P2-338 DIAGNOSTIC AND FOLLOW-UP PROBLEMS OF MEDICAL CARE FOR PRADER-WILLI SYNDROME CHILDREN IN RESOURSE-LIMITED SETTINGS

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INTRODUCTION

Prader-Willi syndrome (PWS), a multisystem disorder, results of the absence of expression of paternal genes from chromosome 15q11.2-q13; it occurs with the prevalence of 1/10000-1/30000 in different populations. In real clinical practice PWS still remains a challenge for doctors, especially in resource-limited settings. In Belarus, PWS is underdiagnosed; its real rate is unknown.

AIM AND METHODS

We analyzed and described clinical course and care problems in 10 pediatric PWS patients (3M; 7F) aged 7,4±3,3 years (1,7÷12,3), all have microdeletion of paternally inherited 15q11.2-q13 region. Mean follow-up time is 4,1±2,6 years (0,5÷7,6).

All patients are under follow-up and receive treatment with growth hormone (GH) in a specialized paediatric and adult's endocrinology center in Minsk.

RESULTS

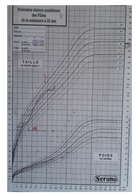
CHARACTERISTICS OF THE PATIENTS IN PERINATAL PERIOD

gestational intrauterine hypoxia – 10/10
IUGR – 5/10; C -section - 6/10
severe muscle hypotonia as neonates – 10/10 needed feeding tubes as neonates – 10/10
chriptorchidism in boys at birth – 3/3
Neurological/ clinical genetic exam as neonates – 10/10
no one baby was diagnosed by geneticists with PWS in neonatal period

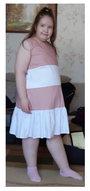
FEATURES OF THE PATIENTS UNDER FOLLOW-UP

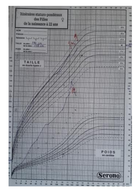
facial dysmorphism, hypotonia, speech delay – 10/10
overweight / obesity before 2 y.o. – 9/10
GH treatment - 10/10
mean time on GH - 1,9±1,2 (0,3÷3,5) y.
1st y. GV with GH - 10,7±1,1 cm/ year
central hypothyroidism – 5/10
central adrenal insufficiency – 0/10
day and ? night sleep apnea (clinically) – 3/10; more?
polysomnography – 1/10
premature adrenarche - 3/7 girls
metformine treatment – 2/10
scoliosis – 4/10
orchidopexy - 3/3 boys
self-picking – 4/10
psychiatric medication – 1/10





Patient N.D.
At the age of 2 years (no GH) and 6,8 years (after 3,3 years of treatment with GH – an impressing improvement in growth, body composition, behavour, metabolic control, neuro- and speach development)





Patient K. S.
At the age of 11,8 years (no GH) and 12,6 years (after 9 months of treatment with small doses of GH – an improvement in body composition - 10 kg of wheight loss, 6 cm plus in growth; easier eating and general behaviour control and better metabolic parameters)

N.D. story

the 1st pregnancy (i/u hypoxia),
the 1st delivery at 36 wks by CS
BW 2150 gr, BL 44 cm
muscle hypotonia since birth,
feeding tube for 1,5 mo.
genetic diagnosis – at 0,4 y.o. - PWS confirmed
MPH - 0,75 SDS
excessive weight gain – after 2 y.o, even with strong eating behaviour control; no obesity in the family

	at GH start	at GH stop	at GH restart
Age,y.o.	3,3	6,8	8,1
Mean GV, cm/	4,0	9,2	0
GH dose, mg/kg/m2	-	1,2	0,6
H-SDS	-1,75	1,0	-1,0
BMI-SDS	+1,3	-1,0	-0,5
IGF-1-SDS	-1,0	**2,6**	-1,8
BA/CA	0,6	**1,1**	1,0
PA, y.o.	-	**6,3**	slow progress
Sleeping problems	??	**7,6**	**not repeated**
Polysomnography	NA	day sleep hypopnoe	under planning
LT4	±	+	+
Scoliosis	-	-	+

K.S. story

the 2nd complicated pregnancy
1st delivery at 41 wks by CS
BW 2600gr, BL 48 cm - IUGR
muscle hypotonia, feeding tube since birth
familial story of metabolic obesity and T2DM
excessive weight gain – after 1 y.o, no strong food control
genetic diagnosis – at 4,5 y.o. - PWS confirmed
MPH – 1,0 SDS
WAS SENT TO PED ENDO SPECIALIZED CENTER AFTER 11 Y.O.

	before GH	on GH
Age,y.o.	11,8	12,8
Mean GV, cm/y	3,0	6,0
GH dose, mg/kg/m2	-	0,25 to 0,4
H-SDS	+1,0	+1,1
BMI-SDS	+3,2	+2,8
IGF-1-SDS	**-2,5**	**-1,8**
BA/CA	1,1	1,1
Tanner stage	1 (B1P2Ax2)	2 (B2P3Ax3)
Sleeping problems	??	??
Polysomnography	NA	under planning
LT4	-	+
Scoliosis	-	?

PATIENTS' (n= 10) CHARACTERISTICS at the AGE of GENETIC DIAGNOSIS, BEFORE and on GH TREATMENT

Parameter	Molecular genetic diagnosis	The 1st visit to pediatric endocrinologist	At the start of GH treatment	The last visit on GH treatment
mean age, years	2,4±1,9 (0,4÷6,3)	3,2±1,6 (0,5÷5,4)	5,2±2,9 (1,0÷11,8)	7,4±3,3 (1,7÷12,3)
Height-SDS	-0,4±0,3	-0,1±1,1	-0,3±1,4	0,7±1,7
BMI-SDS	0,3±1,0	2,2±1,3	2,2±1,0	1,8±1,2
IGF-1 SDS	-	-	-0,9±1,8	0,5±1,5
BA/ CA	-	-	0,7±0,3	0,9±0,3
GH dose, mg/m2/day	-	-	1,1±0,4*	0,7±0,4**

* - GH dose was calculated as syndromic in some patients (in mg/kg/week) first;
** - GH dose was recalculated; including the pts after GH restartment

Reasons for GH interruption (5/10)

- high IGF-1 level when on GH
- BA progression
- high metabolic risks
- not enough compliance of patients' family

Reasons for GH restartment (5/10)

- good families' compliance
- poor growth velocity
- weight gain
- more difficult eating behavior control
- muscular hypotonia worsening
- speach development retardation

CONCLUSIONS

- **Poor awareness and lack of knowledge** about **PWS** in different paediatric specialists (neonatologists, general paediatricians, neurologists, even geneticists) leads to **a delayed PWS diagnosis** and postponed treatment / rehabilitation of the children. **Education of medical professionals is mandatory.**
- Severe perinatal muscular hypotonia at any age, feeding neonatal problems, chriptorchidism in boys since birth, as well as developmental delay and overweight / obesity early in life are **strong indications for PWS genetic diagnosis**.
- As **PWS** patients may have different endocrine problems and GH is a recognised treatment for children and adolescents, **the earlly 1st visit to paediatric endocrinologist** is beneficial for the patients.
- **PWS** is a condition that requires **life-long medical and social patients' support**, a unique **multidisciplinary care system is required.**
- **The fondation of PWS families' organization in Belarus,** with professional medical, legal, social support would help to attract more attention of the society to **special needs** of our patients , to facilitate **access to diagnostic /treatment and improve quality of life in PWS .**

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