

CASE REPORT

OLGU SUNUMU

**COMBINED CENTRAL DIABETES INSIPIDUS AND CEREBRAL SALT WASTING SYNDROME AFTER
HEMORRHAGIC STROKE-FIRST REPORT**

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ABSTRACT

Disorders of water and electrolyte hemostasis such as diabetes insipidus (DI) and cerebral salt wasting syndrome (CSWS) have been described after cerebral insults, but combined DI and CSWS has rarely been reported in patients with traumatic intracranial hemorrhage (ICH). To the best of our knowledge this is the first report of combined DI and CSWS in an adult patient following hemorrhagic stroke: a previously healthy 40-year-old woman developed dysarthria and progressive decline in consciousness while lecturing. Cerebral computed tomography (CT) showed hyperdensity in the right basal ganglia, indicating ICH. Urgent digital subtraction angiography (DSA) was normal, external ventricular drainage (EVD) was placed and barbiturate coma was initiated. At the second day, she developed DI, which responded to desmopressin. From the 4th day, serum concentration of sodium started to decrease gradually, urine specific gravity increased, and massive polyuria that was unresponsive to desmopressin occurred. Based on test results, combined DI and CSWS was diagnosed and a triple treatment was initiated with high doses of hypertonic saline, desmopressin and a fludrocortisone. Water and electrolyte disturbances improved gradually and she was discharged after 28 days with a GOS-E of 7.

Keywords: Diabetes insipidus, cerebral salt wasting syndrome, spontaneous intracranial hemorrhage, brain hemorrhage.

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HEMORAJİK İNME SONRASI KOMBİNE SANTRAL DİYABET İNSİPIDUS VE SEREBRAL TUZ KAYBI SENDROMU-İLK RAPOR

ÖZ

Beyin hasarı sonrası diyabet insipidus (DI) ve serebral tuz kaybı sendromu (STKS) gibi su ve elektrolit hemostaz bozuklukları tanımlanmıştır, ancak kombine DI ve STKS travmatik intrakraniyal kanamalı (IKK) hastalarda nadiren bildirilmiştir. Bildiğimiz kadarıyla yazımız yetişkin bir hastada hemorajik inmeyi takiben gelişen kombine DI ve STKS'nin ilk raporudur: 40 yaşında sağlıklı bir kadın ders anlatırken ani dizartri ve giderek artan bilinç kaybı gelişmiştir. bilgisayarlı beyin tomografisinde (BBT) sağ bazal gangliyonda intraserebral kanama (ISK) ile uyumlu hiperdens lezyon gösterildi. Acil yapılan digital subtraction anjyografisi (DSA) normaldi, eksternal ventriküler drenaj (EVD) yerleştirildi ve barbitürat koma başlandı. İkinci gün desmopressine yanıt veren DI gelişti. 4. günden itibaren serum sodyum konsantrasyonu yavaş yavaş azalmaya başladı, idrar dansitesi arttı ve desmopressine yanıt vermeyen masif poliüri oluştu. Test sonuçlarına göre, kombine DI ve STKS tanısı konulan hastaya yüksek dozlarda hipertonic salin, desmopressin ve fludrokortizon ile üçlü tedavi başlatıldı. Su ve elektrolit bozuklukları kademeli olarak düzeldi ve 28 gün sonra Glasgow Outcome Scale-Extended (GOS-E) 7 ile taburcu edildi.

Anahtar Sözcükler: Diabetes insipidus, serebral tuz kaybı sendromu, spontan intraserebral kanama, beyin kanaması.

INTRODUCTION

Disorders of water and electrolyte hemostasis such diabetes insipidus (DI) and cerebral salt wasting syndrome (CSWS) have been described after traumatic brain injury, neoplasia, infection, and ischemic stroke (1,2), but combined DI and CSWS has rarely been reported in literature in patients with traumatic intra cranial Hemorrhage (ICH) (3). To the best of our knowledge, this is the first report of combined DI and CSWS in an adult patient after hemorrhagic stroke.

CASE REPORT

While lecturing at work, a previously healthy 40-year-old woman suddenly developed dysarthria and vomiting followed by progressive decline in consciousness. Initial level of consciousness was stupor; a detailed examination revealed left hemiparesis and asymmetrical plantar reflex. Intubation was performed. Cerebral computed tomography (CT) showed hyperdensity in right basal ganglia indicating intracranial hemorrhage (ICH) associated with intraventricular hemorrhage (IVH) in the lateral and 3rd ventricles accompanied by a midline shift about 3 mm (Figure 1). Urgent digital subtraction angiography (DSA) was done which was normal. External ventricular drainage (EVD) was placed into the left lateral ventricle and she was admitted to stroke care unit (SCU). After surgery she was placed under mechanical ventilation, barbiturate coma was initiated and hyperthermia was treated aggressively. She had no previous history of

known illness or drug use, and laboratory data were normal at the initial evaluation.

On the second day following admission, she had a significant increase in urine volume of about 6000 ml over 24 hours with urine specific gravity of 1.005 (urine osmolality was not measured) and a plasma sodium concentration of 149mmol/L, blood urea nitrogen of 56 mg/dl, and blood glucose of 140 mg/dl; thus, serum osmolality was estimated at 326 mosm/kg. Based on the above results and since she was not on any diuretic, diabetes insipidus (DI) was suspected and treatment with desmopressin was initiated. Fluid replacement was provided to correct volume depletion. Her urine flow rate declined, which was the expected response to desmopressin.

On the fourth day, the serum concentration of sodium started to decrease gradually. On the fifth day, Sodium (Na) concentration was 136 mmol/L, urine specific gravity was 1.020, and polyuria was resistant to desmopressin. Massive polyuria (urine volume of more than 10 L/day) developed and hyponatremia became progressively more severe. On the sixth day, urine spot analysis showed that urine Na concentration was 250 mEq/L with a serum Na concentration of 132 mEq/L. The patient was hypovolemic with central vein pressure (CVP) of 4-5 cm H₂O. At this time the patient was not on mannitol or other diuretics. Serum pro-BNP level was tested on day 15 and was within normal limits. To avoid a further decline in Na concentration, which also worsens brain cell swelling, a hypertonic sodium chloride (NaCl) 5% infusion was started with the goal of a serum Na concentration of 145-150 mmol/L. Since the

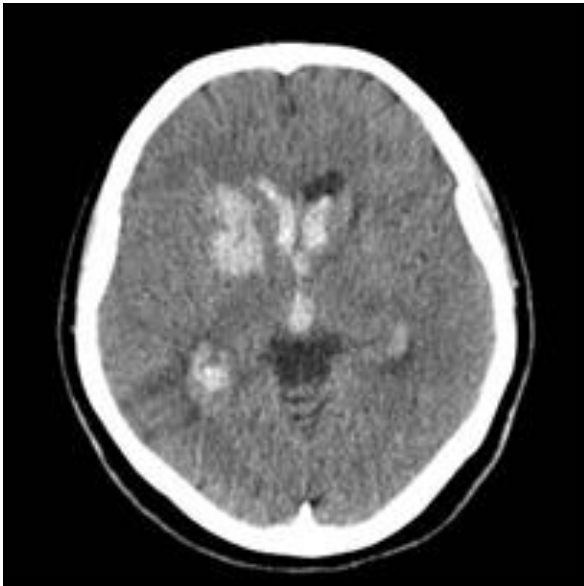


Figure 1. Cerebral computed tomography (CT) showing hyperdensity in right basal ganglia indicating intracranial hemorrhage (ICH) associated with intraventricular hemorrhage (IVH).

hyponatremia was very resistant to treatment despite hypertonic saline replacement, the desmopressin was suspended. Fluid replacement with isotonic serum equal to urine output was continued. Based on patient's history (hemorrhagic stroke), massive polyuria (more than 10 L/day) resistant to desmopressin, high normal urine specific gravity (1.030), high urine Na excretion and decreasing serum Na concentration, we speculated that salt wasting syndrome (SWS) was added to DI. Maximum 24h urine volume was about 16 L/day on the 9th day and the maximum hypertonic NaCl 5% infusion rate needed to maintain serum Na concentration at a high normal level was 80cc/h (equal to 133 ml/h of NaCl 3%). On the 11th day, since the serum Na concentration was stable in the normal range, desmopressin was restarted for better control of polyuria.

Based on the previous case studies, treatment for combined DI and CSWS (triple therapy) was continued using hypertonic saline, desmopressin and fludrocortisone (0.1 mg every 12 hours). Urine volume decreased significantly to less than 10 L/d.

Control brain computed tomography (CT) scans were done at regular intervals with no evidence of hydrocephalus. The barbiturate coma was continued for 5 days. On the 14th day, the patient started to awaken gradually and was

extubated on the 18th day. External ventricular drainage (EVD) was withdrawn on the 19th day.

Desmopressin, hypertonic saline infusion and fludrocortisone continued until 20th, 25th and 28th (discharge day), respectively. Before discharge a brain MRI was conducted to rule out cavernous angioma as a cause of cerebral hemorrhage and pontine demyelination, with normal results. On the 28th day the patient was discharged with slight weakness of the right hand with a modified Rankin Scale of 2 and Glasgow outcome Scale-Extended (GOS-E) of 7. Informed consent was obtained from the patient for this report.

DISCUSSION AND CONCLUSION

Combined diabetes insipidus (DI) and cerebral salt wasting syndrome (CSWS) has rarely been reported in neurological disease (3). In this syndrome, DI generally comes before CSWS (3). DI presents first with polyuria, hypotonic urine, and hypernatremia, and responds to desmopressin. CSWS presents later, and the combined syndrome of DI and CSWS should be suspected if: 1) massive polyuria (over 10 L/day, rare in patients with DI or CSWS alone) with no response to desmopressin alone; 2) high 24h urine Na excretion with normal serum Na concentration (DI increases / CSWS decreases serum Na concentration); 3) normal urine specific gravity (DI decreases / CSWS increases urine specific gravity); and 4) high urine osmolarity (more than serum osmolarity).

It is very important to note that the short transition time from DI to combined syndrome must be correctly and quickly recognized by the attending physician. In such patients, an increase in urine volume may erroneously be interpreted as inadequate treatment with vasopressin and may result in dose increment; since continuing desmopressin without replacing Na loss is a "fatal error". Because this patient had both a very large amount of urine volume and a very high urine Na excretion, infusion of high amounts of hypertonic saline was required to prevent a severe and lethal degree of hyponatremia. Thus infusion of a hypotonic solution is contraindicated in such patients. In a similar patient with combined syndrome reported by Laredo, a 42-year-old previously healthy female with subarachnoid hemorrhage had a sudden decrease in serum Na concentration from 155 mmol/l to 123 mmol/l over a period of 24h, resulting in death (4). Recognition of the short transition time from DI to

combined syndrome is crucial and a very high rate of mortality and morbidity has been reported without proper treatment (5).

Our case also showed that in patients with combined syndrome how extreme urine Na loss can be, and that it can also safely be replaced with very large amounts of hypertonic saline.

Another point worth noting is that vasopressin was able to be discontinued earlier than hypertonic NaCl infusion and fludrocortisone in this case. Unlike cases reported by Wu (3), it seems that CSWS lasted longer than DI in this patient.

To best of our knowledge this is the first report of combined diabetes Insipidus (DI) and cerebral salt wasting syndrome (CSWS) in an adult patient after spontaneous intra cranial hemorrhage (ICH). Recognition of the short transition time from DI to combined syndrome is crucial. Once diagnosed, triple treatment with hypertonic saline, desmopressin and a mineralocorticoid should be started to balance fluid volume and Na concentration. A very large amount of Na replacement may be needed. Most physicians are unaware of the incidence of this combined syndrome which may be a reason for under reporting and high mortality of such patients.

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Concept: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Design: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Data Collection or Processing: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Analysis or Interpretation: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Literature Search: TM, ESH, FM, AM, JE, AT, BB, YS, ESG. Writing: TM, ESH, FM, AM, JE, AT, BB, YS, ESG.

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