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CLINICAL CASE

Adipsic central diabetes insipidus as a result of neurosarcoidosis

Diabetes insípida central adípsica como resultado de neurosarcoidosis

RADMILA MILOSHESKA[1*], IVANA MICKOVSKI[1,2], AND DANIELA BUKLIOSKA ILIJEVSKA[1,3]

[1]Department of Endocrinology, Diabetes and Metabolic Diseases, City General Hospital 8th September, Skopje; [2]Medical Sciences Faculty, Goce Delcev University, Stip; [3]Department of Pulmonology and Allergology, City General Hospital 8th September, Skopje. North Macedonia

ABSTRACT

Sarcoidosis is a systemic multisystem inflammatory disorder of unknown etiology characterized by the presence of non-caseating granulomas. Neurosarcoidosis leads to hypothalamus-pituitary axis dysfunction, and the most common clinical manifestation is the onset of arginine vasopressin deficiency. We present a case involving a 46-year-old female patient with neurosarcoidosis and associated changes in the hypothalamus-pituitary axis, leading to clinical manifestations of hypopituitarism and an atypical presentation of arginine vasopressin deficiency. The diagnosis of neurosarcoidosis has not been confirmed throughthrough biopsy due to its associated high risk and accessibility challenges. However, based on the computed tomography and magnetic resonance imagingcomputed tomography and magnetic resonance imagingresults and the clinical presentation, the patient received hormone replacement therapy with levothyroxine 25 mcg, hydrocortisone 20 mg + 10 mg, and desmopressin 50 mcg to alleviate the clinical symptoms. Notably, the diagnosis of arginine vasopressin deficiency could not be confirmed based solely on clinical characteristics due to the absence of polydipsia and polyuria. In addition, the classic water deprivation test was inconclusive due to persistent hypernatremia, which was confirmed by ruling out other potential causes of hypernatremia. Neurosarcoidosis presents a diverse clinical profile and poses challenges in diagnosis and treatment, particularly in patients with disorders affecting the hypothalamus-pituitary axis and non-typical arginine vasopressin deficiency.

Keywords: Neurosarcoidosis. Arginine vasopressin deficiency. Hypernatremia.

RESUMEN

La sarcoidosis es un trastorno inflamatorio sistémico de etiología desconocida caracterizado por la presencia de granulomas no caseificantes. La neurosarcoidosis conduce a una disfunción del eje hipotálamo-hipofisario y la manifestación clínica más frecuente es la aparición de una deficiencia de arginina-vasopresina. Presentamos el caso de una paciente de 46 años de edad con neurosarcoidosis y cambios asociados en el eje hipotálamo-hipófisis, dando lugar a manifestaciones clínicas de hipopituitarismo y una presentación atípica de deficiencia de arginina-vasopresina. El diagnóstico de neurosarcoidosis no se ha confirmado mediante biopsia debido al alto riesgo asociado y a las dificultades de accesibilidad. Sin embargo, con base en los resultados de la tomografía computarizada y la resonancia magnética, así como en la presentación clínica, la paciente recibió terapia hormonal sustitutiva con levotiroxina, hidrocortisona y desmopresina para aliviar los síntomas clínicos. Cabe destacar que el diagnóstico de deficiencia de arginina-vasopresina no pudo confirmarse basándose únicamente en las características clínicas debido a la ausencia de polidipsia y poliuria. Además, la prueba clásica de privación de agua no fue concluyente debido a la hipernatremia persistente, que se confirmó descartando otras posibles causas de hipernatremia. La neurosarcoidosis presenta un perfil clínico diverso y plantea retos en el diagnóstico y el tratamiento, sobre todo en pacientes con trastornos que afectan al eje hipotálamo-hipófisis y déficit de arginina-vasopresina no típico.

Palabras clave: Neurosarcoidosis. Déficit de arginina-vasopresina. Hipernatremia.

***Correspondence:**
Radmila Milosheska
E-mail: neshovskaradmila@gmail.com

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INTRODUCTION

Sarcoidosis is a systemic disease characterized by the development of granulomas. Predominantly affecting the lungs and lymphatic system, it infrequently involves the central nervous system, occurring in approximately 5-15% of cases[1]. Central nervous system involvement manifests as dysfunction of the hypothalamus-pituitary axis, often resulting in panhypopituitarism and arginine vasopressin deficiency[1-3]. Arginine vasopressin deficiency presents with symptoms such as increased thirst, polydipsia, and polyuria and is managed with desmopressin, a synthetic analog of antidiuretic hormone (ADH), administered throughthrough various routes, including oral, intranasal, subcutaneous, and intravenous[3]. We report an atypical arginine vasopressin deficiency presenting without polydipsia and polyuria but with persistent hypernatremia.

CASE REPORT

A 46-year-old female patient presented at the emergency center with symptoms of diarrheal syndrome, hypotension (blood pressure 90/60 mmHg), weakness, and malaise persisting for 33 days. Ten years ago, the patient was diagnosed with pulmonary sarcoidosis, which was verified by lung computed tomographytomography and pathologically confirmed by invasive bronchoscopy. She has been undergoing immunosuppressive therapy with methotrexate and prednisone, taking frequent breaks when her condition improves. Furthermore, she had diabetes mellitus type 2 on the glucagon-like peptide-1 receptor agonist (GLP-1RA) therapy and metformin. Due to a history of pulmonary sarcoidosis and type 2 diabetes mellitus treated with GLP-1RA therapy, medication side effects were initially suspected. Laboratory tests revealed elevated sodium 160 mmoL/L (136-145 mmol/L), potassium within the normal range 3.8 mmol/L (3.5-5.1 mmol/L), elevated urea 18.1 mmoL/L (2.8-7.2 mmol/L), elevated creatinine 227.6 μmol/L (50.4-110.5 μmol/L), and normal blood glucose levels (Table 1), adrenocorticotropic hormone (ACTH) 5.61 pg/mL (5.0-46.0 pg/mL), and cortisol 1.35 μg/dL (5.0-25.0 μg/dL). The patient was admitted to the endocrinology department for treatment, including continuous rehydration therapy with hypotonic sodium chloride solution 0.45%, calculated using the Adrogue-Madias formula for slow correction of hypernatremia, which improved her clinical condition.

On the 3rd day of hospitalization, the patient's neurological symptoms worsened, leading to visible hallucinations, pronounced vertigo, and vomiting. A neurological assessment and brain magnetic resonance imaging (MRI) showed a 24 × 16 mm solid mass in the suprasellar, retrochiasmal region of the hypothalamus, with signs of chiasm compromise and involvement of the interpeduncular cistern and pressure on the third cerebral ventricle. An MRI of the pituitary gland revealed a pronounced empty sella phenomenon, with a dominant suprasellar cistern and significant adenohypophysis lumen thinning (Figs. 1 and 2). Although highly suspected to be neurosarcoidosis, biopsy for histological confirmation was not feasible due to the mass location and technical constraints. Corticosteroid therapy was initiated, and prednisone 10 mg/day ledled to improved general condition and improved laboratory findings (Tables 1 and 2). A follow-up examination 11 month later showed the patient to be in good health, but laboratory results indicated hypernatremia at 160 mmoL/L. The hormonal status assessment revealed ACTH < 5 pg/mL, cortisol 23.6 μg/dL (5.0-25.0 μg/dL), follicle-stimulating hormone 1.7 mIU/mL (2.8-11.3 mIU/mL), luteinizing hormone 0.2 mIU/mL (1.1-11.6 mIU/mL), estradiol 29.8 pg/mL (20.0-160 pg/mL), prolactin 50.1 ng/mL (1.9-25.0 ng/mL), thyroid-stimulating hormonehormone 7.1 μIU/mL (0.3-4.3 μIU/mL), and fT4 0.6 ng/dL (0.8-1.7 ng/dL (0.8-1.7 ng/dL), indicating hypopituitarism (Table 3). Substitution therapy with hydrocortisone 20 + 10 mg and levothyroxine 25 mg/day was initiated with improvedhormonal levels (Table 3). Despite substitution therapy with corticosteroids, the patient experienced persistent asymptomatic hypernatremia, dry mouth, dry skin, reduced skin turgor, and the absence of polydipsia and polyuria, raising suspicion of arginine vasopressin deficiency. Low natriuresis 55 mmol/L (ref. value 100-200 mL) and urine

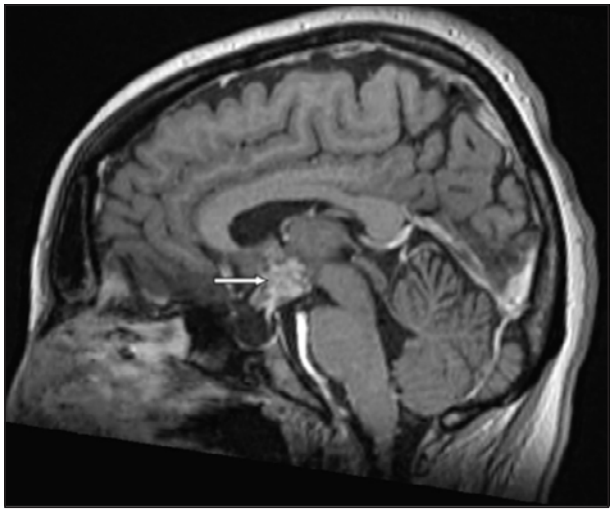

Figure 1. Magnetic resonance imaging sagittal T1 section, solid mass in the suprasellar, retrochiasmal region of the hypothalamus.

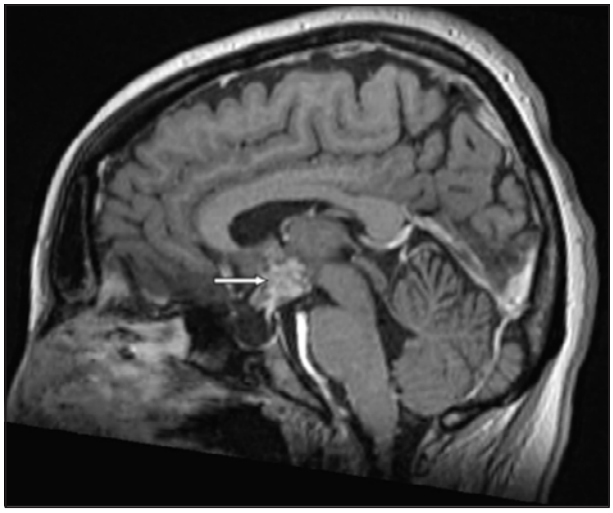

Figure 2. Magnetic resonance imaging axial section, solid mass with involvement of the interpeduncular cistern, and pressure on the third cerebral ventricle.

Table 1. Laboratory parameters on the first day of hospitalization and after therapy with prednisone 10 mg and hypotonic 0.45% sodium chloride solution

Parameters	1st day	After therapy	Reference values
Sodium	160 mmol/L	142 mmol/L	136-145 mmol/L
Potassium	3.8 mmol/L	2.7 mmol/L	3.5-5.1 mmol/L
Urea	18.1 mmol/L	11.5 mmol/L	2.8-7.2 mmol/L
Creatinine	227 μmol/L	159 mmoL/	50.4-110.5 μmol/L
Calcium	3.0 mmol/L	1.3 mmol/L	2.1-2.5 mmol/L
Magnesium	1.1 mmol/L	0.8 mmol/L	0.7-1.1 mmol/L
Phosphor	1.6 mmol/L	1.2 mmol/L	0.8-1.6 mmol/L
Glycemia	5.4 mmol/L	4.5 mmol/L	4.1-5.9 mmol/L
LDH	202 U/L	208 U/L	81-234 U/L
AST	69 U/L	61 U/L	5-37 U/L
ALT	50 U/L	39 U/L	6-55 U/L

LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

osmolality (< 300 mOs/kg) compared to high serum osmolality (335 mOs/kg) suggest arginine vasopressin deficiency. Clinical symptoms and laboratory data indicate dehydration but no thirst. Because the water deprivation test was contraindicated due to high sodium levels, desmopressin 50 mcg/day was initiated. The patient's diuresis and water intake were monitored, resulting in normalized sodium levels and a decrease in degradation products and osmolality

Table 2. ACTH and cortisol levels on 1st day and after 1 month

ACTH	Cortisol	Evaluation time
5.61 pg/mL	1.35 μg/dL	First day
< 5.00 pg/ml	23.6 μg/dL	After 1 month
5.0-46.0 pg/mL	5.0-25.0 μg/dL	References value

ACTH: adrenocorticotropic hormone.

Table 3. Laboratory parameters after 11 month and after therapy with levothyroxine 25 mcg and hydrocortisone 20 mg + 10 mg

Laboratory examination	After month	After therapy	References value
Sodium	160 mmol/L	160 mmol/L	7.0 mmol/L
Potassium	3.8 mmol/L	3.5 mmol/L	3.5 - 5.1 mmol/L
FSH	1.7 mIU/mL	1.9 mIU/mL	2.8-11.3 mIU/mL
LH	0.2 mIU/mL	0.5mIU/mL	1.1-11.6 mIU/mL
TSH	7.1 μU/mL	3.0 μU/mL	0.3-4.3 μIU/mL
fT4	0.6 ng/dL	0.7 ng/dL	0.8-1.7 ng/dL
Estradiol	29.8 pg/mL	< 20.0 pg/mL	20.0-160 pg/mL
Prolactin	50.1 ng/mL	53.9 ng/mL	1.9-25.0 ng/mL
Urea	21.6 mmol/L	18.5 mmol/L	2.8-7.2 mmol/L
Creatinine	323 μmol/L	250 μmol/L	50.4-110.5 μmol/L

FSH: follicle-stimulating hormone; LH: Luteinizing hormone; TSH: thyroid-stimulating hormone.

Table 4. Sodium level before and after treatment with desmopressin 50 mcg/day

Parameters	Before treatment	With desmopressin	References value
Sodium	160 mmol/L	142 mmol/L	7.0 mmol/L
Potassium	3.8 mmol/L	2.8 mmol/L	3.5 - 5.1 mmol/L
Urea	18.5 mmol/L	12.6 mmol/L	2.8-7.2 mmol/L
Creatinine	250 μmol/L	144 μmol/L	50.4-110.5 μmol/L

(Table 4), which implicitly confirmed the diagnosis of atypical arginine vasopressin deficiency. Cortisol deficiency followed by appropriate substitution has led to notable clinical improvements in the patient's condition (Table 2). However, this improvement may obscure the underlying issue of arginine vasopressin deficiency, particularly in cases where thirst remains intact. The ongoing presence of significant hypernatremia highlights the importance of considering this potential condition.

DISCUSSION

Neurosarcoidosis is a complex disease with diverse clinical presentations, often affecting the central nervous system at various levels, particularly the hypothalamus, pituitary gland, and cranial nerves[3]. Diagnosis presents a significant challenge due to non-specific symptoms and the difficulty of obtaining a definitive diagnosis through biopsy and pathohistological analysis[3]. The dysfunction of the pituitary gland leads to various endocrine dysfunctions, with arginine vasopressin deficiency being a common initial symptom. Imaging methods such as brain MRI are often used to aid in diagnosis. Although confirmation through biopsy and pathohistological findings is preferred, it is not always feasible[3-5]. The emergence of endocrinological manifestations of the disease, particularly arginine vasopressin deficiency, may mask other conditions and contraindicate the water deprivation test[5]. Treatment for patients with neurosarcoidosis primarily involves hormone replacement therapy, specifically ADH analog desmopressin, and additional corticosteroid therapy if indicated[5]. In cases where patients cannot tolerate steroid monotherapy, second-line medications, such as immunosuppressants, are considered.

CONCLUSION

The management and treatment of neurosarcoidosis present a significant challenge due to its diverse clinical manifestations and associated endocrinological dysfunctions, impacting the patient's quality of life. The complexity of diagnosing neurosarcoidosis often leads to impediments and complications, emphasizing the critical importance of prompt and comprehensive treatment, which can ultimately be lifesaving.

AUTHORS' CONTRIBUTION

Literature review, critical review, and manuscript preparation held by all authors.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest about this manuscript.

ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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