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Arginine vasopressin deficiency (central diabetes insipidus) with partial empty sella: a case report

Kibret Enyew Belay[1*], Rebil H. Jemal[2], Ayele H. Kebede[2], Meron G. Tulu[3], Alamirew Enyew Belay[4], Asteway Mulat Haile[5] and Samuel A. Demisse[3]

Abstract

Background Arginine vasopressin deficiency (central diabetes insipidus) is defined as a reduction in the release of arginine vasopressin (AVP) resulting in a variable degree of polyuria. Partial empty sella refers to an enlarged sella turcica that is not completely filled by pituitary gland. It can be either primary or secondary and its manifestation ranges from asymptomatic cases to isolated posterior pituitary, isolated anterior pituitary or both anterior and posterior pituitary dysfunctions. Diabetes insipidus caused by a partially empty sella is rare.

Case presentation The patient, an 18-year-old Ethiopian woman who presented with long standing headache, increased urination, increased thirst, absence of menses and weight loss. Urine and serum osmolality was done and suggested diabetes insipidus. On further workup, brain magnetic resonant imaging was done and partially empty sella was diagnosed.

Conclusion Diabetes insipidus secondary to partially empty sella is uncommon. In patients presenting with headache and anterior or posterior pituitary dysfunction, empty sella should be considered, whether partial or complete.

Keywords Partially empty sella, Diabetes insipidus, Arginine vasopressin deficiency

Introduction

The pituitary gland is a structure that protrudes from the base of the brain at sella turcica. In adults, it measures approximately 12 mm in transverse diameter and 8 mm in anterior-posterior diameter and weighs between 500 and 1000 milligram. The pituitary gland consists of two distinct lobes, the anterior pituitary or adenohypophysis and the posterior pituitary or neurohypophysis. The mature pituitary gland has a dual embryonic origin - the anterior and intermediate lobes of the pituitary are derived from the oral ectoderm, whereas the posterior pituitary is derived from the neural ectoderm [1].

Arginine vasopressin deficiency (central diabetes insipidus) is characterized by decreased release of arginine

*Correspondence:
Kibret Enyew Belay
enyewkibret1@gmail.com
[1]Department of Internal Medicine, Endocrinology and Metabolism Unit, Bahir Dar University, Bahir Dar, Ethiopia
[2]Department of Internal Medicine, Adama Hospital Medical College, Adama, Ethiopia
[3]Department of Internal Medicine, Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia
[4]Department of Adult Health Nursing, Bahir Dar University, Bahir Dar, Ethiopia
[5]Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia

vasopressin (AVP), also known as antidiuretic hormone (ADH), resulting in varying degrees of polyuria. It can be caused by disorders affecting one or more of the sites involved in AVP synthesis and secretion: the hypothalamic osmoreceptors, the supraoptic or paraventricular nuclei, or the superior part of the supraopticohypophyseal tract, but rarely by damage to the neurohypophysis [2]. Partial empty sella is an enlarged sella turcica that is not completely filled by pituitary tissue as seen by imaging. It is a loss of pituitary concavity while the gland still occupies > 50% of the sella, with a thickness of ≥ 3 mm. On the other hand, a complete empty sella is radiographically defined as a pituitary gland thickness of ≤ 2 mm with > 50% of the sella occupied by cerebrospinal fluid [3]. If the pituitary gland shrinks or becomes flattened, it cannot be seen on an magnetic resonance imaging (MRI) scan [4].

Incidental radiographic findings of an empty sella are prevalent in up to 35% of the general population. While empty sella was initially considered clinically insignificant, a subset of patients exhibits endocrine or neuro-ophthalmologic manifestations which are diagnostic of empty sella syndrome (ESS) [5]. Symptoms in this clinical condition can include headache or vision loss associated with idiopathic intracranial hypertension (IIH), cerebrospinal fluid (CSF) rhinorrhea, or features of hypopituitarism [6]. Pituitary function disturbances in empty sella syndrome happen with somatotroph, followed by lactotroph, gonadotroph, corticotroph, and thyrotroph abnormalities in that specific order [5].

There is limited report on the association of central diabetes insipidus with empty sella. Only a few case reports have been described. A case report by Sonika Malik et al. in 2021 reported a 32-year-old woman with isolated posterior pituitary dysfunction who responded to desmopressin treatment. Magnetic resonance imaging (MRI) of the pituitary gland showed a predominantly empty sella [7]. In another case report, a one-year-old male child with an empty sella turcica was diagnosed with arginine vasopressin deficiency and treated with intranasal desmopressin therapy [8]. In a study by E. Cacciari et al., the hypopituitarism occurred due to empty sella were isolated growth hormone deficiency, combined pituitary hormone deficiency, hypogonadotropic hypogonadism, idiopathic delayed puberty, and precocious puberty. No patients with isolated diabetes insipidus had empty sella [9]. Here we report a case of posterior pituitary dysfunction in the form of central diabetes insipidus associated with empty sella syndrome in a young female patient.

Case presentation

An 18-year-old female patient presented with a 4-year history of headaches that have worsened over the past 2 years. The pain is severe and global, which she rates as 10 out of 10. One year and 8 months ago she started having polydipsia of about 15 L per day and associated excessive urination which she quantifies as similar to the amount of intake of 13–15 L per day. She wakes up to 10 times a night to urinate. Her first menstruation was at the age of 13, but she has a history of amenorrhoea of 1 year and 6 months duration. She has a history of weight loss of 10 kg in one year from 51 kg to 41 kg. She also has a history of epigastric discomfort and indigestion. Since the onset of her symptoms, she has missed a lot of classes due to her illness and her academic performance has dropped significantly. Otherwise, she has no history of trauma, surgery, radiation, polyphagia, cough or fever. Her medication history is significant only for intermittent use of antacids and analgesics. She didn't take drugs that may cause osmotic diuresis like mannitol.

She has no personal or family history of diabetes, hypertension, asthma, or heart disease. On examination, her vital signs are normal. Her body mass index is 16 kg/m2. Axillary and pubic hair appeared normal. There are no other significant findings. Her initial urine specific gravity was low (1.005). Her initial random urine osmolality test was 150 mOsm/kg. After overnight water deprivation test, the serum osmolality increased to 298 mOsm/kg however the urine osmolality was still low (210 mOsm/kg). The amount of urine during water deprivation test was 3 L over 8 h. Her urine specific gravity after water deprivation test was 1.006. Intravenous desmopressin challenge test was not done due to unavailability. However, after the patient started on low dose oral desmopressin her symptoms significantly improved and her urine specific gravity normalized to 1.020 on follow-up at the outpatient department visit. Her urine osmolality becomes 600 mOsm/kg. Serum beta human chorionic gonadotropin (βhCG) level was 1.2 mIU/mL (normal: < 5 mIU/mL), serum alpha-fetoprotein (AFP) level was 7 ng/ml (normal: 0 to 40 ng/mL), serum IgG4 level was 28 mg/dl (normal: <140 mg/dL), and serum soluble interleukin-2 receptor was 203 U/mL (normal: 158–623 U/mL). Baseline laboratory investigations are summarized in Table 1.

She had a normal chest x-ray. Magnetic resonant imaging (MRI) of the brain shows a partial filling of the pituitary fossa by CSF and a pituitary gland measuring 3.68 mm, which is small for her age and fulfills the criteria for a partial empty sella as shown in Fig. 1. There is no sign of intracranial hypertension. Pelvic ultrasound was normal. The patient is currently on follow-up in the endocrine outpatient department on desmopressin and improved symptoms.

Table 1 Laboratory investigation summary of an 18 years old patient with diagnosis of Arginine Vasopressin Deficiency (Central Diabetes Insipidus) with partial empty Sella

Laboratory investigation	Result	Reference range
White blood cell count	2,800/ mcL	4,000–10,000/ mcL
Hemoglobin level	14.3 g/dL	11.6–15 g/dL
Platelet count	325,000/mcL	150,000-400,000/mcL
Fasting blood sugar	79 mg/dL	70–100 mg/dL
Hemoglobin A1C	5.6%	< 5.7%
Erythrocyte sedimentation rate	1 mm/hr	< 20 mm/hr
Creatinine	1.32 mg/dL	0.6–1.3 mg/dl
Blood urea nitrogen	7 mg/dL	6–24 mg/dl
Aspartate transferase (AST)	36 U/L	8–40 U/L
Alanine transaminase (ALT)	16 U/L	7–42 U/L
alkaline phosphatase (ALP)	192 U/L	44–167 U/L
Albumin	4.95 g/dL	3.4–5.4 g/dL
Total protein	8.07 g/dL	6–8.3 g/dL
Prolactin	10.15 ng/mL	< 25 ng/mL
Thyroid-Stimulating Hormone (TSH)	1.69 mIU/L	0.5-5 mIU/L
Triiodothyronine (T3)	1.09 nmol/L	0.9-2.8nmol/L
Thyroxine (T4)	11.17 µg/dL	5–12 µg/dL
Basal cortisol	17 mcg/dL	5–25 mcg/dL
Potassium	4.3 mEq/L	3.6–5.2 mEq/L
Sodium	141 mEq/L	135–145 mEq/L
Chloride	104 mEq/L	96–106 mEq/L
Total calcium	9 mg.dl	8.5 and 10.5 mg/dL

Discussion

Diabetes insipidus is a rare presentation in patients with partial empty sella, despite the association of an empty sella with other pituitary hormone abnormalities [10]. The neurohypophysis is protected from excessive injury compared to the anterior pituitary due to the specific anatomical difference between the anterior and posterior pituitary. In particular, the vascular supply in the neurohypophysis has an anastomotic ring along the infundibular process from the medial and lateral arteries of the inferior hypophyseal arteries. This may be the reason why posterior pituitary involvement is less common than anterior pituitary involvement [3].

There is limited literature on arginine vasopressin deficiency associated with empty sella. The first of these was published in 1973 and described a 43-year-old woman with diabetes insipidus and postpartum galactorrhoea [11]. Marano et al. described a posterior empty sella in two children with central diabetes insipidus [12]. In our patient, the patient's anterior pituitary hormone function tests were all normal. She presented as a case of posterior pituitary deficiency and empty sella. The association could be coincidental.

Lambert et al. have also described a similar case but with both anterior and posterior pituitary dysfunction. They hypothesized that an empty sella may be due to necrosis of a previous pituitary adenoma, most commonly a prolactinoma, but again in our patient, we did not suspect this from the clinical presentation as the prolactin level was normal and the involvement was exclusively posterior pituitary [13]. The prevalence of empty sella ranges from 8 to 35% [3–5], with an increasing incidence due to the advancement and accessibility of various neuroimaging modalities. Our patient didn't have any clinical features that can suggest growth hormone deficiency, unlike other studies that have shown prominent growth hormone deficiency [6–8]. Contrary to other studies, our patient presented with diabetes insipidus, which is a rare manifestation of empty sella (1.5%) [10].

About 29.6% of patients had arginine vasopressin deficiency in a series of patients with Sheehan's syndrome, all of these patients had an increased thirst threshold [14]. Our patient has no history of pregnancy and doesn't have Sheehan's syndrome. The presentation of central diabetes insipidus in this patient is due to a primary partial empty sella. The prevalence of migraine headache is higher in women with a ratio of 3 to 1. This may have contributed to the higher prevalence of incidental partial empty sella in this particular population, as they may be exposed to neuroimaging modalities that help to diagnose and detect asymptomatic (and clinically silent) partial empty sella. In our case, the patient is a female with a four-year history of intermittent severe headaches that have worsened in the last two years, which is similar to other studies and case reports [10].

This patient had a classic presentation of central diabetes insipidus and amenorrhoea of four years' duration, possibly caused by her significant weight loss. Hormonal analysis showed normal levels of cortisol, follicle-stimulating hormone, luteinizing-hormone, thyroid function test and prolactin. Her initial urine specific gravity was low (1.005), which corresponded to a diluted urine with an osmolarity of 150 mosmol/L [15, 16]. Only urine osmolality above 700 mOsm/kg excludes diabetes insipidus. Her serum sodium concentration is also in the higher part of the reference range which is more suggestive of diabetes insipidus [17]. After overnight water deprivation test, the serum osmolality increased to 298 mOsm/kg and the urine osmolality was still low (210 mOsm/kg) which helps us to exclude primary polydipsia for sure. In normal conditions urine osmolality should have to rise usually to over 750 mOsm/kg. Further IV desmopressin test was not done due to local unavailability. However, the patient was started on desmopressin 60 µg po once at bedtime and her total urine output decreased significantly to 5 L/day. After adjustment to desmopressin 60 µg in the morning and 120 µg po at night, her fluid intake urine output normalized and urine specific gravity normalized. This confirms the diagnosis

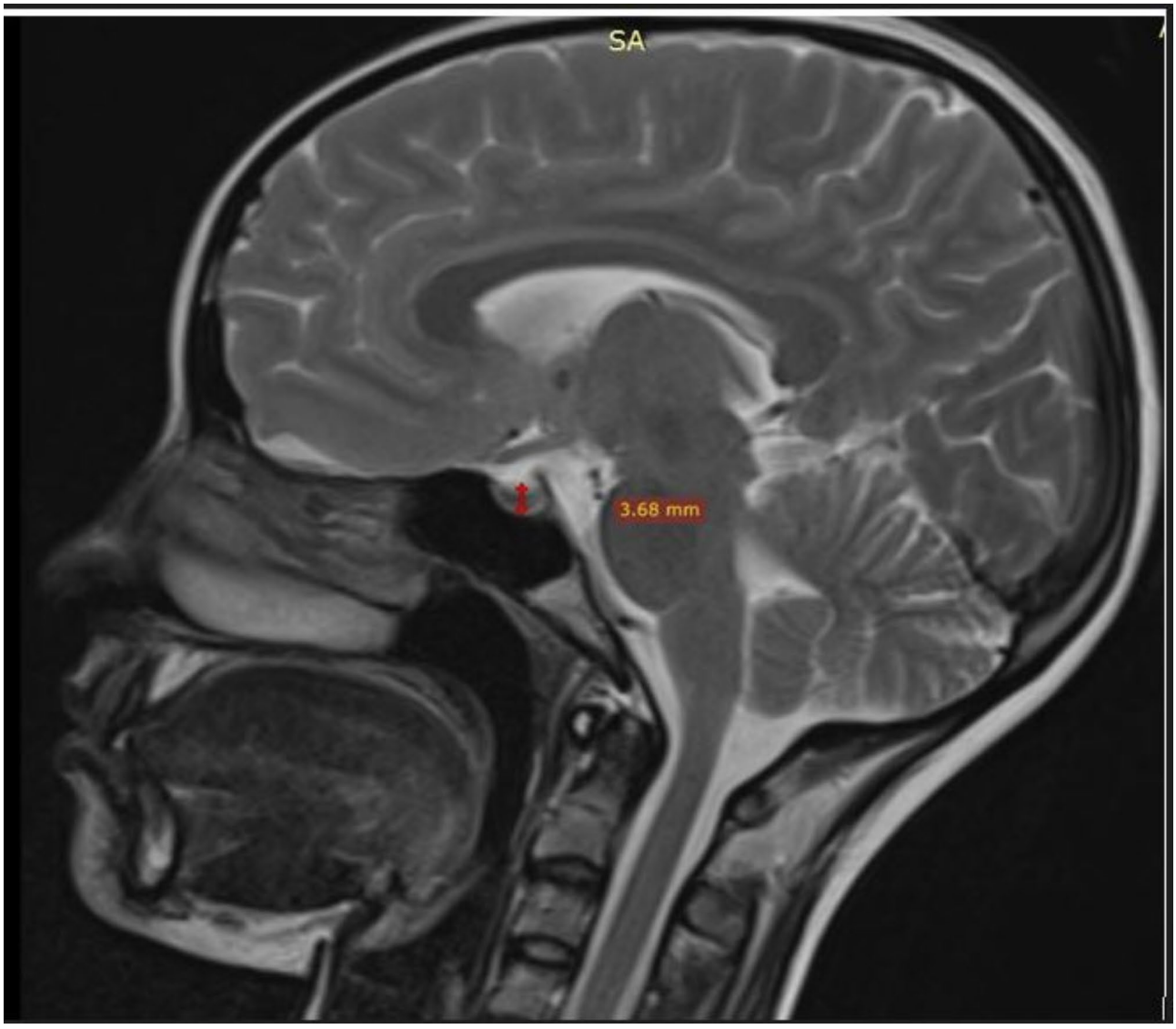

Fig. 1 Brain MRI of an 18 years old female patient with partial empty sella and the diameter of the pituitary gland

of arginine vasopressin deficiency (central diabetes insipidus) with partial empty sella.

A high incidence of pituitary dysfunction has been documented in patients with primary empty sella syndrome. These included panhypopituitarism, secondary hypogonadism, hyperprolactinemia, isolated adrenocorticotropic hormone deficiency, and diabetes insipidus [18]. In our case study, MRI of the brain showed a slightly prominent and CSF-filled sella with a partially flattened and thinned pituitary gland, with the conclusion of a partially empty sella. There is no mass on the MRI that suggests the possible differential diagnosis like craniopharyngioma, germinoma, pinealoma, or a metastasis, lymphomas, Langerhans cell histiocytosis. Lack of involvement of the hypothalamus and normal infundibular stalk makes langerhans cell histiocytosis and sarcoidosis unlikely. No other organ involvement seen in this patient that suggests IgG4 related disorder or IgG hypophysitis. Additional investigations such as beta human chorionic gonadotropin (βhCG), alpha-fetoprotein (AFP) levels, serum IgG4 level, and soluble interleukin-2 receptor were also normal. A repeat MRI is planned to see any change of the imaging within six months to a year period.

The patient is currently being followed up at the endocrine clinic. The radiological grade of partial empty sella tends to remain constant over time. However, due to the theoretical risk of progression, a re-evaluation of the endocrine, neuro/ophthalmological, and radiological picture after months is reasonable. If no progression is observed, additional surveillance could be even less frequent and limited to those patients who clinically require it [3].

Conclusion

Arginine vasopressin deficiency secondary to partial empty sella is a very rare condition with very few reports. We should consider partial empty sella as a possible cause of arginine vasopressin deficiency if supported by pituitary imaging after other common causes have been excluded.

Abbreviations

MRI Magnetic Resonant Imaging
CSF Cerebrospinal Fluid

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Author contributions

All the authors were involved in manuscript preparation, critical analysis, and revision of the manuscript.

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Data availability

All data sets on which the conclusions of the case report are based are to be available as a medical record document and available from the corresponding author on reasonable request from the editors.

Declarations

Ethical approval and consent to participate

The institution does not require ethical approval for the publication of a single case report.

Consent for publication

Written informed consent was obtained from the patient for publication and use of images. The written consent is available for review by the Editor-in-Chief of this journal upon inquiry.

Competing interests

The authors declare no competing interests.

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