Secondary hyponatremia to inappropiate secretion of antidiuretic hormone Siadh in diagnosed patient of bladder cancer in treatment with chemotherapy: exclusion diagnosis?

Losada Vila Beatriz[1*], Carmen Pantin Gonzalez[2], Beatriz Anton Pascual[3], Nadia Sánchez Baños[4], David Gutiérrez Abad[5]

[*]Hospital University of Fuenlabrada, Calle Camino del Molino, Madrid, Spain

Abstract

This is a 65-year-old patient diagnosed in January 2018 of an epidermoid bladder carcinoma with bone involvement (extensive) with pain secondary to lumbar involvement, which starts treatment with antialgic radiotherapy followed by chemotherapy (Cisplatin+Gemcitabine) with palliative aim.
However, after the first cycle of chemotherapy, his general state deteriorated, with hallucinations and somnolence, which is why his Primary Care Physician attributes the dose of morphine (110 mg/12 hours) and pregabalin that had been prescribed by intense pain. Descends dose up to 70 mg and suspends pregabalin but continues with drowsiness, so he goes to the Emergency Department. Analytical is performed showing Creatinine of 2.5 mg/dL (0.4-1.2), Potasium 7.2 mmol/L (3.5-5.1), Sodium 117 mmol/L (135-145), pH 7.23 (7.32-7.43), Bicarbonate 18 mmHg (22-29).
Given that the patient was dehydrated, correction was initiated with fluid therapy (Saline 0.9%) and antihyperkalemia measures (salbutamol, resincalcium) with control in 6 hours that objective improvement of renal function to Creatinine 2.05 mg/dL, Potassium 6 mmol/L, Sodium 119 mmol/L, stable pH in 7.24 and bicarbonate 16 mmHg.
Initially, therefore, improvement of renal function was seen but persistence of hyponatremia and metabolic acidosis. Urine ions are requested: urinary sodium 51 mmol/L, urine osmolality 574 mOsm/kg, and plasma osmolarity 210 mOsm/kg, compatible with SIADH. We added tolvaptan 30 mg daily with progressive improvement, so it is suspended after 3 weeks after restarting chemotherapy again.

Keywords: Vaptan, Hiponatremia, Chemotherapy, Bladder carcinoma, Neurological deterioration.

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Clinical Case

A 65-year-old patient with cardiovascular risk factors (arterial hypertension, diabetes mellitus and dyslipidemia in treatment) who came to the Emergency Department due to deterioration of the general condition in the last week coinciding with the first cycle of chemotherapy (Cisplatin+Gemcitabine). He refers more disorientation, confused, and has fallen on 3 times, without traumatic brain injury. No headache. No other neurological focus. He has presented little water intake in the last days.

Valued by his Primary Care Physician, he attributed the deterioration to the high dose of morphine (110 mg/12 hours) and pregabalin that had been prescribed for intense pain. Descends dose up to 70 mg and suspends pregabalin but continues with drowsiness, so he goes to the Emergency Department.

Analytics

Creatinine 2.5 mg/dL (0.4-1.2), Potasium 7.2 mmol/L (3.5-5.1), Sodium 117 mmol/L (135-145), pH 7.23 (7.32-7.43), Bicarbonate 18 mmHg (22-29).

After hydratation, creatinine improved up to 2.05 mg/dL, Potassium 6 mmol/L, but Sodium still in 119 mmol/L. Urine ions are requested: Urinary sodium 51 mmol/L, Urine osmolality 574 mOsm/kg.

Other tests: Plasma osmolarity of 210 mOsm/kg, TSH in range.

So with the diagnosis of neurological deterioration in probable relationship to metabolic cause (hyponatremia) +/- opioids +/- progression of tumor disease; and Hypo-mole-normovolemic hyponathraemia in probable relation to inappropriate secretion of andiuretic hormone (SIADH) +/- diuretics and antidepressants he was admitted.

From the neurological point of view, it impresses with a metabolic cause (hyponatremia) that justifies the progressive neurological deterioration. A computerized computed tomography (CT) scan was requested that excludes cerebral metastasis.

As metabolic causes before this hyponatremia with hypoosmolarity with normal volume and natriuresis, we must rule out the presence of SIADH. Although it is true that the diagnosis should be made after suspending thiazide (if it persists, SIADH is confirmed) and that osmolarity should have

been requested immediately after reaching the emergency room, in this case intense water replacement was initiated given that the patient was hypotensive and with deterioration of renal function due to the low water intake in the previous days. It was the next day, once the renal function was corrected with intense serum therapy, when after verifying that the sodium levels remained at low limits, when urine osmolarity was requested, urine sodium levels as well as TSH (in range), so that SIADH was confirmed. The use of sodium deficit calculation formulas is contraindicated in the treatment of hyponatremia with severe neurological symptoms.

In our case after starting hydric replacement and completely stop morphine (leaving only intravenous resuscitations) the neurological picture recovered.
At 6 o'clock, although low levels of Na persisted (119 mmol/L), the creatinine and potassium levels had improved, so water correction and antihyperkalemia measures were maintained. It did not show signs of water overload, so it remains the same until the next day.

Afterwards, the same dose of morphine could be reintroduced, suspending pregabalin and duloxetine. Performed TSH levels, in range, so that hypothyroidism is ruled out as a cause of hyponatremia. It maintains diuresis around 1500 cc per day.
Valued by nephrology since sodium persisted in 123, tolvaptan was started at a dose of 30 mg/day. Reassessed at 24 hours, the levels increased to 128 meq/L, so after two days maintaining levels above 125 meq/L we proceeded to discharge. Continued follow-up in consultations, maintaining figures of 130 mEq/L and being able to receive a second cycle of chemotherapy, for which tolvaptan was suspended by the third week.

Discussion

For the management of the SIADH the most important step is your suspicion. In the event of a neurological deterioration in a patient with cancer, in addition to ruling out concomitant medication as opioids, an urgent analysis should be performed to control the analytical levels of ions such as sodium, potassium, or urea [1,2]
In our case, the symptomatology was moderate, but since the patient was dehydrated, physiological saline was started. Vaptans (not recommended in hyponatremia <120 mmol/L) could also have been initiated due to moderate symptoms. Other indications of the vaptans are when there is impossibility for hydric restriction or failure of the restriction, Na<125 mmol/l with a high risk of developing symptomatic hyponatremia or a patient in the ICU. Therefore, given that it persisted at levels <125 and scarce response options despite chemotherapy, it was decided to add tolvaptan on the 4th day. However, we did not perform adequate management according to clinical practice guidelines, maintaining its neurological severity for more than 24 hours [3,4].

The dose of tolvaptan is 30 mg per day. If at 24 hours the increase in Sodium levels is less than 5 meq/L, it should be increased to 60 mg. If not, the same dose is continued and close monitoring is carried out, since except for idiopathic (senile) causes, the duration of treatment usually does not exceed 4 weeks. It should be taken into account that the administration of CYP3A4 inducers (such as rifampin, barbiturates) decreases the action of tolvaptan, as well as cyclosporine [5].

Conclusion

Once hyponatremia is confirmed, if the patient shows signs of dehydration, intense water replacement should be performed, but if hyponatremia persists after said correction, SIADH should be excluded.

The antidepressants such as duloxetine are at high risk of worsening the neurological situation, so they should be discontinued although sudden suspension should be avoided. Also drugs such as cisplatin can contribute to deteriorate renal function, lower magnesium levels and worsen the neurological situation.

The diagnosis of SIADH is confirmed with plasma Sodium levels below 135 mEq/L, urinary sodium elimination >40 mEq/L, urinary osmolarity>100 Osm/kg and decreased plasma osmolarity. Our patient after hydric correction and diuretic withdrawal and tolvaptan is maintained at discharge with Na 133 mmol/L.

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***Correspondence to**

Losada Vila Beatriz,

Hospital University of Fuenlabrada,

Calle Camino del Molino, 2, 28942 Fuenlabrada,

Madrid, Spain,

E-mail: beatriz.losada@salud.madrid.org