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RARE GENETIC SYNDROMES THAT DETERMINE TYPE 1 DIABETES MELLITUS ON THE EXAMPLE OF THE SAMARKAND REGION

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Annotation
The polymorphism of the clinical picture of Wolfram, Rogers and Alstrom syndromes, similar to many other genetic syndromes, makes it difficult to diagnose. Diagnosis of syndromes also takes time, since clinical symptoms do not appear at the time of the manifestation of the disease, but, as a rule, only after a few years. The staging of manifestations also varies. However, molecular genetic studies contribute to the early detection of these syndromes.
The study region does not have the ability to conduct research at the molecular genetic level, as a result of which the data provided in this article will be based mainly on the clinical manifestation in patients of disorders characteristic of each of the presented syndromes. Most cases come from isolated communities or other communities where consanguinity is common (explained by autosomal recessive inheritance).
The studied patients applied for admission initially with a diagnosis of diabetes mellitus, only a further study of the patients, their medical history, as well as concomitant diseases made it possible to verify Wolfram, Rogers and Alstrom syndromes.
The purpose of the study: to assess the prevalence and association of type 1 diabetes with rare genetically determined syndromes on the example of the Samarkand region.

Design: single center retrospective study.

Keywords: type 1 diabetes mellitus, Wolfram's syndrome, Rogers' syndrome, Alstrom's syndrome

Introduction

Wolfram syndrome is a complex of multiple organ disorders caused by genetic causes, including diabetes and diabetes insipidus, sensorineural hearing loss, and atrophy of the optic

nerves. According to the literature, sensorineural hearing loss occurs in the 2nd decade, and bladder atony develops only by the 3rd decade. In this case, the initial manifestations of bladder innervation disorders in the form of its dysfunction appeared already in the 1st year, and sensorineural hearing loss formed by the 4th year of the disease. Atrophy of the optic nerve head in the patient developed, as in other studies, within 1 year after the onset of diabetes mellitus. The sequence of development of the entire picture of the disease does not always coincide with the classical course of the syndrome, which makes timely diagnosis difficult.

Thiamine sensitive megaloblastic anemia (TRMA, Rogers syndrome) is a rare recessive genetic syndrome with early onset of thiamine sensitive megaloblastic anemia associated with diabetes and sensorineural deafness. Anemia is one of the main manifestations of TRMA, often found early in life (infancy or childhood). It is a macrocytic regenerator anemia without iron deficiency. Diabetes is another mandatory component of TRMA, usually beginning early (often before the age of 5 years). The onset is acute, with significant hyperglycemia and the need for rapid initiation of insulin therapy. The last manifestation of Rogers syndrome is sensorineural hearing loss due to vitamin B1 deficiency. Hearing damage is often detected in childhood and usually later than anemia and diabetes. Partial hearing loss can indeed go unnoticed in the first few months or years of life. Hearing damage is caused by the presence of the THTR-1 transporter in the inner hair cells, which is a structure located in the organ of Corti.

Alstrom's syndrome is a genetic pathology in which obesity, retinitis pigmentosa, type 2 diabetes mellitus, sensorineural hearing loss, dilated cardiopathy, and nephropathy develop. A number of symptoms and their combination are also found in other genetic syndromes (Lawrence-Moon-Beadle syndrome; Bardet-Beadle, Prader-Willi). One of the central symptoms of the disease is early obesity, which occurs in 98% of patients. Body weight at the birth of a child may be within the normal range, but the next 2 years there is an intensive increase. The body length at birth does not differ from the norm, in the future children grow rapidly, and the differentiation of the skeleton is usually 1–3 years ahead of the chronological age. However, the final height of patients is below the 3rd precentile. From the first months of life (5–15 months), the child has nystagmus and photophobia. An ophthalmological examination reveals retinitis pigmentosa, leading to blindness in less than 10 years. Insulin resistance develops between 18 months and 4 years of age. The appearance of acanthosis nigricans confirms this symptom. Type 2 diabetes mellitus is usually diagnosed in the second or third decade of life. Among other endocrine disorders, hypothyroidism (up to 17%), hyper- and hypogonadotropic hypogonadism, cryptorchidism, hirsutism in girls with pathological development of the mammary glands, polycystic ovaries, irregular menstruation or amenorrhea are noted. Puberty is often delayed. Hepatolienal syndrome is detected in 86% of patients under the age of 8 years. It is accompanied by an increase in the level of hepatic transaminases in serum.

Materials and methods of research

The study included 409 patients with a verified diagnosis of type 1 diabetes mellitus. Of which 284 (69.43%) were children (1-15 years old), 125 (30.56%) were adolescents (15-18 years old). Among the total number of patients, 4 (0.97%) patients with Rogers syndrome were identified , 6 (1.46%) patients with Wolfram syndrome, 1 (0.24%) patient with Alstrom syndrome. Born

from consanguineous marriages with the syndrome of Rogers 3 (75%), Wolfram 4 (66%), Alstrom 1 (100%). Children born from closely related marriages account for 72.72% of the total number of patients with genetically determined syndromes.

Conclusion

Currently, genetically determined forms of type 1 diabetes mellitus are ignored by specialists due to various manifestations, rare occurrence and lack of awareness of medical personnel. There is also the problem of closely related marriages in remote regions of the Samarkand region, which increases the frequency of these pathologies. In turn, they lead to early disability of patients. For this reason, it is necessary to carry out educational work to increase the awareness of medical personnel and prevent entry into closely related marriages. There is a clear association between the presence of genetic syndromes in a patient with determining type 1 diabetes and children born from closely related marriages.

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