

Case Reports

A Thirteen-year-old Boy with 'Idiopathic' Central Diabetes Insipidus

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Abstract

Central diabetes insipidus is a rare disease in childhood and adolescence. This case report described a 13-year-old boy with polyuria and polydipsia for 2 years and water deprivation test confirmed central diabetes insipidus. Magnetic resonance imaging of brain revealed absence of posterior pituitary bright spot in T1-weighted image but otherwise normal study. The finding of 'idiopathic' central diabetes insipidus posed special challenge in subsequent follow-up in order to detect evolving anterior pituitary endocrinopathy. Also it is unclear about the frequency of serial imaging study of the brain so as to reveal possible neoplastic tissue. Besides, it is essential to disclose the nature of the findings and the follow-up plan to patient without causing undue anxiety.

Key words

Central diabetes insipidus; Hypothalamo-pituitary region; Magnetic resonance imaging

Introduction

Central diabetes insipidus (DI) is a rare disorder owing to various causes e.g. cerebral malformation, trauma, hypoxic brain damage, infection, tumour, autoimmune or mutation in gene encoding for arginine vasopressin.¹ With availability of magnetic resonance imaging (MRI) the underlying anatomical lesion, if present, can be demonstrated. However, it is not uncommon to reveal, apart from the absence of posterior pituitary bright spot, a normal hypothalamo-pituitary region. This type of 'idiopathic' central DI requires careful follow up for possible evolving anterior pituitary endocrinopathy. Serial imaging of the central nervous system (CNS) is necessary to achieve early detection of possible neoplastic structures.

Case Report

A 13-year-old boy was presented with polydipsia, polyuria, nocturia and decreased height velocity for 2 years. He passed urine for 7 times during daytime and each voiding was of large volume. He also had nocturia for 2 times every night i.e. at 3 hours and 6 hours after onset of sleep and had to drink water afterwards. The total urine output was 3800 ml/m²/day and his daily life was disturbed by his polyuric state. His appetite was normal and had no subjective weight change before presentation. There was no headache or visual field defect. The height velocity decreased to 1 cm per year for the last 2 years before presentation. The patient was the second child of a non-consanguineous couple and was delivered at full term vaginally. Apart from allergic rhinitis requiring intermittent drug treatment from General Practitioners, he was otherwise healthy without previous hospitalisation. No family history of diabetes mellitus or diabetes insipidus was noted.

Physical examination revealed an alert boy without dysmorphic features or mid-line defects. The body weight and height were 2 kg and 7.1 cm below 3rd percentile respectively. There was no upper to lower segment body disproportion. Visual field was normal by confrontation test and fundi were normal. He remained pre-pubertal with testicular size at 2 ml. Examination of

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other systems were normal.

Urine was negative for glucose and ketone. Fasting plasma glucose was 4.4 mmol/L. Paired early morning serum and urine osmolalities were 289 mOsm/kg and 106 mOsm/kg respectively. Serum sodium level was 141 mmol/L and morning cortisol was 112 nmol/L. Thyroid function test and serum prolactin were normal. Bone age was 9.6 years according to Tanner and Whitehouse. Water deprivation test was performed for suspected DI. When weight loss of 5% was achieved, the simultaneous serum and urine osmolalities were 296 mOsm/kg and 152 mOsm/kg respectively, with serum sodium at 145 mmol/L. After subcutaneous desmopressin acetate was given, the urine osmolality increased to 546 mOsm/kg. Further urine sample could not be obtained within remaining test time, but central DI was very likely. Oral desmopressin acetate was started with marked decrease in urinary frequency and volume, and with subsidence of nocturia. Total daily urine output was decreased to 1200 ml/m²/day. After stabilisation on oral desmopressin and priming with testosterone, anterior pituitary function test was performed using soluble insulin, thyrotrophin-releasing hormone and luteinising hormone-releasing hormone. The basal and trough plasma glucose were at 4.7 mmol/L and 1.6 mmol/L respectively and hypoglycaemic symptoms were present, signifying adequate stress. Peak serum growth hormone was 25 mIU/L, indicating adequate growth hormone secretion. The peak cortisol was impaired at 324 nmol/l. The responses from thyroid-stimulating hormone and prolactin were normal. The responses from follicle-stimulating hormone and luteinising hormone were compatible with early puberty. Serum α -feto protein and β -human chorionic gonadotrophin were not raised. In view of central DI and mild impairment of cortisol response, MRI study (with gadolinium contrast) of hypothalamo-pituitary area was performed. The study showed that the posterior pituitary bright spot on T1-weighted image was absent. The size of anterior pituitary gland was within normal for age. The pituitary stalk was in mid-line position and was not thickened. No focal lesion was detected in the brain parenchyma.

The latest follow-up was 8 months after presentation. The symptoms of central DI were under control of oral desmopressin. The annualised height velocity was 6.2 cm per year. He was in stage 2 in genitalia, stage 1 in pubic and axillary area according to Tanner staging. The testicular size was 4 ml. Serum α -feto protein and β -human chorionic gonadotrophin were not raised.

Discussion

Water balance in the body is maintained by thirst sensation which controls fluid intake, and also by kidneys which control fluid excretion under the influence of 8-arginine vasopressin (AVP). AVP is produced in the paraventricular and supraoptic nuclei of the hypothalamus and is transported to and stored in posterior pituitary gland.¹ Polyuric state should be confirmed by recording the exact volume of input and output states. Daily urinary volume exceeding 2000 ml/m²/day is defined as polyuria and calls for further investigation.² Preliminary investigations are necessary to rule out the more common condition of diabetes mellitus by checking urine for glucose and ketone, and by fasting plasma glucose level. Paired morning serum and urine osmolalities are ordered to screen for concentrating defect of kidneys. Water deprivation test followed by desmopressin acetate is necessary for definitive diagnosis. Once central DI is confirmed, the anterior pituitary function should also be assessed for possible endocrinopathy because of close anatomical proximity. MRI (with gadolinium contrast) of the hypothalamo-pituitary region is needed for anatomical diagnosis and raised serum tumour markers may give a clue to underlying aetiology.

Our patient had typical symptomatology of polyuria and was confirmed to have central DI by water deprivation test. Although the peak urine osmolality was 546 mOsm/kg, the dramatic relief of thirst sensation and the marked decrease in daily urine output after oral desmopressin were very suggestive of central DI. At presentation, the child had decrease in height velocity for 2 years. Anterior pituitary function test was normal except mildly impaired cortisol response. MRI of brain revealed absence of posterior pituitary bright spot but no other anatomical defect i.e. 'idiopathic' central DI.

Central DI is a rare disease entity in childhood and adolescence and a large tertiary referral centre received about 3.0 to 3.2 patients per year.^{3,4} The aetiology included head trauma, familial, tumour of CNS, malformation of CNS, granuloma, hypoxic brain damage, infection of CNS.¹ However, a cause could not be found in 13.3% to 24% of patients at initial presentation.^{3,4} The subsequent management strategy for such 'idiopathic' central DI is uncertain at this moment. Previous case reports showed that patients could have initial 'idiopathic' central DI but later found to have growth hormone insufficiency and other anterior pituitary hormone deficiency owing to intracranial

tumours. The time lag ranged from 2.1 to 11.2 years,⁵ occasionally up to 21 years,⁶ although only computed tomograms but not MRI were used in serial scanning those patients. The data from a retrospective study suggested that an underlying structural lesion was unlikely when central DI was either isolated or associated with growth hormone deficiency only; but the likelihood increased significantly when gonadotrophin deficiency was present.³ During follow up for patient with 'idiopathic' central DI, attention should be made to the occurrence of evolving anterior pituitary endocrinopathy, both in clinical features and by anterior pituitary function test. When other hormonal disturbances were present in addition to growth hormone insufficiency, especially hyperprolactinaemia, CNS germinoma should be suspected.⁷ Besides, other systemic manifestations of possible aetiology should be looked for, e.g. Langerhans cell histiocytosis.

Another unique entity is the finding of absent posterior pituitary bright spot with thickened pituitary stalk. In multi-centred studies, precise aetiology (Langerhans cell histiocytosis) was found in 15% of the cases, with further 4% and 15% confirmed Langerhans cell histiocytosis and germinoma respectively after a mean follow up period of 5.5 ± 3.6 years. The diagnosis for the rest of the group remained unknown, although some of the patients had normal pituitary stalk at certain moment during follow up.^{8,9}

The finding of 'idiopathic' central DI, especially if associated with anterior pituitary endocrinopathy, should never be considered as a benign entity. Patients should be followed up closely for possible emerging neurological or endocrine disturbances. Serial CNS imaging, preferably

with MRI of brain with gadolinium contrast,¹⁰ is necessary in order to achieve early detection of a growing intracranial tumour. An algorithm for the subsequent follow up and management of central DI has been proposed, which also stresses on serial MRI of brain.²

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