FAMILY FORM OF NEPHROGENIC X-LINKED DIABETES INSUPLIUS

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ABSTRACT

There is a global trend towards an increase in the prevalence of diabetes insipidus. Symptoms of nephrogenic diabetes insipidus (NDI) with X-linked inheritance appear in men and women with heterozygous mutations, and are characterized by an isolated symptom complex of polyuria, polydipsia, and hyposthenuria. In children, more often than in adults, when fluid is limited, a clinical picture of water deficiency dehydration develops with hypernatremia, hyperthermia and plasma hyperosmolality. This manuscript presents a case of NND, a familial form, X-linked in male patients. At the same time, in the female line of the family, the mother and grandmother also had an increased need for water; the use of minirin was ineffective. In the older and younger brothers, clinical manifestations of diabetes insipidus in the form of severe thirst and polyuria were noted from infancy; after examination, a diagnosis of diabetes insipidus was made and the drug desmopressin was prescribed. Due to the lack of effect from the use of desmopressin, an analysis of the exons and adjacent regions of the introns of the AQP2 and AVPR2 genes was carried out using the polymerase chain reaction method and subsequent direct sequencing. No mutations were identified in the AQP2 gene. A hemizygous substitution S315I was detected in the AVPR2 gene. The familial X-linked form of NND was confirmed. Hypothiazide is recommended, with constant use of which only slight positive dynamics are observed.

Keywords: diabetes insipidus; hereditary nephrogenic diabetes; children; polyuria; polydipsia; AQP2 and AVPR2 genes

INTRODUCTION

Diabetes insipidus (DI) is a disease in which large volumes of urine with low specific gravity are excreted (polyuria). The prevalence of diabetes insipidus in the population is 0.004–0.01% (US Census Bureau, Population Estimates, 2004). It is believed that ND affects both women and men equally often. The peak incidence occurs at ages 20–40 years [1, 2]. Hereditary (congenital) ND manifests itself as an isolated symptom complex of polyuria, polydipsia, hyposthenuria, or occurs in the structure of a hereditary disease as one of the syndromes [3]. Nephrogenic diabetes insipidus (NDI) manifests itself as an acquired disease in most patients, but very rarely has a hereditary origin. Currently, 4 hereditary forms of congenital NND are known in children and adult patients: X-linked recessive, caused by mutations of the AVPR2 gene, autosomal dominant and autosomal recessive, caused by mutations of the AQP2 gene, NND due to mutations in the SLC14A1 and SLC14A2 genes, encoding urea transporters UT -1 and UT 2 [4–6]. In approximately 90% of cases, it is caused by defects in the vasopressin receptor (V2) and has an X-linked pattern of inheritance. In other cases, the disease is inherited autosomal recessively (9%) or autosomal dominant (1%) and is caused by mutations in the AQP2 gene, which encodes the renal collecting duct water channel regulated by vasopressin. To date, 36 mutations of the AQP2 gene have been described [7, 8]. NDI is caused by the failure of renal collecting duct cells to respond to the antidiuretic effects of arginine vasopressin. The action of this antidiuretic hormone in the kidney is regulated by three subtypes of G protein-coupled AVP receptors. Renal collecting duct cells are unable to reabsorb water, and the kidneys produce large amounts of low-concentration urine as a result of AVPR2 gene mutations in patients with X-linked NND. Children suffering from NND are emotionally labile, irritable, they experience memory loss, inattention, absent-mindedness, restlessness or lethargy, asthenoneurotic syndrome, and delayed physical development. Constant thirst and polyuria determine the behavioral stereotype of children with congenital NDD. In children, the dominant desire is to quench thirst and urinate. When patients with NDI are limited in fluid, a clinical picture of water deficiency dehydration develops with hypernatremia, hyperthermia and plasma hyperosmolality [9]. CASE DESCRIPTION We present a case of NND, familial form, X-linked, in male patients observed in the endocrinology department of the Children's City Clinical Hospital No. 8 in the city of Chelyabinsk. For the first time, patient A. was transferred to the endocrinology department for further examination and treatment from the intensive care unit at the age of 1 year 9 months with complaints of severe thirst, polyuria more than 3 liters per day, and periodic intense headaches. According to the life history, the boy was born at 39 weeks with a birth weight of 3750 g, 51 cm long. Physical and neuropsychic development in the first years of life corresponded to

age standards. Previous illnesses - rarely ARVI. Allergy history is not burdened. Denies injuries, surgical interventions and blood transfusions. When clarifying the family history, it was established that in the family on the female side, the mother and grandmother of the child had an increased need for water (the mother drank and excreted in urine up to 8-10 liters per day, the grandmother - about 7-8 liters per day), according to mother of the child, the prescription of Minirin to her was ineffective, and therefore was canceled independently; no other treatment was prescribed. History of the disease In patient A., thirst and polyuria increased from infancy (according to the mother, he could excrete more than 3 liters per day in urine, in proportion to the volume of fluid drunk). At the age of 1 year 8 months he entered a preschool institution, where the child was limited in fluid intake, as a result of which the boy began to develop swelling and increase over time, his state of health was disturbed, a change in consciousness appeared, including stupor, and therefore he was hospitalized in the intensive care unit, where the necessary therapeutic measures were carried out with a positive effect. When conducting laboratory diagnostic screening, the following indicators attracted attention: in urine tests - urine density 1002, decreased urine osmolarity (240 mOsm/kg), in a biochemical blood test - hypernatremia over 148 mmol/l. Taking into account complaints of polydipsia, polyuria (3–5 l/day) with reduced urine density, family history and medical history with characteristic clinical manifestations, the child was diagnosed with diabetes insipidus of central origin. Treatment with desmopressin was prescribed at a dose of 0.1 mg per day; it is noteworthy that within a year the dose was increased to 0.3 mg/day. Given the lack of necessary observation and examination (parental refusal), the child received the prescribed therapy uncontrolled for 8 years. At the age of 10 years, the boy was re-examined in the endocrinology department, where it was found that, against the background of regular intake of desmopressin 0.3 mg/day, the symptoms of polyuria and polydipsia increased to 7–10 liters per day. At the same time, a second child, 4 years old, from this family was examined with clinical manifestations of ND in the form of severe thirst and polyuria (more than 4–5 l per day), which, according to the mother, were noted from the age of 3 months, and at the age of 7 months he was also diagnosed with diabetes insipidus. The drug desmopressin was prescribed. Results of physical, laboratory and instrumental studies When examining the child A. the condition was of moderate severity. My health is not affected. A boy with a hypersthenic build.

DISCUSSION

Congenital NDI is a rare hereditary disorder characterized by the absence of antidiuretic effect when taking vasopressin, manifested by increased production of low-density urine and severe thirst. The severity of the disease varies from a mild form

with polyuria and polydipsia to a severe dehydration crisis with anorexia, decreased physical performance, fever and constipation [1, 2]. In our case, the patient's overweight increases with age, to the point of obesity. Women are in most cases healthy or asymptomatic carriers. In our case, the boy had episodes of dehydration, including due to limited fluid intake. In connection with polyuria and polydipsia, insomnia appears, which is accompanied by physical and mental asthenia [9].

CONCLUSION

ND is a relatively rare disease that is not only a medical problem, but also a social and psychological one. When thirst appears in a child, it is necessary to promptly diagnose diseases accompanied by severe polydipsia, since fluid restriction in childhood is often the cause of severe metabolic disorders. Timely correct diagnosis of this disease allows you to avoid severe complications and prescribe adequate treatment. The main treatment method for ND of central origin still remains the administration of desmopressin, while confirmed ND requires the prescription of hypothiazide or a combination of hypothiazide with indomethacin or amiloride. Considering that X-linked diabetes insipidus is currently a disease with an unfavorable outcome, medical genetic examination is recommended for children with clinical manifestations and laboratory indicators of NDI.

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