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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Forgotten cause of severe hyponatremia

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SUMMARY

Introduction Sheehan syndrome is (pan)hypopituitarism because of postpartum pituitary infarction due to massive obstetrical hemorrhage. Enlargement of the pituitary gland, smaller sellar region, disseminated intravascular coagulation or autoimmunity are predisposing factors. The absence of lactation after labor and the inability to resume the menstrual cycle later are presenting symptoms. Some patients with Sheehan's syndrome have a sudden onset of severe hypopituitarism immediately after labor, most often in the form of severe hyponatremia. Central adrenal insufficiency is the most usual cause of hyponatremia, although in some cases the syndrome of inappropriate antidiuretic hormone secretion has been also described.

Case report A 39-year-old female patient was admitted to the Intensive Care Unit due to severe hyponatremia with neurological symptoms (Na 103 mmol/L, Cl 72 mmol/L, K 3.7 mmol/L), and absence of lactation. Previously, on the sixth postpartum day, she was admitted to the Obstetrics and Gynecology Clinic due to severe headache, nausea, vomiting, and blurred vision. The symptoms persisted since labor, which was complicated with severe hemorrhage (1000 ml) due to obstetric complications. Treatment began with the 3% hypertonic saline solution with restriction of fluid intake. In regard to panhypopituitarism, replacement therapy with hydrocortisone and levothyroxine was initiated. Diabetes insipidus was excluded. Growth hormone replacement therapy and combination of progesterone and progestogens was started during follow-up.

Conclusion Early diagnosis of Sheehan's syndrome is essential. Pituitary insufficiency in these patients has a great diversity in presentation, that can sometimes result in coma and death.

Keywords: postpartum hemorrhage; Sheehan syndrome; panhypopituitarism

INTRODUCTION

Hyponatremia defined as sodium level < 135 mmol/l is a frequent electrolyte disorder, and it can be found in patients with endocrinopathies [1]. In hospital setting, the incidence of hyponatremia is as high as 30% [2, 3]. Most commonly seen endocrinopathies together with euvolemic hyponatremia are the syndrome of inappropriate antidiuretic hormone secretion (SIADH), adrenal insufficiency and hypothyroidism [3]. Sheehan syndrome (ShS) is (pan) hypopituitarism on the grounds of postpartum pituitary infarction due to massive obstetrical hemorrhage. Signs and symptoms of ShS are mild and nonspecific, so the diagnosis can be easily missed or delayed [4]. Nationwide retrospective study in Iceland found the incidence of ShS of 5.1 per 100,000 females, while according to the KIMS database (Pfizer International Metabolic Database) the incidence of ShS was found to be 3.1 in 1034 patients with growth hormone deficiency. Occurrence of ShS in developed countries is estimated to be exceedingly rare due to highly developed obstetrical care [5]. Here we present a case of acute onset of hyponatremia in a patient who experienced hemorrhage during labor.

CASE REPORT

A 39-year-old female patient was admitted to hospital five days after parturition because of altered sensorium. Five days earlier she had given birth to a healthy newborn, but the labor had been complicated with extensive obstetrical hemorrhage. On admission, the patient was adynamic and confused, with signs of anemia but without signs of obstetrical bleeding. She reported that lactation was not established. She did not have polyuria or polydipsia. Blood was drawn for initial laboratory tests; the results are shown in Table 1. Due to severe overt hyponatremia, she was treated with 3% saline solution and further investigation was indicated. The results of endocrinological tests are shown in

Table 1. Initial blood results

Parameter	Value
Sodium (mmol/l)	103
Potassium (mmol/)	3.7
Chlorine (mmol/l)	72
Hemoglobin (g/l)	105
RBC ($\times 10^{12}$)	3.7
WBC ($\times 10^{9}$)	11.06
Hematocrit (%)	27.9
CRP (mg/L)	29.4

RBC – red blood cells; WBC – white blood cells; CRP – C-reactive protein

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Table 2. Endocrinological test results

Endocrinological test	Value
FSH (IU/L)	< 0.1
LH (IU/L)	< 0.5
PRL (ng/mL)	12.2
ACTH (pg/mL)	3
hGH (ng/mL)	0.12
IGF-1 (ng/mL)	134.8
Cortisol 8 a.m. (nmol/L)	14.5
24-hour urine sodium excretion (mmol/day)	83
Anti-TPO Ab (IU/ml)	1.4
Anti-Tg Ab (ng/ml)	18.6

FSH – follicle-stimulation hormone; LH – luteinizing hormone; PRL – prolactin; ACTH – adrenocorticotropic hormone; hGH – human growth hormone; IGF-1 – insulin-like growth factor 1; Anti – TPO Ab – thyroid peroxidase antibody; Anti – Tg Ab – antithyroglobulin antibodies

Table 2. Endocrinological testing showed panhypopituitarism. Parenteral hydrocortisone was introduced, and after a few days, levothyroxine was added. All the signs and symptoms of severe hyponatremia resided after the therapy and did not appear again after the hydrocortisone initiation. Magnetic resonance imaging of the pituitary gland was done, and it revealed enlarged pituitary with apoplexy without bleeding (Figure 1). On subsequent ambulatory check-ups, panhypopituitarism persisted, and a replacement dose of estrogen and progesterone was given, along with growth hormone therapy initiation. So far, we have been following this patient for three years and panhypopituitarism seems to be definite. She has been feeling well and has been asymptomatic.

Written consent for the publication of this article was obtained from the patient.

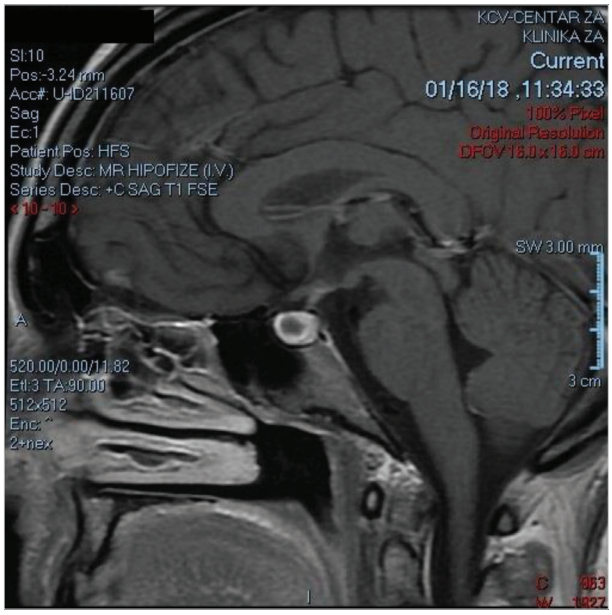

Figure 1. Enlarged pituitary with apoplexy without bleeding

DISCUSSION

ShS can be a life-threatening condition thus making a delay in diagnosis detrimental. It emerges because of extensive postpartum hemorrhage which leads to pituitary hypoperfusion and necrosis [6, 7]. Nowadays, ShS diagnosis is rare in developed countries, but in under-developed and developing countries it can be seen more often. With improving obstetrical care, the incidence of ShS is less frequent, but more than 40 years ago, the prevalence of this condition was around 100–200 per 100,000 females [8]. Miljić et al. [9] presented a retrospective study on 260 patients with hypopituitarism treated at their specialized endocrinological unit during a decade, and among those patients, two had ShS. Due to the rarity of this condition, nowadays, in countries with well-developed health care the data regarding the ShS incidence is not fully established [4, 8, 10]. Signs and symptoms of ShS are nonspecific and gradual in onset. The time from onset to the diagnosis is one month to 27 years [11, 12, 13]. Our patient had the abrupt onset of signs and symptoms of severe overt hyponatremia due to central adrenal insufficiency. Earlier reports of deaths due to diminished cortisol level in unrecognized partial or complete hypopituitarism after labor emphasize the need to reintroduce ShS as possible cause of rapid onset of worsening state in females after delivery [14, 15, 16]. Hyponatremia in ShS is mainly the consequence of central adrenal insufficiency i.e., the lack of cortisol. It is known that SIADH is the most common reason for euvolemic hyponatremia. There are clear diagnostic criteria for SIADH, nevertheless it is not always the case that the central adrenal insufficiency is priorly excluded [17, 18, 19]. Further contribution to the severity of hyponatremia comes from hypothyroidism as a part of hypopituitarism in the presented patient. Hyponatremia in isolated hypothyroidism is rare, and mostly the consequence of primary hypothyroidism. Proposed mechanism for the hyponatremia in hypothyroid patients is the elevation of antidiuretic hormone together with mild renal impairment [20–23]. Symptomatic hyponatremia should be urgently solved with intravenous 3% saline solution according to current guidelines, having in mind that too fast elevation of sodium can result in pontine myelinolysis [1, 24, 25, 26]. Timely diagnosis of ShS is needed in order to initiate adequate hormonal supplementation, and the hydrocortisone and levothyroxine are of vital significance.

ShS is a rare condition in developed countries and the significance of the risk it carries might be neglected. Central adrenal insufficiency can be component of ShS, thus contributing to the severity of syndrome. With timely diagnosis and adequate therapy, significant morbidity and, in some cases, mortality might be avoided.

Conflict of interest: None declared.

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Занемарени узрок хипонатремије тешког степена

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САЖЕТАК

Увод Шиханов синдром настаје услед исхемијске некрозе хипофизе због постпарталног крварења, а карактерише га различит степен хипопитуитаризма. Повећан волумен хипофизе, мања селарна регија, дисеминована интраваскуларна коагулација или аутоимуност су предиспонирајући фактори. Изостанак лактације постпартално и касније немогућност успостављања менструалног циклуса су најчешћи презентујући симптоми. Мали број болесница са Шихановим синдромом има нагли настанак тешког хипопитуитаризма непосредно постпартално, најчешће у виду хипонатремије тешког степена која се може детектовати већ у акутној фази после порођаја. Централна адренална инсуфицијенција је највероватнији узрок хипонатремије, мада је у појединим случајевима описан и синдром неадекватне секреције антидиурезног хормона.

Приказ болесника Болесница стара 39 година примљена је на Одељење ургентне интерне медицине због тешке хипонатремије праћене неуролошком симптоматологијом (*Na* 103 *mmol/L*, *Cl* 72 *mmol/L*, *K* 3,7 *mmol/L*), уз податак о изостанку лактације. Претходно је шестог постпарталног дана рехоспитализована на Клинику за гинекологију и акушерство, због тешке главобоље, мучнине, повраћања, замућења вида. Тегобе перзистирају од момента терминског вагиналног порођаја, током ког је болесница изгубила око 1000 *ml* крви због акушерских компликација. Започето је лечење применом хипертоног раствора натријума уз накнадну рестрикцију уноса течности. У оквиру дијагностикованог панхипопитуитаризма започета је супституциона терапија хидрокортизоном и потом левотироксином. Искључено је постојање инсипидног дијабетеса. Током даљег праћења, уведена је супституциона терапија хормоном раста и комбинацијом прогестерона и прогестагена.

Закључак Рана дијагноза Шихановог синдрома је од суштинског значаја. Питуитарна инсуфицијенција код ових болесница има велики диверзитет у презентацији, што понекад може да резултира комом и смрћу.

Кључне речи: постпартална хеморагија; Шиханов синдром; панхипопитуитаризам