CASE REPORT

Diabetes insipidus as an early clinical manifestation of pineal tumor

José S.S. Diniz¹, Eduardo A. Oliveira², Marina M. Servilha³

Abstract

Objective: to present a pineal tumor diagnosed after long clinical course of diabetes insipidus.

Case Report: a ten years old male patient, with symptoms of polyuria, polydipsia and nocturia for 18 months was admitted at the Nephrology Unit with the diagnosis of nephrogenic diabetes insipidus. Six months prior to his admission, he had been submitted to a computed tomography scan, which was considered inconclusive. The diagnosis of central diabetes insipidus was confirmed by a water deprivation test. A head magnetic resonance imaging demonstrated two masses suggesting germinoma.

Conclusions: our observations show that patients with central diabetes insipidus need close clinical, laboratory and neuroradiological follow-up in order to detect the intracranially tumors in an early stage.


Introduction

Central diabetes insipidus is a disorder characterized by polyuria and polydipsia due to vasopressin (antidiuretic hormone) deficiency caused by a lesion at the hypothalamo-hypophyseal axis. It may be secondary to infections, trauma, tumors, and other pathologic processes that damage this axis.¹ Frequently, central diabetes insipidus is wrongly considered idiopathic if not associated with other neurological signs and symptoms.² On the other hand, tumors in the pineal region are rare, being responsible for 0.4-1% of all intracranial masses in childhood.³ The clinical presentation of these tumors is highly variable, ranging from disorders of the pubertal development to neurological symptoms of intracranial masses. Yet, central diabetes insipidus may be an isolated initial manifestation of pineal tumors, and an adequate clinical approach may contribute to an earlier diagnosis of these tumors. In this study, we present the report of a case that illustrates the difficulties in the diagnosis and the frequent delay in the approach of this neurological condition.

Case report

A 10 year-6-month old, male child was referred to the Pediatric Nephrology Unit at Hospital de Clínicas, Universidade Federal de Minas Gerais, with history of polydipsia, polyuria, and nocturia for 18 months. He had performed encephalic computed tomography 6 months before, which showed the thickening of the hypothalamo-hypophyseal infundibulum; this finding was not considered significant (Figure 1A).
The patient was then considered to have diagnostic suspicion of nephrogenic diabetes insipidus. The urinary volume in 24 hours was approximately 6.5 l; the water ingestion of liquids was 5 l. On the physical examination at the moment of admission, he weighed 28,900 g (5-10th percentile) and was 133 cm high (25-50th percentile), with no other alterations (including neurological evaluation). There were no signs of development of secondary sexual characters. Arterial pressure was 80/50 mmHg. On the preliminary evaluation, the examinations presented the following results: urinalysis (density = 1,005, pH = 6, glycosuria = 0); serum biochemistry (glycemia at fasting = 93 mg/dl, urea = 19 mg/dl, creatinine = 0.9 mg/dl, sodium = 144 mEq/L, potassium = 3.7 mEq/L, chloride = 102 mEq/L); venous gasometry (pH = 7.378, pCO₂ = 50.3, HCO₃ = 28.8, BE = +4.8); hemogram (Hb = 11.6 mg/dl, Ht = 35%, leukocytes = 5,900 cells/mm³); vasopressin = 2.2 pg/ml, plasmatic osmolality = 288 mOsm/kg. The ultrasonographic study of the urinary tract revealed kidneys with normal volume for the age, besides the absence of calculi and nephrocalcinosis.

These results characterized the presence of diabetes insipidus, so performance of a water deprivation test was indicated. The results of the test may be observed in Figure 2: after a 6-hour fasting period, there was no increase in the urinary concentration; 2 hours after the stimulus with desmopressin (0.2 ml = intra-nasal 20 mcg), there was an evident increase in urinary osmolality.

Thus, after the test, we verified the presence of central diabetes insipidus, and a therapy with DDAVP was initiated, and magnetic resonance imaging of the central nervous system was indicated. The therapy with vasopressin (an intra-nasal 20 mcg/day dose) resulted in the complete regression of the symptoms and in the normalization of the laboratory findings (urinary density and osmolality).
Magnetic resonance imaging showed two isodense intraparenchymal lesions, with a homogeneous contrast concentration: the first, placed at the anterior part of the third ventricle, invading hypophyseal optic chiasma, infundibulum, and hypophyseal stalk. The other lesion, with the same characteristics, was located at the posterior portion of the third ventricle. Cerebral ventricles presented normal volume in anatomical position. Basal cisterns and peripheral sulci had a normal aspect (Figure 1B-1D).

Considering the radiological and clinical findings, the most probable diagnostic hypothesis was pineal tumor; among these tumors, germinoma is the most common histological type. We required preliminary complementation with serum and liquor dosages of HCG and alpha-fetoprotein, which presented normal results. After evaluation by the Neurology Service at Hospital de Clínicas, Universidade Federal de Minas Gerais, radiotherapy was indicated, and it has been performed with a satisfactory clinical response.

The present report illustrates the difficulties in diagnosing these tumors. The only initial clinical presentation was diabetes insipidus. The typical symptomatology lasted for 18 months and, after a simplified initial investigation, it was considered idiopathic. Some problems called our attention in this case: initially, the child was not submitted to the basic investigation of diabetes insipidus, that is, water deprivation test and stimulus with desmopressin. Later, he was submitted to a computed tomography, and, considering the findings, we discarded the presence of central diabetes insipidus and referred him to a nephrology service, due to a suspicion of nephrogenic diabetes insipidus.

In our opinion, when a status of polyuria and polydipsia is present, it is important to establish the unequivocal diagnosis of diabetes insipidus. Initially, the status of pathologic polyuria and polydipsia must be characterized, in general, above 2 l/m²/day, interfering with the child’s normal activities (the child frequently wakes up during the night to drink water or presents nocturia). Besides that, the pediatrician must be alert to the data about the child’s longitudinal growth and to the signs of associated endocrine or neurological alterations, such as precocious puberty and visual disorders, on the physical examination. The following examinations should be included in the preliminary evaluation: determination of serum osmolality, sodium, potassium, glycemia, calcium, urea, and the evaluation of urine, osmolality, density, and glycosuria. Serum osmolality higher than 300 mOsm/kg, with urine osmolality lower than 300 mOsm/kg, characterizes the presence of diabetes insipidus. After the characterization of the clinical status, the patient should be submitted to the water deprivation test, in order to identify the origin of the problem (whether central or nephrogenic). The test is performed after a nocturne period of maximum tolerated fasting, the child being followed with clinical and laboratory evaluations for a period of 8 to 10 hours.

Some comments on the difficulties in the identification of germinative cell tumors situated in the central nervous system should be made. The initial clinical presentation of our case was only diabetes insipidus. There are several reports about this manifestation associated with other findings in patients with tumors in the pineal region.

The clinical presentation of the germinomas at the central nervous system is highly variable, depending on the patient’s age and on the location of the tumor. Tumors at the pineal region usually present signs of increased intracranial pressure and pubertal disorders. In contrast, suprasellar lesions determine endocrine and visual disorders. Unfortunately, the diagnosis of germinomas at the central nervous system, especially of those located at the sella turcica area, is very difficult and usually obtained late.

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Discussion

Germinomas are rare tumors originated from primordial germinative cells. They arise in regions of the medium line, such as gonads, retroperitoneum, mediastinum, diencephalon, and the ocular orbit. Independently of the region, they are identical, both from the optic or electronic microscopy, and from the histochemical analysis points of view. Friedman established the term germinoma, which has a widely accepted teratoid nature and unknown etiology.

The incidence of germinomas varies according to the region: in Japan and Taiwan, they represent 2 to 9% of intracranial tumors, while in eastern countries, this percentage is consistently lower, varying from 0.4 to 1%. They occur mainly among during adolescence and in young adults, and predominate in male children. They are malign tumors, frequently multifocal and that may originate metastases in the central nervous system or other organs.

Figure 2 - Result of the water deprivation test, stimulus with desmopressin. Two hours later, an important increase in the urine osmolality occurs.

- serum osmolality
- urinary osmolality
- Desmopressin

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et al.\textsuperscript{15} report diabetes insipidus in 80\% of their patients, but most times associated with cephalgia, vomiting, diplopia, and other symptoms. In other studies, there are reports varying around 30 to 50\%, and they are almost always accompanied by other manifestations.\textsuperscript{1,16,17} Yet, there are reports of central diabetes insipidus as an initial sing for germinomas. Ramelli et al.\textsuperscript{2} report seven cases of these tumors; in six children, the isolated initial manifestation was central diabetes insipidus. More recently, Dokek et al.\textsuperscript{11} described two other cases. Some authors emphasize the early occurrence of diabetes insipidus in the clinical course of germinomas.\textsuperscript{18}

Another important information concerns the time interval between the beginning of the symptoms and the diagnosis. In our case, there was an 18-month interval between the first manifestations of diabetes insipidus and the detection of the tumor. This fact is not rare considering germinomas of the central nervous system. Bulger et al.\textsuperscript{19} also report an 18-month interval between the manifestation and the diagnosis in a 14-year-old teenager. It is interesting to comment that, similarly to our case, this patient was initially submitted to a computed tomography, which failed in detecting any abnormality in the central nervous system. In the cases reported by Ramelli et al.,\textsuperscript{2} there was a variable time interval (between 12 and 66 months) for these cases of isolated manifestation of central diabetes insipidus, while for the case with manifestation associated with visual disorders, this interval was of only 3 months. Though in prognostic studies there are no correlations between the time interval from the initial manifestation up to the diagnosis of the tumor and survival, the latter is strongly associated with the tumor extension and with the presence of metastases.\textsuperscript{10} Thus, the early diagnosis, in the initial course of the disease, will benefit the patients, possibly lengthening survival.

The approach to these tumors is still controversial. Previously, several studies recommended craniotomy and biopsy to establish a definitive diagnosis.\textsuperscript{15} However, some authors, according to their growing experience, have indicated radiotherapy, based in clinical, neuroradiological, and neuroendocrine parameters.\textsuperscript{16} In our case, the procedure was to indicate radiotherapy based on these parameters, and the clinical response has been satisfactory up to the present moment.

Conclusions

Our case report emphasizes the difficulties in the diagnosis of tumors at the pineal region. Germinomas may have central diabetes insipidus as their isolated manifestation. The symptoms of diabetes insipidus may precede the alterations in the computed tomography. Whenever a clinical status suggestive of diabetes insipidus is present, the pediatrician should perform a complete clinical investigation and an adequate preliminary approach, considering that the presence of these tumors cannot be discarded, even in cases of an initially normal neurological examination.

References


Correspondence:
Eduardo A. Oliveira
Rua Patagônia, 515/701
CEP 30320-080 – Belo Horizonte, MG, Brazil
E-mail: eduolive@ medicina.ufmg.br