МЕЖДУНАРОДНЫЙ ЦЕНТР НАУЧНОГО СОТРУДНИЧЕСТВА
«НАУКА И ПРОСВЕЩЕНИЕ»

НАУКА и ПРОСВЕЩЕНИЕ
МЕЖДУНАРОДНЫЙ ЦЕНТР НАУЧНОГО СОТРУДНИЧЕСТВА

МОЛОДОЙ УЧЁНЫЙ

СБОРНИК СТАТЕЙ V МЕЖДУНАРОДНОЙ НАУЧНО-ПРАКТИЧЕСКОЙ КОНФЕРЕНЦИИ,
СОСТОЯВШЕЙСЯ 23 ЯНВАРЯ 2024 Г. В Г. ПЕНЗА

ПЕНЗА
МЦНС «НАУКА И ПРОСВЕЩЕНИЕ»
2024

УДК 001.1
ББК 60
М75

Ответственный редактор:
Гуляев Герман Юрьевич, кандидат экономических наук

М75
МОЛОДОЙ УЧЁНЫЙ: сборник статей V Международной научно-практической конференции. В 2 ч. Ч. 1. – Пенза: МЦНС «Наука и Просвещение». – 2024. – 264 с.

ISBN 978-5-00236-199-1 Ч. 1
ISBN 978-5-00236-198-4

Настоящий сборник составлен по материалам V Международной научно-практической конференции «**МОЛОДОЙ УЧЁНЫЙ**», состоявшейся 23 января 2024 г. в г. Пенза. В сборнике научных трудов рассматриваются современные проблемы науки и практики применения результатов научных исследований.

Сборник предназначен для научных работников, преподавателей, аспирантов, магистрантов, студентов с целью использования в научной работе и учебной деятельности.

Ответственность за аутентичность и точность цитат, имен, названий и иных сведений, а также за соблюдение законодательства об интеллектуальной собственности несут авторы публикуемых материалов.

Полные тексты статей в открытом доступе размещены в Научной электронной библиотеке **Elibrary.ru** в соответствии с Договором №1096-04/2016К от 26.04.2016 г.

УДК 001.1
ББК 60

ISBN 978-5-00236-199-1 Ч. 1
ISBN 978-5-00236-198-4

UDC 616-007. 19

CLINICAL CASE JF COMPLETE DYSGENESIS OF THE GONADS

KALMENOVA PERIZAT ESENKELDIYEVNA,
Candidate of Medical Sciences, Associate Professor.
RASHIMBETOVA VENERA MUSTAFAYEVNA,
Magistr,
PERNEBEKOV ERLAN ANARBEKULY
Resident
International Kazakh –Turkish university named after Khoja Ahmed Yasawi,
Shymkent campus, Shymkent

Abstract: in the article, the authors present a clinical case of Swayer's syndrome or complete dysgenesis of the gonads in a patient over 7 years of age, present anamnestic and clinical data, analysis of laboratory and instrumental research results. During the examination of a patient with a hereditary variant of the hormone - resistant nephrotic syndrome-Denis-Drash syndrome, an increase in the level of gonadotropins in the presence of a female phenotype was found, which, in turn, was the reason for conducting a cytogenetic study of blood lymphocytes (karyotyping). Chromosomal pathology was detected in the patient - inversion of sex 46, XY. Also, the female phenotype, the behavior of the girl corresponds to the passport gender. Identification of a patient with hormone-resistant nephrotic syndrome and karyotype 46, XY in the female phenotype obliges doctors to conduct a molecular genetic study of the WT1 gene.
Key words: Swayer syndrome, disorders of genital formation, pure dysgenesis of the gonads, nephrotic syndrome, Denis-Drash syndrome.

КЛИНИЧЕСКИЙ СЛУЧАЙ: СИНДРОМ СВАЙЕРА

Калменова Перизат Есенкельдиевна,
к.м.н., доцент
Рашимбетова Венера Мустафаевна,
магистр, старший преподаватель
Пернебеков Ерлан Анарбекулы
резидент
Шымкентский кампус, Международный казахско-турецкий университет имени Х.А.Ясави

Аннотация: В статье авторами представлен клинический случай синдрома Свайера или полной дисгенезии гонад у пациентки старше 7 лет, проанализированы анамнестические и клинические данные, результаты лабораторных и инструментальных обследований. В процессе обследования пациентки с наследственным вариантом гормонорезистентного нефротического синдрома - Дениса-Драша, при наличие женского фенотипа было выявлено повышение уровня гонадотропинов, что послужило поводом для проведения цитогенетического исследования лимфоцитов крови (кариотипирование). У пациентки была выявлена хромосомная патология – инверсия пола 46, XY. А также установлен женский фенотип, поведение девочки адекватно паспортному полу. Выявление у больного с гормонорезистентным нефротическим синдромом кариотипа 46, XY при женском фенотипе должно обуславливать врачей в проведении молекулярно-генетического исследования гена WT1.

Ключевые слова: синдром Свайера, нарушение образования половых органов, чистый дисгенез гонад, нефротический синдром, синдром Дениса-Драша.

In 1955, Dr. Gerald Swayer (G. I. M. Slayer) first described two phenotypic women with primary amenorrhea, normally developed external genitalia and vagina, hypoplasia of the uterus and without ovaries. In this case, the genotype of these women was 46 XY. Complete gonadal dysgenesis, Swyer's syndrome, is a disorder of sexual differentiation characterized by a complete lack of androgenization of the external genitalia and stability of the Muller structures due to insufficient synthesis of the anti-Muller hormone. Patients have female phenotypic traits, being karyotype 46, Hu. This pathology occurs with a frequency of 1 per 80,000 [1]. The epidemiological age for detection of Swyer's syndrome is usually 18 to 23 years, B. According to Temime, which described 5 clinical cases of patients with Swayer syndrome, the average age of detection is 17.6 years [1-5]. The study of this deviation of testicular differentiation contributed to the identification of the SRY gene, which is a determinant factor in testicular development. Up to 20% 46, XY complete dysgenesis of the gonads is explained by mutation or destruction of the SRY – this gene is the precursor of testicular differentiation, which occurs in the seventh week of embryo development. In 80% of cases, genetic changes in SRY are not detected. Duplication of the dax21 and WNT4 genes in the location of chromosomes 31 and 1p 35–1 and autosomal mutations at the 9p and 12q sites can also cause gonadal dysgenesis [4-6]. In addition to SRY, other genes are also involved in testicular formation and differentiation, among which the nrob1 (DAX -1) gene located on the X chromosome, as well as the nr5a1 (SF-1), WT1 and Sox9 autosomal genes are the best studied. The Wilms tumor gene encodes a transcription factor that plays a crucial role in the formation and differentiation of the kidneys and gonads. Mutations in the WT1 gene were detected in patients with the WAGR complex (Wilms tumor, aniridia, various types of genitourinary pathologies, mental retardation), Fraser syndrome and Denis - Drash syndrome (early renal failure, diffuse mesangial sclerosis, different degrees of dysgenesis of the gonads, high risk of developing Wilms cancer) [7]. The latter syndrome is characterized by the early debut of nephrotic syndrome in children with PS (pseudohermaphroditism). All patients with Denis-Drash syndrome come to chronic renal failure.

In most publications devoted to the clinical description of Swyer's syndrome, the main complaints that often occur in patients are primary amenorrhea, less often-a delay in secondary sexual characteristics. Patients have a female phenotype, the external genitalia are formed by the female type, however, manifestations of hyperandrogenia in the form of hirsutism and clitoral hypertrophy are characterized [8]. Most often, patients will be of medium or high height, with poorly developed secondary sexual characteristics. The examination reveals high levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) gonadotropins at low levels of estradiol. Since the dysgenetic gonads are capable of producing androgens, an increase in testosterone levels may be recorded. Ultrasound of the pelvis reveals hypoplasia of the uterus and ovaries. Cases of successful pregnancy in gonadectopic women with dysgenesis of the gonads 46, XY using assisted reproductive technologies have been described [5].

46, XY in patients with complete dysgenesis of the gonads, the risk of gonadal cancer is with a frequency of 37 to 45%, which requires their early removal for preventive purposes. Gonadoblastoma and dysgerminoma are the most common malignant tumors. Isolated cases of embryonic carcinoma have also been described. With age, the risk of neoplasia increases: for example, at 15 years old it is 15%, at 20 years old-16%, at 30 years old– 27,5 % [3, 9, 10]. Currently, in the domestic endocrinological literature, Swyer's syndrome is not described as one of the main manifestations of the hereditary variant of nephrotic syndrome in children (Denis-Drash syndrome).

The goal is to propose an analysis of the state of complete dysgenesis of the gonads in a 7.7-year-old patient for the timely diagnosis of this pathology.

Materials and methods: an analysis of the clinical condition of Swyer's syndrome (complete dysgenesis of the gonads) in a 7.7-year-old girl was carried out.

Results and their discussion: clinical case: Patient A., 7.7 years old, complained of periodic weakness and was led by his parents to an appointment with a pediatric endocrinologist.

Life story: the child was born from the 4th pregnancy, an emergency birth that occurred at the 40th week of gestation. The course of pregnancy and childbirth passed without exception. The weight at birth is 3800 G, the body length is 54 cm. At the age of 1.5, he fell ill with chickenpox and spent. At birth, the sex of the child is defined as "female". Medical history. Since 2018, the child has been diagnosed with ICD against the background of nephrotic syndrome, in the report of a nephrologist, a multiresident variant (Denis-Drash syndrome: nephrotic syndrome, mutation of the WT1 gene, karyotype 46 Hu). Chronic kidney disease 3G, A3 (43.57 ML/57 mL/min). The first episode of nephrotic syndrome was detected in mid-June 2018 (3 years old) after a print disease: swelling of the eyelids, vomiting, headache, oliguria appeared. In the analysis dated 15.06.2018: ESR 22 mm/h, cholesterol 6.9 mmol/L, Total Protein 48.8 G/L, albumin 26.5 g/l, creatinine 54.4 μmol/L, proteinuria 13.2 13.2 g/L. the patient received the following treatment : prednisolone 35 mg/day 18.07-29.08.2018 (6 weeks)→ another 2 40 mg / day week + Solu-medrol pulse injection September 12,14,16. Against the background of corticosteroid therapy, proteinuria of 3.3 g/l-0.99 g/l was preserved.

Attempts to treat nephrotic syndrome with prednisolone and cytostatics turned out to be ineffective, steroid resistance was established. In view of the ineffectiveness of the treatment of nephrotic syndrome with drugs of the glucocorticoid line and cyclosporines in this disease, previously prescribed therapy was discontinued. In addition, the further appointment of immunosuppressive therapy can lead to a number of complications, disruption of social adaptation and, most importantly, a decrease in the likelihood of effective sex correction and kidney transplantation. Further, the child was prescribed a consultation with a children's endocrinologist, and the endocrinologist, in turn, sent the patient to determine the level of follicle-stimulating and luteinizing hormones in the blood serum in order to diagnose pathologies of the gonads.

From November 2022, the diagnosis of subclinical hypothyroidism is examined by a children's endocrinologist. The patient takes Euthyrox at a dose of 25 mg. The hereditary Anamnesis for kidney diseases is painless. A history of hereditary endocrine pathology is serious: the sister has diffuse goiter, the grandmother has diabetes. For the first time, she was examined by an endocrinologist at the age of 7 with complaints of periodic weakness. At the time of inspection: height 125 cm, growth SDS: 041, weight - 22 kg, SDS BMI – 1.14 kg/m2. The external genitals are formed according to the female type. Sexual development Tanner on Ma0 P0 Me0.

According to the results of a biochemical examination on 19.12.2022, a significant increase in the level of gonadotropins (FSG = 126 mm/ML (0-11. 1), LG = 16.9 (0.3-3.1 mm/ML) was found with a normal estradiol level of 5.0 pg/ml (6.0-57.0) against the background of taking Euthyrox in a dose of 25 mg of the patient. Ultrasound of the small pelvis organs (ultrasound examination) made 07.10.2022: the body of the uterus is determined. The right and left ovaries are determined. The size of the uterus and ovaries corresponds to 2-7 years. Karyotype -46 Hu. The structure of the external genital organs is in accordance with the female type.

Thyroid ultrasound (ultrasound): Grade 2 thyroid hyperplasia. The results of a study of thyroid hormones from 20.10.2022 showed an increase in Thyroid - Stimulating Hormone against the background of normal T4 (free) and antibodies to thyroid peroxidase : TSH-6.49 μme (0.6 - 4.84), T4 free-1.08 ng/dL (0.97-1.67), at K TPO -11.5 IU/mL (0-18).

Ultrasound of the kidneys (ultrasound) 08/08/2022: right kidney: the topography has not changed. Dimensions: 86.0 mm x 31.0 mm. Intrarenal structures are not differentiated in all sections. The parenchyma is uniform, diffuse-increased. The plate-Calyx system is not expanded. Left kidney: the topography has not changed. Dimensions: 77.0 mm x 34.0 mm. Intrarenal structures are not differentiated in all sections. The parenchyma is uniform, diffuse-increased. The plate-Calyx system is not expanded. Diagnosis: Echo symptoms of diffuse kidney changes.

Nephrobiopsia results No. 24618-30 dated 04.10.10.18: focal-segmental glomerulosclerosis fibrosis of the intermediate tissues (segmental sclerosis of vascular loops -75 %, focal sclerosis-25%).

Objective data. Height - 125 cm, body weight - 22 kg, BMI = 1.14 kg / m2, ad-90/50 mm Hg.GG. St., heart rate-90 KD / min. The condition is satisfactory. The physique is proportional. The skin is clean, of medium moisture and elasticity. The subcutaneous fat layer is sufficiently developed, the distribution is uniform. The muscles are satisfactorily developed. Breathing is vesicular, there are no wheezing. Heart tones are clear, rhythmic. The tongue is clean and moist. The abdomen is soft, painless, accessible for deep palpation. The

liver does not protrude beyond the edge of the costal arch. Diuresis is sufficient. Large bowel movements are regular, daily, shaped. The thyroid gland is not palpable, uniform, soft, elastic, nodules are not palpable. Sexual development: by type of woman. Sexual development Ma0 P0 Me0.

The results of laboratory tests. 12.08.2022 general blood test: hemoglobin 122 g/l, erythrocytes 4.36 ×1012, leukocytes 13.54 ×109, platelets 365×109, hematocrit 37.10%, lymphocytes 34.10%, monocytes 6.30%, eosinophils 5.30%, neutrophils 52.60%, ESR 30 mm/h. 12.08.2022 biochemical blood test: sodium 139 mmol/L, phosphorus-3.1 mg /dL, glucose-5.0 mol/L, potassium 5.1 mmol/L, ionized calcium 1.25 mmol/ L, urea 10.05 mmol/L, creatinine 93.84 μmol/L, SHFH (SCF) 42, 25 ml/min, Total Protein 52.99, G/L, albumin 27.60 g/l, immunoglobulin a 2.49 g/l, immunoglobulins m 1.98 g/l, immunoglobulin G 0.29 g/l, ast 20.3 – units/l, alt – 9.4 units/ml, cholesterol – 3.0 mmol/l, ast 22.70 units / l, alt 11.20 units / l, SRB 0.80 units / L, glucose 4.36 mmol / l. results of laboratory tests. 12.08.2022 complete blood count: hemoglobin 122 g/l, erythrocytes 4.36 ×1012, leukocytes 13.54 ×109, platelets 365×10 9, hematocrit 37.10%, lymphocytes 34.10%, monocytes 6.30%, eosinophils 5.30%, neutrophils 52.60%, ESR 30 mm/h. Biochemical blood test dated 12.08.2022: sodium 139 mmol / L, phosphorus-3.1 mg / dL, glucose-5.0 mol / L, potassium 5.1 mmol / L, ionized calcium 1.25 mmol / L, urea 10.05 mmol / L, creatinine 93.84 μmol / L, GFR 42, 25 ml / min, Total Protein 52.99, G / L, albumin 27.60 G/L, immunoglobulin a 2.49 g/l, immunoglobulins m 1.98 G/L, immunoglobulin G 0.29 g/l, ast 20.3 – units/L, alt – 9.4 units/mL, cholesterol – 3.0 mmol/l, ast 22.70 units / l, alt 11.20 units / L, CRP 0.80 units / L, glucose 4.36 mmol / l. total urine analysis dated 08/12/2022. specific gravity 1010, protein 4.13 g/l. General urine analysis dated 12.08.2022-specific gravity 1010, protein 4.13 g / l.

Cytogenetic study of blood lymphocytes (karyotyping): chromosomal pathology – inversion of sex 46, XY. The patient has a female phenotype, this behavior corresponds to the passport gender. Molecular genetic study (full exomic): in heterozygous composition, 9 intron (out of 9) of the WT1 gene.

Conclusion

The results of laboratory and instrumental studies (karyotype 46, Hu, the presence of a Y-specific marker, an increase in the level of gonadotropins and thyroid stimulating hormone, hyperplasia of the thyroid gland of the 2nd degree, the presence of Altered gonads) were given the following clinical diagnoses: subclinical hypothyroidism, disorders of sex formation 46, Hu, "complete" dysgenesis of the gonads, Swyer's syndrome.

Recommendations of a children's endocrinologist to the patient:

1.monitoring by a pediatrician, neurologist, endocrinologist at the place of residence.

2.taking Euthyrox 25, 1 tablet on an empty stomach, 20 minutes before meals (avoid taking iron and calcium supplements for 2 hours).

3.surgeon's consultation (given the high risk of gonadoblastoma formation in a patient with complete dysgenesis of the gonads 46 Hu, it is recommended to remove them early prophylactically in adolescence, and then prescribe hormone replacement therapy).

4.revision after 2 months with the results of laboratory tests of testosterone, TSH, T4-free, AMG.

Thus, complete dysgenesis of the gonads of the described patient in the form of Swyer's syndrome, together with nephrotic syndrome and a mutation in the WT1 gene, is one of the manifestations of Denis-Drash syndrome.

Nephrotic syndrome in Denis-Drash syndrome is morphologically characterized by diffuse mesangial sclerosis, which inevitably progresses at birth or in the first years of life and is subsequently followed by the development of CRS. The presence of nephropathy determines the specificity of the syndrome, which can be in full form or incomplete form, consisting of three components of the Triad, where nephrotic syndrome is combined with Wilms tumor or pathology of sex formation [11].

Given the complexity of diagnosing Denis-Drash syndrome, karyotyping is a necessary study in the management of patients with hormone-resistant nephrotic syndrome (early development of kidney failure).

Determination of karyotype 46, XY in a patient with hormone-resistant nephrotic syndrome in the female phenotype entails the need to conduct a molecular genetic study of the WT1 gene. The use of Prednisolone and cytostatics in children with Denis-Drash syndrome leads to a deterioration in the condition of patients and an increase in the degree of proteinuria, contributes to an increase in sclerotic changes in the kidney tissue and an exacerbation of the disease with an earlier result in CSF.

46, complete dysgenesis of the gonads at XY is a complex type of violation of genital formation. All girls with primary amenorrhea should conduct a hormonal profile and ultrasound of the small pelvis, based on the results of which it is necessary to resolve the issue of the need to conduct a cytogenetic study. Due to the high risk of malignant tumors in Swyer's syndrome, early diagnosis is important. Radical surgical treatment and the ability to choose hormone replacement therapy improve the prognosis and preserve the reproductive potential of patients.

References

1. Coutin A. S., Hamy A., Fondevilla M., Savigny B., Paineau J., Visset J. Pure 46,XY Gonadal Dysgenesis // J Gynecol Obstet Biol Reprod.- 1996. -Vol. 25, Is. 8. -P. 792–796.
2. Верховых Е. В., Гирш Я. В., Калинченко Н. Ю. Клинический случай чистой дисгенезии гонад – синдрома Свайера // Вестник СурГУ. Медицина.- 2022.- № 2 (52).- С. 65–68. DOI 10.34822/2304-9448-2022- 2-65-68
3. Газизова Г. Р., Валеева Ф. В., Шайдуллина М. Р., Акбирова Э. И. Синдром Свайера // Медицинский вестник Юга России.- 2020.- Т. 11, № 3.-С. 65–68. DOI 10.21886/2219-8075-2020-11-3-65-68.
4. Dimitri P., Cohen M., Wright N. Indications for Familial Screening and Gonadectomy in Patients with 46,XY Gonadal Dysgenesis // Int J Gynaecol Obstet.-2006.-Vol. 95, Is. 2.-P. 167–168. DOI 10.1016/ j.ijgo.2006.05.035.
5. Ben Temime R., Chechia A., Attia L. et al. Swyer Syndrome: Report of 5 Cases // J Gynecol Obstet Biol Reprod. -2008.-Vol. 38, Is. 3.-P. 220–225. 5. Carrillo A. A., Berkovitz G. D. Genetic Mechanisms that Regulate
6. Carrillo A. A., Berkovitz G. D. Genetic Mechanisms that Regulate Testis Determination // Rev Endocr Metab Disord.-2004.-Vol. 5, Is. 1.-P. 77–82.
7. Hossain A., Saunders G. F. // J. Biol. Chem. -2001. - Vol. 276. - P. 16817-16823
8. Chen M. J., Yang J.-H., Mao T.-L., Ho H.-N., Yang Y.-S. Successful Pregnancy in a Gonadectomized Woman with 46,XY Gonadal Dysgenesis and Gonadoblastoma // Fertil Steril.-2005.-Vol. 84, Is. 1.-P. 217.e5-217.e6.
9. Chen M. J., Yang J.-H., Mao T.-L., Ho H.-N., Yang Y.-S. Successful Pregnancy in a Gonadectomized Woman with 46,XY Gonadal Dysgenesis and Gonadoblastoma // Fertil Steril.-2005.-Vol. 84, Is. 1.-P. 217.e5-217.e6.
10. Diessner J., Stuber T., Niederle B., Pawlik M., Dietl J., Honig A. XY Gonadal Dysgenesis – Development of a Germ Cell Tumor: Case Report // Eur J Gynaecol Oncol.-2013.-Vol. 34, Is. 6.-P. 572–57
11. Mueller R.F. The Denys-Drash syndrome.//J Med Genet.-1994,- Vol.31.-P. 471–477.