Esthesioneuroblastoma presenting as syndrome of inappropriate antidiuretic hormone secretion

Esthésioneuroblastome se présentant comme un syndrome de sécrétion inappropriée d'hormone antidiurétique

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Abstract

Hyponatremia is the most common fluid electrolyte disorder in hospitalized patients. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is the main cause of normovolemic hyponatremia, it can be caused by diverse etiologies: malignant tumors are the most feared cause that clinician persists in finding. Exceptionally, SIADH can complicate Esthesioneuroblastoma (ENB) or olfactory neuroblastoma, a rare tumor of the nasal sinus cavities. We report the case of a 26-year-old female patient admitted for recurrent headaches and vomiting, with a profound normovolemic hyponatremia at the initial assessment. Biological explorations have concluded in a SIADH. Imaging showed a mass of the left nasal cavity with extensions to the ipsilateral paranasal sinuses. The biopsy of the lesion, under endoscopic control, was inconclusive. The anatomopathological study, after surgical removal, concluded in ENB. The postoperative evolution was marked by the normalization of the natremia.

Key words: Hyponatremia; Syndrome of inappropriate antidiuretic hormone secretion; Esthesioneuroblastoma

Résumé

L'hyponatrémie est le trouble électrolytique le plus fréquent chez les patients hospitalisés. Le syndrome de sécrétion inappropriée d'hormone antidiurétique (SIADH) est la principale cause d'hyponatrémie normovolémique, il peut être causé par diverses étiologies : les tumeurs malignes sont la cause la plus redoutée que le clinicien s'obstine à rechercher. Exceptionnellement, le SIADH peut compliquer l'Esthésioneuroblastome (ENB) ou neuroblastome olfactif, qui est une tumeur rare des fosses nasales. Nous rapportons le cas d'une patiente de 26 ans admise pour céphalées et vomissements récurrents, avec une hyponatrémie normovolémique profonde au bilan initial. Les explorations biologiques ont conclu à un SIADH. L'imagerie a montré une masse de la cavité nasale gauche avec des extensions aux sinus paranasaux homolatéraux. La biopsie de la lésion, sous contrôle endoscopique, n'était pas concluante. L'étude anatomopathologique, après ablation chirurgicale, a conclu à un ENB. L'évolution postopératoire était marquée par la normalisation de la natrémie.

Mots clés: Hyponatrémie ; Syndrome de sécrétion inapproprié d'hormone anti-diurétique ; Esthesioneuroblastome

INTRODUCTION

Hyponatremia is a frequent clinical situation in common medical practice. True hyponatremia is classified according to the state of the extracellular sector into hypovolemic, normovolemic and hypervolemic. Normovolemic hyponatremia is related to syndrome of inappropriate antidiuretic hormone (SIADH) after ruling out hypothyroidism, primary or secondary adrenal insufficiency, and hypopituitarism. SIADH is a specific entity, defined by a normovolemic hyponatremia associated with an abnormally high level of antidiuresis compared to the natremia. SIADH have multiple etiologies especially neoplastic ones. SIADH is a classic mechanism of hyponatremia, found in approximately 50% of patients suffering from cancer (1).

Esthesioneuroblastoma (ENB) is a rare malignant tumor of the sino-nasal cavities that may represent an unusual etiology of SIADH. About thirty cases have been published in the literature (2)

We report in our study the case of a 26-year-old female patient presented with SIADH secondary to esthesioneuroblastoma.

CASE REPORT

A 26-year-old female patient presented with recurrent headaches, abdominal pain and vomiting.

On the day of admission, she was normohydrated, her blood pressure was 120/80 mmHg, her heart rate was 74 bpm, her neurological and respiratory condition was normal

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and she had no melanodermia, goiter or cervical adenopathy. The initial laboratory investigations showed: hyponatremia of 120 mmol/l (verified on two other samples); kalemia = 4.4 mmol/l; mild hypocalcemia of 2.12 mmol/l; protidemia = 66 g/l; glycemia = 5.3 mmol/l; urea = 3.17 mmol/l; creatinine = 61 µmol/l; plasmatic osmolarity = 257 mosmol/l; TSH=2.1mUI/l.

An acute adrenal insufficiency was suspected and the patient received an intravenous isotonic saline and hydrocortisone.

Despite iterative isotonic saline infusions and hydrocortisone administration, hyponatremia persisted.

To push the investigation further, a urinary ionogram was requested and showed a urinary osmolarity above 100 mosmol/l.

The diagnosis of adrenal insufficiency was questioned and ruled out by a 250 µg Synacthen test (performed after stopping hydrocortisone) which showed a cortisol peak of 255 ng/ml.

The diagnosis of SIADH was then retained considering: true hyponatremia with plasmatic hypotonia, modest improvement of the natremia after intravenous saline infusion, inadequate antidiuresis with high urinary osmolarity, clinical euvolemia, absence of kidney, adrenal or thyroid failure, absence of loop diuretic intake and low urea at 3.17 mmol/l.

Despite moderate water restriction (0.5 liter/24h), loop diuretics (20 mg per day of furosemide) and an oral salt intake, the hyponatremia persisted (132 mmol/l).

As part of the SIADH etiological investigations, a thoraco-abdominal CT didn't show any neoplastic process. A brain CT showed the presence of a tissular mass in the sinonasal cavities. A magnetic resonance imaging (MRI) of the facial area confirmed the presence of a tumor, developing in the left nasal cavity with high T2 and low T1 signal and extending to the left maxillary sinus and anterior ethmoidal cells, measuring 40x25 mm (Figure 1).

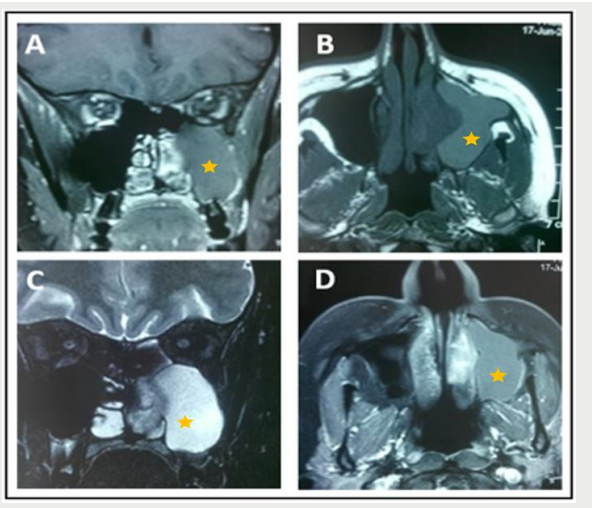

Figure 1. MRI of the facial area showing the tumor (yellow star) in the left nasal cavity with low T1(Show in coronal (A) and axial (B) T1-weighted sequences), and high T2 signal (Shown in (C) coronal T2-weighted sequence). A moderate contrast enhancement is show in (D) an axial T1-weighted sequence after fat saturation and gadolinium injection.

The patient was then referred to the otolaryngology for evaluation of the nasal mass. An endoscopic biopsy was inconclusive. Trans-nasal endoscopic surgery was then performed.

Histological examination of hematoxylin and eosin-stained slides demonstrated a proliferation of round small cells, arranged in nests or sheets, separated by a richly vascularized fibrous stroma and forming frequently the Homer-Wright pseudorosettes.

The tumor was immunoreactive for chromogranin, glial fibrillary acid protein, neuron-specific enolase, and synaptophysin. It was not immunoreactive for cytokeratin, CD99 and Glial fibrillary acidic protein (GFAP). The ki-67 was at 2% (Figure 2).

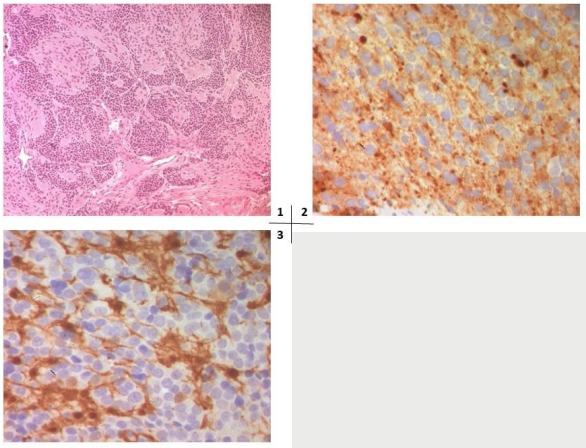

Figure 2.
1. Proliferation of small round blue cells arranged in nests and lobules set in a neurofibrillary stroma. Few Homer Weight pseudorosettes are seen (H&E stain, original magnification 10x)
2. The tumor cells show positive cytoplasmic finely granular staining for Synaptophysin(Synaptophysin immunostain).
3. S-100 immunostain highlights sustentacular cells surrounding nests of tumor cells (S-100 immunostain).

The final pathology interpretation of the excised mass was consistent with grade 2 esthesioneuroblastoma with clear surgical margins.

The search for metastases was negative. Her case was presented at a multidisciplinary tumor board, and the consensus opinion was that she would not require any adjuvant radiation or chemotherapy.

Iterative biological controls after surgery have shown the stability of the natremia (between 135 and 136 mmol/l), in favor of the resolution of SIADH and its accountability to the tumor.

The patient has been followed for 2 years since surgical treatment and has not demonstrated any recurrence of disease. Her sodium levels continue to be normal.

DISCUSSION

This case this case illustrates an atypical form of ENB by its mode of revelation: SIADH. SIADH in the most common cause of normovolemic hyponatremia in clinical practice (3).

The diagnostic criteria of SIADH according to Spasovski et al. (4) are: effective serum osmolality below 275 mOsm/kg, urine osmolality over 100 mOsm/kg, effective osmolality, clinical euvolemia, urine sodium concentration over 30 mmol/l with normal dietary, salt and water intake, absence of adrenal, thyroid, pituitary or renal insufficiency, no use of diuretic agents. In our patient, clinical criteria of SIADH were clearly established.

Paraneoplastic SIADH is found in 3% of head and neck cancers particularly those originating from neuroendocrine system such as ENB (5).

ENB is a rare type of cancer that originate from the olfactory neuroepithelium of the superior turbinate, the cribriform plate, and along the superior septum. Its prevalence is estimated at 0.4 cases/1,000,000 (6). It affects both sexes equally. The distribution by age shows bimodal pattern with peaks in the 2nd and 6th decade, our patient was 26-year-old.

The clinical presentation oscillates between an indolent paucisymptomatic tumor and a particularly aggressive lesion

with extensive locoregional spread and/or metastases (7). There is a 2% prevalence of ENB-associated SIADH in the literature with most patients initially presenting with signs secondary to hyponatremia as is the case with our patient (8).

Plesencia et al. (9) showed that hyponatremia associated with ANB was deeper compared to other SIADH etiologies which is the case of our patient where the natremia was frankly low at 120 mmol/l.

SIADH does not appear to correlate with tumor aggressiveness since it has been described in different stages lesions, ranging from small indolent tumors to particularly invasive tumors (10).

Our patient had a low-grade tumor that starts from the left nasal cavity and extend to the left maxillary sinus and anterior ethmoidal cells. There does not appear to be a relationship between the location of the tumor and the degree of malignancy.

Testing for anti-diuretic hormone by immunohistochemistry is usually positive in this type of tumor, but Nakano et al.(11) reported an interesting clinical case of an ENB revealed by SIADH which resolved after surgery but ADH immunohistochemical research was negative. in our case, immunohistochemical research for ADH was unfortunately not carried out.

The initial management of ENB involves a careful examination of the nasal cavity with the realization of a biopsy, which may confirm the diagnosis by showing typical histologic features of ENB. Imaging workup is undeniably a crucial step in the preoperative evaluation of the tumor (12).

The treatment pillars for the ENB are represented by surgery, radiotherapy and chemotherapy (7): The classic surgical approach is the craniofacial resection but endoscopic trans-nasal surgery is increasingly being carried out, especially for early stages (Kadish A and B); radiotherapy depend mainly on the tumor stage, the histological grade and the state of the surgical margins; chemotherapy is indicated in advanced stages (Kadish C and D).

Our patient had endoscopic removal of the tumor, chemotherapy and radiotherapy are not indicated because of the histological low grade of the tumor.

Generally, total removal of the tumor is accompanied by a total resolution of paraneoplastic syndromes and in particular SIADH. Its persistence is indicative of incomplete surgery. In our patient postoperative evolution was marked by spontaneous normalization of the natremia which highly suggest that the SIADH was due to the ENB.

In this sense we can suggest that the periodic measurement of plasma sodium might be an easy and cost-effective method to detect cases of tumor recurrence and should be considered in all patients who have had SIADH due to ENB during follow-up.

CONCLUSION

SIADH is the most cause of normovolemic hyponatremia in clinical practice. While most ENBs present with typical symptoms of nasal obstruction and epistaxis in late stages of disease, uncommon manifestations should be considered as well like hyponatremia due to paraneoplastic SIADH. The advantage in these cases is that surgical treatment cures the hyponatremia.

Abbreviations list:

ENB: Esthesioneuroblastoma

GFAP: Glial fibrillary acidic protein

MRI: Magnetic Resonance Imaging

SIADH: Syndrome of Inappropriate Antidiuretic Hormone

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