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THE IMPORTANCE OF EARLY DETECTION OF DIABETES INSIPIDUS IN CHILDHOOD - CASE REPORT

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SUMMARY

Introduction: Diabetes insipidus (DI) is a disease that occurs due to inappropriate secretion of anti-diuretic hormone from the pituitary, or as a result of disorder in which the level of the kidneys cannot adequately respond to the secretion of this hormone. Also, it is known as central diabetes insipidus. The most common causes are head traumas, tumors of the hypothalamus and pituitary glands, inflammatory processes, histiocytosis, anomalies in the development of brain. It can appear in the form of familial diabetes insipidus or in certain syndromes (Wolfram syndrome). It is characterized by hypotonic polyuria higher than 3l/24h (which persists if even taking liquids stops), then by nocturia and compensatory polydipsia. Enuresis often occurs among children. Case report: A boy, aged 11, lives with his mother and brothers. Mother noticed that the boy was urinating frequently in last few months (diuresis 4.6 l/24h, and 3.25 l/24h). After two months, the boy developed double images and severe headaches, vomiting, inability to see, squinting in the right eye and headache in the back of the head. MNR of the endocranium indicates the presence of a tumor formation. The tumor was surgically removed, and the boy started with chemotherapy and radiotherapy. Due to persistent diabetes insipidus, the boy started using desmopressin-acetate - in tablet form. Active substance desmopressin - acts in the same way as the natural hormone vasopressin and regulates the kidney's ability to concentrate urine. The positive effect of taking the drug appeared after three weeks from the start of taking the therapy. Conclusion: Central (neurogenic) DI occurs as a result of a relative or absolute deficiency of antidiuretic hormone, which is responsible for the osmolality of body fluids. Based on this case, we want to show the importance of early diagnosis of the disease in order to improve the prognosis and the necessity of careful monitoring of these patients.

Key words: diabetes insipidus; antidiuretic hormone; dieresis; tumor; desmopressin-acetate.

SRPSKI

ZNAČAJ RANOG OTKRIVANJA DIJABETESA INSIPIDUSA U DETINJSTVU - PRIKAZ SLUČAJA

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SAŽETAK

Uvod: Insipidni dijabetes (DI) je bolest koja nastaje usled neodgovarajuće sekrecije antidiuretskog hormona iz hipofize ili poremećaja na nivou bubrega koji ne mogu adekvatno da odgovore na sekreciju ovog homona. Naziva se jos i centralni. Najčešći uzročnici su trauma glave, tumori hipotalamusa i hipofize, zapaljenski procesi, histiocitoza, anomalije u razvoju mozga. Moze se javiti i kao familijarni dijabetes insipidus ili u sklopu nekih sindroma (Volframov sindrom). Karakteriše se hipotoničnom poliurijom većom od 3l/24h, koja istrajava čak i nakon prestajanja uzimanja tečnosti, zatim nokturijom i kompezantornom polidipsijom. Enureza se često javlja kod dece. Prikaz slučaja: Dečak, uzrasta 11 godina, živi sa majkom i braćom. Unazad nekoliko dana majka je primetila da dečak učestalo mokri (diureza 4.6 l/24h, i 3.25 l/24h) . Nakon dva meseca, dečaku se javljaju duple slike i jake glavobolje, povraćanje, nemogućnost gledanja, žmiranje na desnom oku i glavoblje u potiljačnom delu glave. MNR endokranijuma ukazuje na prisustvo tumorske formacije. Tumor je operativnim putem odstranjen, a dečaku je određena hemo- i radioterapija. Zbog perzistentnog insipidnog dijabetesa dečak je počeo da koristi desmopressin-acetat - u tabletiranom obliku. Aktivna supstanaca dezmopresin - deluje na isti način kao i prirodni hormon vazopresin i reguliše sposobnost bubrega da koncentriše urin. Pozitivan efekat uzimanja leka javio se nakon tri nedelje od početka uzimanja terapije. Zaključak: Centralni (neurogeni) DI, nastaje kao posledica relativnog ili apsolutnog deficita antidiuretskog hormona, koji je odgovoran za osmolalanost telesnih tečnosti. Na osnovu ovog slučaja, želimo da prikažemo značaj rane dijagnoze bolesti u cilju poboljšanja prognoze i neophodnost pažljivog praćenja ovih bolesnika.

Ključne reči: dijabetes insipidus; antidiuretski hormon; diureza; tumor; desmopresin-acetat

INTRODUCTION

Central diabetes insipidus is a disorder induced by an aberrant release of anti-diuretic hormone from the pituitary gland, or by an issue in which the kidneys' function does not respond adequately to this hormone's output. Because the kidneys are unable to prevent water excretion, frequent urination occurs. The patient grew extremely thirsty and drank copious amounts of fluids. This cycle may persist when sleeping, resulting in nicturia. Peripheral or nephrogenic diabetes is another kind of diabetes insipidus. The arginine vasopressin receptors on tubular cells are absent in this illness. Despite the fact that both types of diabetes produce increased thirst and urine production, the conditions are vastly different (1).

A reduction in antidiuretic hormone synthesis causes central diabetes insipidus. Antidiuretic hormone (ADH) is a hypothalamic hormone that is stored in the posterior pituitary gland and subsequently released. ADH maintains the body's water balance by controlling how much water the kidneys reabsorb. More ADH is generated or released in response to dehydration or hypotension. In the majority of instances of diabetes insipidus, either the hypothalamus or the pituitary gland fails to produce adequate ADH. This causes frequent and significant urine loss (2).

When pathological lesions affect any part of the neurosecretory system, including the hypothalamic supraoptic and paraventricular nuclei, pituitary-hypothalamic tract, and pituitary gland's posterior lobe, ADH secretion and synthesis are diminished. Permanent diabetes insipidus occurs when a disease condition impacts the hypothalamic structures, resulting in the loss of secretory neurons. The loss of the posterior pituitary gland which stores ADH(3) may cause a transitory DI. The renal distal and collecting tubules do not absorb water in the absence of the hormone, leading to polyuria.

Vasopressin (AVP) increases water reabsorption in renal tubular cells by binding to V2 receptors and activating adenyl cyclase. This raises the concentration of cyclic adenosine monophosphate, which activates protein kinase A and phosphorylates protein aquaporin 2. This component subsequently fuses with the apical cell membrane, generating microtubules that allow water to diffuse.

People with central DI had lower aquaporin 2 expression as well as lower aquaporin 3 activity. It is thought that these deficiencies are the primary cause of polyuria in DI patients (4).

The most common causes of DI include head injuries, hypothalamic and pituitary tumors, inflammatory disorders, histiocytosis, and brain development anomalies. It might present as a genetic solitary condition or with specific symptoms (Wolfram syndrome). Because the etiology is uncertain in 30-40% of instances, it is classified as idiopathic diabetic insipidus with a probable autoimmune origin. Central DI with a rapid onset should be suspected of craniopharyngioma or germinoma if it develops before the age of 30, and of metastases if it appears beyond the age of 50 (5).

It is distinguished by nocturia and compensatory polydipsia, as well as hypotonic polyuria of more than 3l/24h (which persists even when liquid intake is halted). Children frequently have enuresis. DI is defined as serum osmolality greater than 300 mOsm/kg and urine osmolality less than 300 mOsm/kg.

Arginine vasopressin medication is used to treat diabetes insipidus. Desmopressin, a synthetic AVP equivalent, is more strong, has a longer half-life, and is easier to use. It is administered intravenously, subcutaneously, or as an intranasal spray. As a palliative therapy, the vasopressor actions of arginine vasopressin have been employed to minimize acute gastrointestinal bleeding. Hyponatremia and water intoxication are rare adverse effects that should be addressed when using these medication (6). The medication's therapeutic impact usually became obvious after three weeks of treatment.

AIM

Our study's goal is to provide a case with both standard and unusual symptoms of diabetes insipidus, as well as to explain the etiology of this condition.

CASE REPORT

A 11 years old lives with his mother and brothers. The boy's mother had noticed him urinating excessively for several months (2-3 times in one hour). He also needs to urinate multiple times during the night. Urination does not cause discomfort, however a tingling feeling may occur.

The patient is awake, oriented, afebrile, eupnoic, and developed normally upon admission to the Regional Hospital. The skull is slightly distorted, but the ocular bulbules and pupils are normal. Overall, the clinical results are normal. Diuresis was 4.6 l on the day of delivery and 3.25 l the next day, corresponding to 0.124 l/kg/BW. RBC: 3.21 x 109/L, HGB: 110 g/L, SE: 8/20 mm/h, serum lucose: 2.9 mmol/l, blood urea: 3.75 mmol/l, creatinine: 56 mmol/l, AST: 21 U/L, ALT: 26 U/L, RF: 10 IU/ml. Urinary tract ultrasonography revealed normal findings. The patient is taken to a tertiary health care facility for verification of the diagnosis and, if necessary, the commencement of therapy.

During the first hospitalization at Institute for Mother and Child (IMC) in New Belgrade, the diagnosis diabetes insipidus (DI) is confirmed. The oral therapy starts with Desmopressin (Minirin) 6,2mg at 1 + 0 + 1/2 per day.

The baseline cortisol level (550mmol) and TSH level (0.97) do not suggest a reduction in pituitary gland output.

The child experiences diplopia and severe headaches particularly in the nape of the neck, occur often throughout the night. He was also unable to blink his right eye. Vomiting occurs three to four times a day.

The MDCT (multi-dector computed tomography) of the endocranium (native and with IV contrast) detected tumor during the repeat hospitalization (AP 2.5 mm, a 19mm, 20mm LL). The tumor obstructs cerebral aqueducts between the third and fourth ventricles, causing hydrocephalus and a rise in both the lateral and third ventricles while leaving the fourth ventricle normal. As a result of fluid transudation via the ependyma, there is visible and early periventricular white matter edema. The condition required surgical treatment in the Institute of Neurosurgery in Belgrade.

At the time of admission to the neurosurgical hospital, the kid is conscious, oriented, active, with normal mental status, with no evidence of pyramidal lateralization. The oftalmology examination revealed exophthalmos and stretched conjunctival blood vessel. The other ocular tests results were normal.

MRI indicated a developing oval tumor in the pineal region (lamina kvadrigemina), dimension 2 x 1.5 x 2 mm, partially solid, partially cystic. The patient underwent single voxel proton MR spectroscopy with short duration (30ms) sequences, which identified the tumor in the pineal gland. The tumor was constituted of lipid / lactoid and lipid tisssue. The presented profile suggests cell proliferation and lymphocyte infiltration, and it corresponds to the emergence of the early germinoma.

Following the surgery preparation, an endoscopic ventriculocisteroskopia and tumor biopsy are performed. Pathohistological studies confirmed the presence of germinoma. Malignant cells were not detected in the cerebrospinal fluid, and beta HCG and alpha-feto protein levels in the serum and cerebrospinal fluid were normal. The membranous area of the floor of the third ventricle was fenestrated during the surgery, and contact was achieved between the interpendicular tanks and the ventricular system.

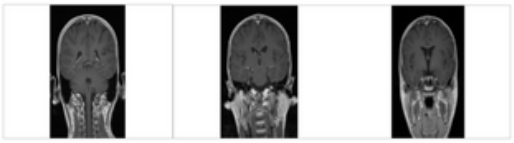

Fig. 1 - 3. Clear withdrawal of chamber system, without acute exacerbation of hydrocephalus with moderate collapse of the chamber

The post-operative course is adequate. A clean retraction of the chamber system, with slight constriction of the chamber and no substantial exacerbation of hydrocephalus, was detected by postoperative MRI, showing that the stoma was operating properly (Figure 1-3). Because of the boy's persistent diabetic insipidus, Minirin Spray therapy was combined with radiation treatment.
The child underwent chemotherapy and radiation therapy for the following five months, with satisfactory subjective and hematological tolerance.
An examination of growth hormone secretion is performed one year following surgery (table 1).

Table 1: Clonidine test results

Time	-30	0	30	60	90	120	150
Growth hormone	1.1	0.6	0.7	4.1	4.4	3.9	2.2

The lack of growth hormone, which had been suspected based on the patient's low growth rate during the previous 18 months, was verified on this occasion. Low growth hormone readings during the glucagon test (GH 1.1,1.2,1.4, 1.7, and 1.8mU/l) and IGF 1 (117 ng/ml) levels at the lower limit indicated growth hormone defficiency.
Following the consultation with the child and his mother, growth hormone substitution treatment was initiated in order to improve muscular and skeletal system development. A control MRI of the endocranium and spine should be performed within 6 months of starting growth hormone prescription. All of the possible risks of this treatment, including the likelihood of tumor recurrence, were reviewed. Hydrocortizone and thyroxine replacement were evaluated during the follow-up since therapy worsened hypocorticism and hypothyroidism.
Somatropin (Genotropin) was received for 26 months at a dosage of 0.03 mg/kg/24h. Check-ups were carried out on a regular basis by neuro-oncologists, neurosurgeons, and endocrinologists. The MRI of the endocranium was performed once a year to ensure that the primary disease has not recurred.
The child is now in good overall health, with no subjective discomfort, no substantial changes in body weight, and no headaches.

DISCUSSION

The most prevalent cause of DI in children and people under the age of 30 is germinoma or craniopharyngeoma, trauma and inflammatory processes, as well as tumor metastases.
Determining the pathophysiology of the vasopressin system has several major clinical consequences. The cerebral vasopressin cells are dispersed throughout the hypothalamus, tumors that induce diabetes insipidus must be either large and/or infiltrative, or positioned in the infundibulum - at the region of confluence of the hypothalamo-neurohypophyseal neuronal tract.
The germinomas causing diabetes iinsipidus can be relatively minor and undetectable by imaging for years after the development of polyuria. As a result, in infants with idiopathic or unexplained diabetes insipidus, assessment of the beta-subunit of human chorionic gonadotropin and MRI scans should be undertaken on a regular basis (7). This unit is frequently released by germinomas and pinealomas.
As a result, the DI may only be the tip of the iceberg, the first and only sign of tumors, possibly malignant ones (8). Early detection of these tumors (e.g., thyroid cancer, lymphoma), may affect survival (8).
In individuals with full central diabetes insipidus, the maximum urine-concentrating capacity is roughly 100mOsm/kg. Patients with untreated diabetic insipidus may survive well for a long time if their thirst and ability to take fluids is retained. If this capacity is compromised for any reason, dehydration occurs quickly, with potential hypotension, collapse, and death.
Vasopressin treatment can be used to treat central diabetic insipidus in children following neurosurgery in the early postoperative period (9, 10). Furthermore, vasopressin and its analogues treatment improves patients' quality of life.
Nocturia should be the trigger that causes the physician to investigate diabetes insipidus as a possible cause. Despite a substantial diuresis (more than 3l/24), our patient was not subjected to fluid restriction or a DDAVP (desmopresin) test. A positive family history (three years older brother had the same complaints and diagnosis) suggests that all patients be subjected to comprehensive genetic testing. The precise cause of this problem was discovered only after an MRI, and the potentially devastating consequences were avoided in this occasion.

CONCLUSIONS

A variety of conditions and diseases can lead to central diabetes insipidus. Clinical examination can provide critical information in the diagnosis of such illnesses. The age of the patient, as well as fluid consumption, vomiting, irritability, sleep problems, and mental impairment, all contribute to the diagnosis.
Based on this case, we want to emphasize the need of early detection in order to enhance patient prognosis and survival, as well as the importance of closely checking the treated persons for symptoms and signs of relapse.

REFERENCES

1. Mishra G, Chandrashekhar SR. Management of diabetes insipidus in children. Indian J Endocrinol Metab. 2011;15 Suppl 3(Suppl3): S180-S187. doi:10.4103/2230-8210.84858
2. Dabrowski, E., Kadakia, R., & Zimmerman, D. (2016). Diabetes insipidus in infants and children. Best practice & research. Clinical endocrinology & metabolism, 30(2), 317–328. https://doi.org/10.1016/j.beem.2016.02.006
3. Kataoka Y, Nishida S, Hirakawa A, Oiso Y, Arima H. Comparison of incidence of hyponatremia between intranasal and oral desmopressin in patients with central diabetes insipidus. Endocr J. 2015;62(2):195-200. doi: 10.1507/endocrj. EJ14-0368. Epub 2014 Nov 7. PMID: 25382102
4. Stojiljković S. Stoiljković M, Bojanić V., Stojiljković N., Radenković S. Uloga akvaporina u poremećajima bilansa vode, Acta Medica Medianae 2007;46(4):66-73, strana 68 (Serbian)
5. Leroy C, Karrouz W., Douillard C, Do Cao C., Cortet Ch., Wémeau JL. Et al. Diabetes insipidus, Annales d'Endocrinologie, Volume 74, Issues 5–6, 2013, Pages 496-507.
6. Shulman LH, Miller JL, Rose LI. Desmopressin for diabetes insipidus, hemostatic disorders and enuresis, Division of Endocrinology-Metabolism, Hahnemann University School of Medicine, Philadelphia, Pennsylvania. 1990 Oct;42(4):1051-7.
7. Zanetta F, Di Dio G, Savastio S, Saccagno A, Petri A, Bellone S, Maghnie M, Bona G. Germinoma: a rare cerebral tumor causing central diabetes insipidus in childhood. Minerva Pediatr. 2008 Feb;60(1):129-33
8. Lukasz C., Obolonczyk L, Sworczak K, Berendt-Oboloncyzk M, Siekierska-Hellmann M. Diabetes insipidus as a main symptom of cancer, Arch Med Sci. 2014 May 12; 10(2): 401–405.
9. Wise-Faberowski L, Soriano SG, Ferrari L, McManus ML, Wolfsdorf JI, Majzoub J, Scott RM, Truog R, Rockoff MA. Perioperative management of diabetes insipidus in children. J Neurosurg Anesthesiol. 2004 Jul;16(3):220-5. doi: 10.1097/00008506-200407000-00006. PMID: 15211159
10. Patti, G., Ibba, A., Morana, G., Napoli, F., Fava, D., di Iorgi, N., & Maghnie, M. (2020). Central diabetes insipidus in children: Diagnosis and management. Best practice & research. Clinical endocrinology & metabolism, 34(5), 101440. https://doi.org/10.1016/j.beem.2020.101440