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Case Report

Arginine Vasopressin Resistance in a Patient with a Pituitary Microadenoma

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Abstract

***Introduction**: This case report presents a unique case of new-onset arginine vasopressin resistance in a 42-year-old patient with a co-existing pituitary microadenoma.*

Clinical case: A 42-year-old male presented to our facility with findings consistent with severe diabetic ketoacidosis, likely triggered by MRSA sepsis. He developed polydipsia and polyuria during his hospital stay, for which he was investigated. Based on the characteristic laboratory findings, a diagnosis of arginine vasopressin resistance was made, but no recognized cause was identified. An MRI study of the pituitary showed a pituitary microadenoma, with clinical and biochemical picture suggesting hypogonadotropic Hypogonadism. He was successfully treated with hydrochlorothiazide and testosterone, allowing for the improvement of his symptoms. Conclusion: Arginine vasopressin resistance (AVP-R) should be considered even if no causes are recognized. Also, it could co-exist with pituitary microadenoma. However, a possible association between these diagnoses is still unclear.

***Keywords**: Arginine vasopressin resistance, Pituitary microadenoma. Case Report, Diabetic ketoacidosis MRSA sepsis. Polydipsia, Polyuria.*

Introduction

Arginine vasopressin deficiency/resistance is a clinical syndrome characterized by polyuria due to a defect in the urinary concentrating mechanism and compensatory polydipsia. In the general population, the prevalence of is approximately one per 25,000–30,000 (2). Arginine vasopressin resistance (AVP-R), previously called nephrogenic diabetes insipidus is acquired and occurs as a complication to numerous common clinical conditions, such as electrolyte disturbances, medications, or secondary to genetic renal diseases (6). However, pituitary adenoma is not a recognized cause of Arginine vasopressin resistance (AVP-R) in the literature.

We report a very interesting case of a man with newly diagnosed arginine vasopressin resistance in whom a pituitary microadenoma was identified. We discuss the challenges faced in determining the cause and emphasize the importance of recognizing this association.

Case Presentation

A 42-year-old male patient known to have diabetes mellitus for five years. In the past three months, patient was not compliant with his antidiabetic medications. Presented to our emergency department complaining of a generalized feeling of unwellness, fatigue, and abdominal pain. Upon initial examination, the patient looked severely dehydrated and drowsy with a Glasgow Coma Scale of 11 out of 15. He was hypotensive with a blood pressure of 92/50 mmHg, tachycardic (heart rate 107/min), tachypnoeic (respiratory rate 27/min) but maintaining saturation on room air and hypothermic (temperature 33.4 degrees). Lab investigations on admission revealed a high anion gap metabolic acidosis with a pH of 6.90 associated with hyperglycemia of 43.5 mmol/L, ketosis with blood ketones of 6.6 mmol/L, glucosuria, and ketonuria. Inflammatory markers were elevated WBC 22 with neutrophilia and a CRP of 104 mg/L. Due to low GCS, a non-contrast brain CT scan was requested, and it was unremarkable. A diagnosis of sever diabetic ketoacidosis (DKA) was made, and management as per the DKA institutional protocol was initiated with insulin infusion and fluid therapy along with empirical antibiotic coverage because of elevated septic markers. Within two days of his admission, the patient was out of DKA; however, he became more confused and spiked a high-grade fever of 38.6 degrees. Blood culture showed growth of Methicillin-Resistant Staphylococcus Aureus. He was transferred to the ICU, and antibiotics were changed from empirical antibiotics to targeted antibiotic therapy based on culture and sensitivity. Bedside Echocardiogram was normal and did not reveal any valvular vegetations.

On day 10 of the patient's admission, it was noted that he had an increase in his urine output; his charted 24-hour urine output was reaching up to 9 L. He also reported increased levels of thirst since his hospital admission. According to the patient, he had been experiencing thirst and an increase in frequency in passing urine in the last few months since he stopped his antidiabetic medications, but never to such an extent. On further questioning to rule out pituitary pathology, he reported having decreased libido and erectile

dysfunction for the past year. Full pituitary hormone panel was sent and revealed only a low testosterone levels with low LH and FSH, full details of the result are shown in (Table 1). Endocrinology services were consulted, and a water deprivation test was requested. Following the administration of intravenous desmopressin, no improvement in urine output, plasma and urine osmolality were noted (Table 2). Based on the clinical picture and laboratory findings, a diagnosis of Arginine vasopressin resistance (AVP-R), was made. Nephrology services were consulted, and after reviewing the patient, no medication or condition typically associated with AVP-R was detected. Furthermore, in view of the evidence of partial hypopituitarism and the prolonged history of symptoms of hypogonadism, a pituitary MRI was done and showed a small lesion of preferential enhancement suggestive of a pituitary microadenoma displayed in Figure 1.

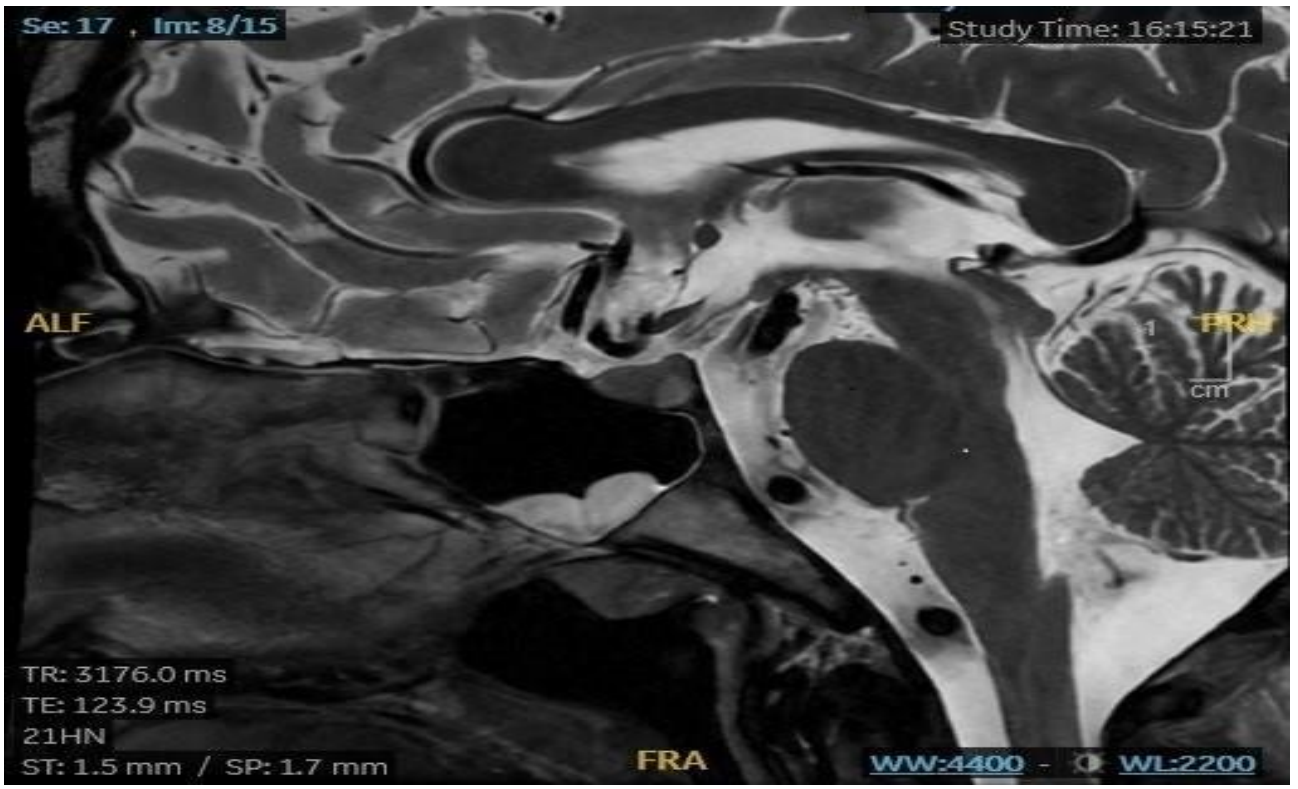

Figure 1. T2 weighted Sagittal MRI of the pituitary showing a small lesion of preferential enhancement measuring 0.43 x 0.58 x 0.52 cm in its maximal anteroposterior, transverse, and cephalocaudal dimensions, respectively involving the posterior aspect of the anterior lobe of the pituitary gland wing as an area of low enhancement in both the dynamic and post-dynamic series.

Table 1. Table 2, Serum biochemical and endocrine values		
Measurements	Patient's results	Reference values
TSH	1.07 mlU/L	0.55 – 4.78 mlU/L
T3	3.04 pmol/L	3.5 – 6.5 pmol/L
T4	9.24 pmol/L	11.5 – 22.70 pmol/L
HbA1c	14 mmol/mol	4.80 – 6.00 mmol/mol
Prolactin	243 ulU/ml	45.00 – 375.00 ulU/ml
LH	1.48 IU/L	1.50 – 9.30 IU/L
FSH	1.31 IU/L	1.40 – 18.10 IU/L
Cortisol 8 AM	870.5 nmol/L	145.40 – 619.40 nmol/L
IGF	24 ng/ml	101 – 267 ng/ml
Testosterone	0.56 pg/ml	6.30 – 17.80 pg/ml
Sodium	145 mmol/L	136 – 145 mmol/L
Potassium	4.23 mmol/L	3.50 – 5.10 mmol/L
Chloride	107 mmol/L	98 – 107 mmol/L
Glucose	18.7 mmol/L	3.9 – 6.1 mmol/L
Calcium	2.18 mmol/L	2.12 – 2.52 mmol/L
Phosphorus	0.75 mmol/L	0.84 – 1.52 mmol/L
Magnesium	0.91 mmol/L	0.70 – 0.99 mmol/L
Creatinine	109 umol/L	62 – 115 umol/L
Urea	6.33 mmol/L	2.10 – 7.10 mmol/L
eGFR	80 ml/min/1.73 m^2	> 90 ml/min/1.73 m^2

Table 2. Serum and urine osmolality values before and after water deprivation test, administration of desmopressin (DDAVP), and hydrochlorothiazide therapy.		
Time and conditions	Serum Osmolality	Urine Osmolality
Reference Values	275- 295 mOsm/kg	50- 1200 mOsm/kg
Pre water Deprivation test	287 mOsm/kg	126 mOsm/kg
Post water deprivation test	293 mOsm/kg	126 mOsm/kg
Post-Intravenous desmopressin	293 mOsm/kg	126 mOsm/kg
Post hydrochlorothiazide treatment	273 mOsm/kg	156 mOsm/kg
Results demonstrated the diagnosis of NDI as defined by < 50% improvement in urine osmolality post administration of Desmopressin		

A multidisciplinary team approach was utilized, and through the combined efforts of the endocrinology and nephrology teams, a treatment regimen was tailored for the patient. For Arginine vasopressin resistance (AVP-R), Hydrochlorothiazide was initiated, 25mg TID, then increased to 50mg TID, after which notable improvement in his condition was detected. The patient was also started on Testosterone 1000mg intramuscular every 3 months for his hypogonadotropic hypopituitarism. For his diabetes, he was discharged on insulin Glargine U300 26 units bed time and lispro 10 units with each meal. Patient was discharged on the 15th day following admission.

Unfortunately, the patient failed to attend his scheduled follow-up clinic appointment, but he was contacted via the phone, and he reported feeling well in himself with no additional issues while taking his medications. He stated his preference to follow up in a different facility, thus further evaluation of his progress was not possible.

Discussion:

Water is essential for life; without it, humans can survive only for days. It is essential for cellular homeostasis and life. (1). Maintaining normal body water balance requires a system that ensures the daily intake of water matches the daily loss. Excretion by the kidney is one of the key factors in the body's ability to adjust to preserve body water balance (2). Increases in plasma osmolality or decreases in blood volume stimulate the

osmoreceptors in the hypothalamus, leading to the secretion of the antidiuretic hormone arginine vasopressin (AVP) from the pituitary gland. (3) Arginine vasopressin deficiency/ resistance is a group of hereditary or acquired polyuria and polydipsia diseases. It is associated with inadequate (ADH) secretion or renal response to it, resulting in its characteristic manifestations of hypotonic polyuria (>50 mL/kg), dilute urine (osmolality <300 mOsm/L), and increased thirst (water intake of up to 20 L/day) (1). ADH facilitates aquaporin (AQP)-mediated water reabsorption via activating the vasopressin V2 receptor (AVPR2) in the collecting duct, thus enabling urine concentration. In Arginine vasopressin resistance (AVP-R), the kidneys cannot respond to ADH. (2). The causes of AVP-R are variable, extending from congenital to acquired causes. Such causes include exposure to drugs including lithium, demeclocycline, and cisplatin, electrolyte disturbances such as hypercalcemia, hypokalaemia, infiltrating lesions (sarcoidosis, amyloidosis, multiple myeloma, etc.), vascular disorders (sickle cell anaemia), and mechanical (polycystic kidney disease, urethral obstruction).(3)

Increased interest in the nature and the causatives of AVP-R has been witnessed in the past decade. Extensive analysis of the drugs contributing to decreasing the Nephrogenic Aquaporins receptors has been studied. Drugs classically implicated include Lithium(4) and Demeclocycline. Newer additions, including Foscarnet and Amphotericin (5), among other nephrotoxic medications such as Cisplatin and Clozapine (6), have been investigated.

Our patient was referred to endocrinology services to investigate his worsening of his symptoms of polyuria and polydipsia, and to exclude Arginine vasopressin deficiency/resistance the instigator. During questioning, one vital finding emerged: the patient had been experiencing erectile dysfunction and decreased libido for a year prior to his admission. As guided by the patient's medical history and the crucial new piece of information learned, our thoughts were directed towards a pathology in the pituitary as a possible explanation for both presentations. Therefore, we proceeded with the water deprivation test alongside an evaluation of his pituitary hormone profile. Lab investigations revealed evidence of hypogonadotropic hypogonadism, thus a pituitary MRI was requested and revealed a pituitary microadenoma. The water deprivation test was conducted based on the hospital protocol, with review and discontinuation of any interfering medications. The test lasted a total of 8 hours, and included the administration of desmopressin injection of 2 µg IV after two consecutive urine osmolaility readings of no variation were obtained. Results demonstrated the diagnosis of AVP-R as defined by < 50% improvement in urine osmolality post

administration of Desmopressin (7).

Although our patient had a complicated hospital course with multiple antibiotic administrations, none of the medications used have had any previously reported links to AVP-R (8). Furthermore, electrolyte imbalances, including hypokalaemia (9) and hypercalcemia (10) which have been reported to play a role in the development of AVP-R, have not been detected throughout his hospital stay. No infiltrative or vascular pathologies were found either.

While the argument that this could be a pituitary incidentaloma might be raised. Our patient reported erectile dysfunction with reduced libido for one year prior to his admission. This particular detail alongside his pituitary hormonal profile which indicated evidence of hypogonadotropic hypogonadism make the diagnosis of incidentaloma very unlikely (11).

Our patient represents an interesting case for two reasons, the first of which is that after extensive investigations, we could not find any plausible cause for his AVP-R. The second is that he was found to have a pituitary microadenoma and AVP-R, an unusual combination. And after conducting an extensive literature review to explore the possibility of the presence of an association between pituitary microadenoma and AVP-R , nothing could be found, making this a case report regarding a rare case of a pituitary micro-adenoma coexisting with AVP-R.

Conclusions:

We report a case of a coexisting pituitary microadenoma with arginine vasopressin resistance, the latter of which had no identifiable cause in our patient. Our take home message is that clinicians should be careful not to be misled by the co-existance of two medical conditions that seem related or part of a single entity during initial assessment. Instead, they should make every effort to consider alternative explanations by looking beyond the obvious cause in order to intervene appropriately early on for the best outcome, as was the case in our patient.

Confirmation of consent for publications: The authors confirm that they have obtained the consent of the patients for publication of the case report on a totally anonymous basis.

Conflict of interest: None

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Compliance with ethical principles: Approval of institutional review board is not required for single case reports or small case series provided patients give consent and reporting is completely anonymous.

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