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Syndrome of inappropriate antidiuretic hormone secretion following transarterial chemoembolisation of hepatocellular carcinoma☆

Síndrome de secreción inadecuada de hormona antidiurética postquimioembolización transarterial de un carcinoma hepatocelular

We present the case report of an 86-year-old woman with a prior history of hypertension and compensated chronic liver disease (in Child-Pugh grade A6) secondary to hepatitis c virus, treated with direct-acting antivirals with sustained virologic response, with large oesophageal varices treated with carvedilol in primary prophylaxis, oedema/ascites controlled with low-dose spironolactone and insomnia treated with lormetazepam, these being the only chronic treatments. Asymptomatic clinical course with preserved renal function (glomerular filtration rate 75 ml/min/1.73 m^2) and normal blood sodium levels. The patient was diagnosed with a 3-cm hepatocellular carcinoma in segment VIII in her six-monthly ultrasound scan. Following deliberation by a multidisciplinary committee, the patient was scheduled for transarterial chemoembolisation with doxorubicin (Adriamicina®). The blood tests performed as per routine clinical practice 24 h after the procedure revealed moderate hyponatraemia (serum Na: 124 mEq/l), which the patient did not have before (Na in plasma: 139 mEq/l previously). In light of this finding, plasma and urine osmolarity was measured, which identified hypoosmolar hyponatraemia (plasma osmolarity: 252 mOsm/kg), high urine osmolarity (463 mOsm/kg), increased urinary sodium excretion (118 mmol/l) and normal extracellular volume. Predominantly asymptomatic, the patient only reported paraesthesia in the distal phalanges of both hands.

Having ruled out other causes of hypoosmolar hyponatraemia (including central nervous system disorders and kidney disease), syndrome of inappropriate antidiuretic hormone secretion (SIADH) following transarterial chemoembolisation was diagnosed following a thyroid function test, coupled with normal baseline cortisol levels. The patient's progression was favourable, with gradual correction of serum sodium levels (serum Na: 134 mEq/l) and clinical improvement after fluid restriction and replacement with 0.9% physiological saline solution at 72 h.

Three months later, the patient remained asymptomatic and with no decompensations of her underlying disease, so a new chemoembolisation session was scheduled. Hypoosmolar hyponatraemia (plasma Na: 127 mEq/l) recurred 24 h following the procedure, having once again had normal baseline sodium levels (plasma Na: 135 mEq/l), which resolved within a similar timescale as before, with no other complications arising.

Discussion

Hepatocellular carcinoma is the most common primary hepatic malignancy. It tends not to respond to curative therapy, although other alternatives are available, like chemoembolisation.[1] This consists of the intra-arterial infusion of a cytotoxic drug and the embolisation of the tumour blood vessels. The most common complication is post-chemoembolisation syndrome, characterised by nonspecific symptoms such as nausea, fever and abdominal pain, which are usually mild in nature and transient.[2] SIADH is characterised by excess antidiuretic hormone in the absence of a physiological stimulus, which inhibits the secretion of free water and gives rise to hyponatraemia. It may be secondary to many different causes, such as medication (including chemotherapy), malignancies, bronchial diseases, hypopituitarism and hypothyroidism, to name a few. Complications arising from moderate to severe hyponatraemia, particularly when onset is acute (less than 24–48 h), range from mild (weakness, muscle cramps, etc.) to potentially fatal (seizures, coma with respiratory arrest). Appropriate treatment for asymptomatic patients consists of fluid restriction, whilst symptomatic patients require urgent but gradual correction of sodium levels to prevent complications, such as central pontine myelinolysis.[3]

In the differential diagnosis, we recommend considering the chronic liver disease itself, as well as chronic treatment with diuretics, beta-blockers and psychoactive drugs as potential causes of hyponatraemia. In addition, the possibility of paraneoplastic SIADH secondary to hepatocellular carcinoma should be ruled out[4] by a complete plasma and urine analysis that includes osmolarity and hormone profiles.

The onset of SIADH after chemoembolisation of hepatocellular carcinoma is a rare complication. In fact, only one other similar case has been reported, which describes

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multifocal hepatocellular carcinoma following transarterial chemoembolisation with cisplatin and accompanied by a reduced level of consciousness, and which resolved within a few days following fluid and electrolyte replacement.[5] No similar cases with doxorubicin have been reported. However, several cases of SIADH after chemoembolisation of other malignancies with liver metastases have been published. The aetiopathogenesis can be hypothesised to be the massive secretion of antidiuretic hormone (ADH) after the tumour lysis of lesions with insignificant baseline production of ADH.[2] It would be plausible to apply this hypothesis to the case of hepatocellular carcinoma presented above. However, given the rarity of this complication and our patient's low tumour load compared to the cases published in the literature, this cannot be confirmed.

It can be concluded that, despite the rarity of this complication, comprehensive plasma and urine testing after chemoembolisation is nonetheless useful for detection, given that it can be potentially life-threatening if not properly treated.

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