stimulation therapy at home.

Prognosis and evolution:

The evolution of the patient may be favourable if the family complies with the recommendations. As positive prognostic factors, we can mention family support and early intervention. Because of the presence of incurable genetic syndrome and a mother suffering from a mental illness, a negative outcome is expected.

CONCLUSIONS

In presenting this case we want to highlight the importance of an enhanced comprehensive screening of egg donors and of preimplantational oocytes in order to avoid mental disorders and other diseases caused by a genetic syndrome.

REFERENCES

1. Ioannides Y, Lokulo-Sodipe K, Mackay DJ, Davies JH, Temple IK. Temple syndrome: improving the recognition of an underdiagnosed chromosome 14 imprinting disorder: an analysis of 51 published cases. J Med Genet 2014;51:195–201.
2. Wang JCC, Passage MB, Yen PH, Shapiro LJ, Mohandas TK. Uniparental Heterodisomy for Chromosome-14 in A Phenotypically Abnormal Familial Balanced 13/14 Robertsonian Translocation Carrier. American Journal of Human Genetics 1991; 48(6):1069-1074.
3. Herbert M, Kalleas D, Cooney D, Lamb M, Lister L. Meiosis and maternal aging: insights from aneuploidy oocytes and trisomy births. Cold Spring Harb Perspect Biol 2015;7:1–20.
4. Dobrescu I. (2016), Manual de psihiatrie a copilului si adolescentului, Ed. Total Publishing Bucuresti.