

# FUNCTIONAL AND TRANSIENT DEFECT OF SODIUM EXCRETION IN COMBINED PITUITARY FAILURE WITH CENTRAL AND PERIPHERAL DIABETES INSIPIDUS: Case report

Ana Coelho Gomes<sup>1</sup>, Ana Filipa Martins<sup>1</sup>, João Martin Martins<sup>1,2</sup>, Sónia do Vale<sup>1,2</sup>, Isabel do Carmo<sup>1,2</sup>

1 – Santa Maria Hospital, Endocrinology, Diabetes and Metabolism Department, Lisbon, Portugal. 2 – Lisbon Medical School, Lisbon, Portugal.

## BACKGROUND

Central and peripheral Diabetes Insipidus are both rare conditions.

Combined they may result in serious hypernatremia and water deficit that may pose a therapeutic challenge.

## CLINICAL PRESENTATION

♀, 52 years-old, Caucasian, teacher

### PAST HISTORY

- Bipolar disorder, treated with lithium occasionally
- July 2008** ⇒ Hypophysectomy due to a non-secreting pituitary macroadenoma, with secondary panhypopituitarism and central diabetes insipidus. Treated with hydrocortisone (20mg+5mg+5mg), levothyroxine 125µg qd and desmopressin PO 0,12mg (tid). Even with this treatment the patient had urinary volumes of about 5-6L per day.
- 2010** ⇒ admitted to the hospital due to hypernatremia

### SYMPTOMS

- 17<sup>th</sup> July 2012** ⇒ admitted to a Psychiatric hospital due to a manic episode ⇒ **Lithium**
- 20<sup>th</sup> July 2012** ⇒ Fever + Acute mental confusion + Extrapyrimal symptoms (head and neck dyskinesia) + diuresis of 7L per day

### PHYSICAL EXAMINATION

- Desoriented, cognitive impairment, delusions
- Dehydrated
- Blood pressure: 110/50mmHg; Cardiac rate: 78bpm
- Afebrile, without focal neurologic signs, meningeal signs or seizures.

## LABORATORY

- Laboratory testing** supported a panhypopituitarism and a central and peripheral diabetes insipidus. Lithium was below the reference level. (Tables 1A, 1B and 1C)

Variable	Values
<b>HEMOGRAM</b>	
Hemoglobin (g/dL)	12.5
Hematocrit (%)	37.9
White-cell count (per mm <sup>3</sup> )	6040
Platelets (per mm <sup>3</sup> )	<b>146000</b> ↓
<b>BIOCHEMISTRY</b>	
Urea (mg/dL)	25
Creatinin (mg/dL)	<b>1.3</b> ↑
Sodium (mmol/L)	<b>153</b> ↑
Potassium (mmol/L)	3,7
Osmolality (mOsmol/Kg)	<b>308</b> ↑
Calcium (mg/dL)	8,7
Phosphorus (mg/dL)	<b>1.2</b> ↓
Albumin (mg/dL)	<b>2.8</b> ↓
Total proteins (mg/dL)	<b>5,6</b> ↓
<b>URINE TEST</b>	
Density	<b>&lt;1.005</b> ↓

Table 1A – Laboratory testing on admission

Variable	Values
<b>ENDOCRINOLOGY</b>	
Thyroid-stimulating hormone (µg/mL)	<b>0,010</b> ↓
Free thyroxine (ng/dL)	0,98
Adrenocorticotrophic hormone (pg/mL)	11,7
Cortisol (µg/dL)	<b>3.8</b> ↓
Renin (pg/mL)	13,7
Aldosterone (pg/mL)	61,4
Follicle-stimulating hormone (U/L)	4,1
Luteinizing hormone (U/L)	1,49
Estradiol (pg/mL)	<b>&lt;19</b> ↓
Prolactin (ng/mL)	<b>&lt;0.3</b> ↓
Parathyroid hormone (pg/mL)	<b>123.5</b> ↑
25-hydroxy Vitamin D (ng/mL)	<b>7,2</b> ↓
Growth hormone (ng/mL)	<b>&lt;0.05</b> ↓
Insulin-like growth factor (ng/mL)	<b>&lt;25</b> ↓
Insulin-like growth factor binding protein 3 (µg/mL)	<b>1,75</b> ↓

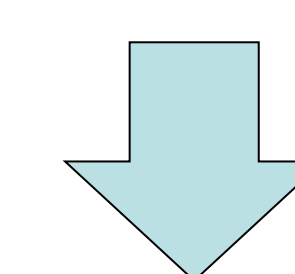
Table 1B – Laboratory testing on admission

Variable	Values
<b>DRUGS IN SERUM</b>	
Lithium (mmol/L)	<b>0.59</b> ↓
<b>DRUGS IN URINE</b>	
Benzodiazepines	<b>POSITIVE</b>
Tricyclic antidepressants	<b>NEGATIVE</b>
Barbiturates	<b>NEGATIVE</b>

Table 1C – Laboratory testing on admission

## TREATMENT

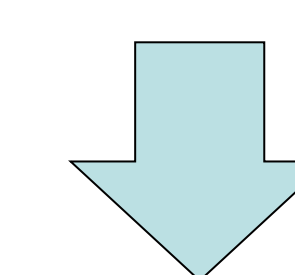
- Sodium chloride (NaCl) 0,9% + 5% dextrose solution ⇒ Total: 2000mL qd
- Nasal desmopressin ⇒ 50µg tid
- Levothyroxine ⇒ 125µg qd
- Hydrocortisone ⇒ 20mg + 5mg + 5mg
- Lithium ⇒ 400mg qd
- Quetiapin (25mg bid), Clomipramin (100mg qd), Sodium valproate (1g qd), Diazepam (2mg tid), Haloperidol (10mg qd), Trihexyphenidyl (1mg qd)



Transferred to the Endocrinology department

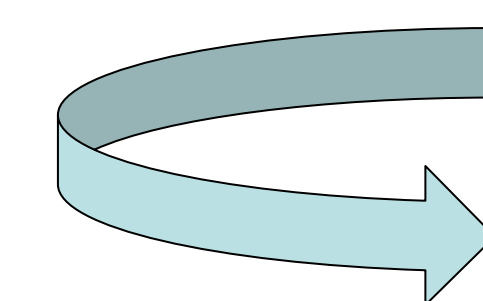
Urine output... **12400mL per day**

- Lithium was interrupted
- Fluid endovenous administration (NaCl 0,9% and 0,45%) ⇒ increased up to 6000mL qd
- Endovenous desmopressin was added ⇒ 4µg bid
- Hydrochlorothiazide ⇒ 50mg qd
- Indometacin ⇒ 400mg qd



Urine output: 6000-7000mL per day  
Serum sodium... **180mmol/L**

- Endovenous desmopressin ⇒ 4µg qid ⇒ 4µg six times a day



Ineffective

- Dialysis ⇒ sodium 155mmol/L (single session)
- Furosemide 40mg qd ⇒ **sodium 132mmol/L**

## EVOLUTION

Variable	20/07	22/07	24/07	27/07	27/07 (after Dialysis)	29/07	29/07 (after furosemide)	09/08
Sodium (mmol/L)	153	165	180	171	155	149	142	133
Potassium (mmol/L)	3,7	3,3	3,4	3,1	3,3	3,6	3,9	4,2
Chloride (mmol/L)			148	142		119		103
Urea (mg/dL)	25	16	27	32	21	32	35	91
Creatinine (mg/dL)	1,3	1,1	1,3	1,0	1,1	1,0	1,1	1,29
Urine output(mL)/ Water balance(mL)		12400/- 3125	6630/-172	6884/-316	/+1000		8650 /-1939	3200/+150

- Oriented
- With logical and consistent speech
- Without cognitive impairment

## DISCUSSION

- Combined Central and Peripheral Diabetes Insipidus may result in serious life-threatening hypernatremia due to massive water loss.
- In this case, Peripheral Diabetes Insipidus was due to lithium therapy and Central Diabetes Insipidus resulted from an hypophysectomy due to a non-secreting macroadenoma.
- Initially, both conditions were conventionally treated.
- However, despite no evidence of hemoconcentration, sodium further increased in a dramatic way.
- This hypernatremia responded to a single dialysis session and in fact dialysis has been proposed as a treatment to refractory hypernatremia.
- This points to a specific sodium excretion defect.
- The most likely explanation is increased renin-angiotensin-aldosterone activity because of volume depletion with increased distal tubule reabsorption of sodium.
- This possibility is supported by the transient nature of the defect and the very good response to furosemide.
- Another possible explanation is a change in the sodium set point due to an hypothalamic defect caused by lithium. In fact it has been described that lithium therapy may induce partial Central Diabetes Insipidus, mainly in patients with other pathologies. However, its mechanism of action is not known.