Triphasic AVP Secretion in Encephalopathy

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Abstract

A patient with encephalopathy developed triphasic changes in the clinical course, starting with diabetes insipidus (DI), then the syndrome of inappropriate ADH secretion (SIADH), and followed by the final phase of DI. The clinical course of encephalopathy was very rapid. The patient lost consciousness completely within only one day after the onset. During the early phase, he lapsed into a condition of "brain death". We could not identify the etiology of the encephalopathy. The triphasic change referred to above is similar to previous reports of cats model after stereotactic destruction of the supraopticohypophyseal tract. We speculate that our case may have been associated with neurohypophyseal dysfunction caused by supraopticohypophyseal tract damage.

A patient with encephalopathy developed triphasic changes in the clinical course, starting with DI, then SIADH, and followed by the final phase of DI. The case is thought to be a human model of neurohypophyseal dysfunction induced by permanent supraopticohypophyseal tract damage.

Case Report

The patient was a 5-year-old male child and had been in good health until the day before admission when he became drowsy. During transfer to our hospital, he developed seizures and episodes of vomiting. On arrival, he was in a coma without any

response to pain. His body temperature was 37°C and his pulse was weak, at 120/min. His respiration was first irregular, 20/min, and subsequently stopped. His blood pressure was 60 mmHg systolic. The liver was not palpable.

His hemoglobin was 16.4 g/dL, hematocrit 46.0%, white blood cell count 14,200/mm³, and platelets 33.9 × 10⁴/mm³. The serum sodium concentration was 136 mmol/L, and potassium 2.9 mmol/L. Blood urea nitrogen (BUN) was 34 mg/dL, and serum creatinine (Cr) 2.0 mg/dL. The erythrocyte sedimentation rate was 6 mm/h, and the C-reactive protein serum level 2.9 mg/dL. SGOT was 100 IU/L, and SGPT 20 IU/L. Urinalysis showed 2+ protein and the sediment contained innumerable red blood cells (RBC) per high power field. Cerebrospinal fluid examination yielded 1 leukocyte/

Fig. 1A.: Clinical course, * AVP < 0.15 pg/ml

mm³, glucose 26 mg/dL, and protein 19 mg/dL. Needle liver biopsy ruled out Reye's syndrome because no fine lipid droplets were observed. The Electroencephalogram (EEG) was flat, and a CT scan of the head revealed marked brain edema.

After admission, respiration and blood pressure were maintained by assisted ventilation and intravenous epinephrine (0.075 micrograms/kg/min) and dobutamine (5 micrograms/kg/min). In order to decrease intracranial pressure, dexamethazone (0.4 mg/kg) and hyperventilation therapy with a respirator were administered. In spite of these maintenance therapy throughout admission, he did not regain consciousness and his EEG remained flat. Thirty-three days after admission he died of pneumonia.

During admission, high and low plasma osmolality (Posm) were alternately measured. His clinical course can be separated into 4

periods (Fig. 1A. and 1B.).

From admission to the 7th hospital day (period 1), in spite of high Posm (340-350 mOsm/kg) and weight loss, urine osmolality (Uosm, 200-300 mOsm/kg) was disproportionately low and the plasma AVP (0.5-0.6 pg/ml) level was low (Hammer M *et al.*, 1980; Milles JJ and Baylis PH, 1979; Robertson GL *et al.*, 1976). These data are consistent with DI.

From the 8th to the 14th hospital day (period 2), in spite of low Posm (230-240 mOsm/kg) and weight gain, Uosm (600-800 mOsm/kg) and plasma AVP (2-4 pg/ml) were definitely high (Hammer M and Landefoged J, 1980; Milles JJ and Baylis PH, 1979; Robertson GL *et al.*, 1976). During period 2, we performed a hypertonic saline loading test (Fig. 2., 5% NaCl 0.05 ml/kg/min for 120 min.). Plasma AVP did not change during this test. These data

Fig. 1B.: Clinical course

Fig. 2.: Hypertonic saline loading test

are consistent with SIADH.

From the 15th to 25th hospital day (period 3), Uosm (50–150 mOsm/kg) and plasma AVP levels (0.4 pg/ml >) were low

(Hammer M *et al.*, 1980; Milles JJ and Baylis PH, 1979; Robertson GL *et al.*, 1976) in spite of high Posm (310–330 mOsm/kg) and weight loss. These data are again consistent with DI.

In the last half of period 3, Uosm transiently increased (320–350 mOsm/kg) despite continuously low plasma AVP (0.4 pg/ml >).

From the 26th to the 33rd hospital day (period 4), we tried 1-deamino-8-D-arginine vasopressin (DDAVP), administered nasally. Uosm rose to a maximum of 445 mOsm/kg from 70 mOsm/kg.

We measured thyroxine and insulin-like growth factor-I during period 1, and the values are 10.0 microgram/dl, and 1.12 U/ml, respectively. However, we did not measure any other anterior pituitary hormones or perform provocation tests for the hormones.

We could not get consent for autopsy.

Discussion

The diagnosis of our patient was encephalopathy of unknown etiology with severe brain damage. In period 1, we could not deny the possibility that renal tubular dysfunction resulted in low Uosm and weight loss, because he had hematuria, proteinuria, and high serum creatinine levels. However, low plasma AVP reflects suppression of AVP release, which contributed to the development of low Uosm and high Posm. There seems to be no doubt that he developed SIADH in period 2 and DI in periods 3 and 4, judging from Posm, Uosm, plasma AVP levels and body weight (BW) measurements. The transient rise in Uosm seen in period 3 despite continuously low plasma AVP may be explained by mechanisms other than AVP, such as decreased glomerular filtration rate or periodic AVP leakage which could not be detected by our measurements.

SIADH followed by permanent DI has been reported in neonatal asphyxia (Khare SK, 1977). Our case is similar to the reported one. The reported case was that of biphasic SIADH and DI. Plasma AVP levels were not described.

A triphasic pattern of urinary excretion is reported in cats and humans after stereotactic destruction of the supraopticohypophyseal tract (Fisher C *et al.*, 1935; Hollinshead WH, 1964; Randall RV *et al.*, 1960). In these animal and human models, the 1st phase is the immediate post-injury rise in urine volume and a fall in urine osmolality. This phase is followed by the second phase of five to seven days during which urine flow falls abruptly and urine osmolality rises. The final phase is characterized by permanent hyposthenuric polyuria. The initial phase is assumed to be secondary to an injury-related neural shock during which time no AVP release occurs. The 2nd phase is thought to be

secondary to the leak of hormone from degenerating neurons. The last phase is considered to be permanent depletion of AVP.

In our case, a triphasic pattern of Posm and Uosm was also observed. Low plasma AVP during period 1 is consistent with suppression of AVP release. Both relatively high plasma AVP during period 2 and the lack of the response of AVP to a hypertonic saline load are consistent with AVP leakage from the neurons. Very low plasma AVP during period 3 and the response to DDAVP during period 4 are also consistent with permanent depletion of AVP.

Thus we speculate that our case with encephalopathy represents neurohypophyseal dysfunction induced by supraopticohypophyseal tract damage because the discrete triphasic pattern of Posm and Uosm changes is similar to that in cats and human models.

The changes in the plasma AVP concentration are consistent with the above speculation. This triphasic response may be secondary to acute or abrupt damage to the tract because cats and human models were those used after acute destruction of the tract. The acute clinical course of our patient and the similarity of duration of each phase (periods 1, 2 and 3) to that of the models support the concept that this triphasic responses may be associated with "acute" damage of the tract.

Because we did not perform an autopsy, we could not obtain pathological data on the supraopticohypophyseal tract and other brain lesions. However, his brain lesion was very diffuse and he was in a condition of brain death. It is possible to speculate that there could be a triphasic response if a patient were in a condition of brain death, which leads to the damage of the tract. It is very difficult to discuss the relationship between brain death and the triphasic response in only one case, since, as far as we know, there are no other reports about the response seen in a patient

with a diffuse brain lesion or in a brain-dead patient.

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