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Case Report

Severe Recurrent Hyponatremia and Acute Renal Failure Due to Shapiro's Syndrome

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1. Abstract

Shapiro syndrome is a rare disorder defined by the clinical trial of relapsing episodes of hypothermia, hyperhidrosis and agenesis of the corpus callosum.

The exact mechanism that leads to hyperhidrosis crises is unknown and its treatment consists of controlling the periodic attacks. Severe temperature deregulation and hyperhidrosis are important hallmarks of this syndrome that can be characterized by strongly fluid loss and electrolyte severe disorder.

All of them can lead to severe recurrent hyponatremia, acute renal impairment and metabolic acidosis as we report in the case below.

2. Introduction

Shapiro syndrome is extremely rare all over the world and approximately fifty cases have been reported.

It was first described in literature by Shapiro and Plum in 1967 and it consists of the triad of spontaneous periodic hypothermia, hyperhidrosis and agenesis of the corpus callosum [1, 2]. The pathogenesis of it is still unclear.

The corpus callosum, formed by interhemispheric associative fibres, represents a constant and continuous communication system between the two cerebral hemispheres. Its absence may determine the symptoms described above.

There was only one report about familiar Shapiro syndrome variant with occurrence of the disease in two siblings with supported inheritance as a cause [3].

The accepted pathophysiological mechanism is the decrease of the 'set point' temperature in the hypothalamus that is considered an important thermoregulatory centre [4]. Hyperhidrosis within hypothermia are considered characteristic hallmark of this rare syndrome [5]. The fluid depletion can be profound and determine hyponatremia, acute renal failure and metabolic acidosis and as we describe in our case report.

3. Case Report

We report the case of a fifty-nine years old adult male Caucasian patient who was admitted for a syncopal episode with non-commotional head injury showing a severe hyponatremia (113 mEq/l, n.v.:135-145 mEq/l), hyperkaliemia (6.9 mEq/l, n.v.: 3.5 - 5.0 mEq/l) and acute renal failure (serum creatinine 4.3 mg/dl, n.v.: 0.7 - 1.3 mg/dl, serum urea 151 mg/dl, n.v.: 15 - 38 mg/dl) following to massive hyperhidrosis (from four to six liter of sweat as estimated from home's relatives) and subsequent mucus-cutaneous severe dehydration.

Physical examination showed significant cutaneous dehydration, dry tongue, systolic arterial hypotension (90 mmHg), sinus tachycardia (92 BPM R) and oligo-anuria (< 300 cc of urine pool/day). His medical history included Shapiro's syndrome with many years of recurrent hospitalizations for episodes of excessive sweating and generalized malaise. During the previous hospitalizations an anxious-depressive syndrome related to the underlying pathology was diagnosed. On examination the patient showed asthenia, arterial hypotension and massive sweating (up to six liters of sweat loss per day) with need for recovery for adequate rapid re-hydration. The crises appeared especially on the night period even if they could have appeared anytime. He also had hypothermia (34.5° – 35°in Celsius grade scale vs normal human body temperature that in basal conditions is commonly considered to be around 36.8 Celsius degrees) for which he was protected with a thermal blanket with constant hot air flow (37 - 38 °C) to avoid frostbite and thermal shock.

Blood admitting exams showed severe hyponatremia (113 mEq/l) and consensual hypochloraemia (78 mEql, n.v.: 98-107 mEq/l), hyperkaliemia (6.2 mEq/l), acute renal failure (serum creatinine 4.3 mg/dl, serum urea 151 mg/dl), metabolic acidosis (pH 7.29,

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n.v.: 7.35-7.45), Bicarbonates 23.8 mEq/l, n.v.: 22-26 mEq/l, excess base -1.9 mEq/l, n-v.: -2+2), nonspecific increase in liver enzymes (GOT 49 Ui/l, n.v.: 8-30, GPT 129 Ui/l, n.v.: 13-57, Gamma-glutammil-traspherase 99 Ui/l, n.v.: 5-85, increase in cholinesterase to 26999 U/L, n.v.: 7000-19000, haemoconcentration (haemoglobin 18.2 gr/dl, n.v.: 14-18 gr/dl), normal plasma osmolarity (288 mOsm/lt-n.v.: 270-300 mOsm/lt) and urinary's one (724 mOsm/kg, n.v.: 400-1100 mOsm/kg).

Thyroid hormone controls showed suppressed thyroid stimulating hormone (TSH 0.11 mUi/ml, n.v.: 0.36-3.74 MUi/ml) and normal thyroid fractions (fT3 2.56 pg/ml, n.v.: 2.0-4.4 pg/ml, fT4 1.13 ng/dl, n.v.: 0.7-1.9 ng/dl).

Blood culture performed because of a single day hyperthermia (37.6°C) was negative.

Among the instrumental exams done during hospitalization, an ECG showed slightly accelerated sinus rhythm, PR interval within the limits and low voltages in the QRS complex. The ECG was the same also during vagal tests stimulation with a small circular massage on the neck sinus.

The brain imaging study (MRI) showed complete absence of the corpus callosum in the various scans (Figure 1-6).

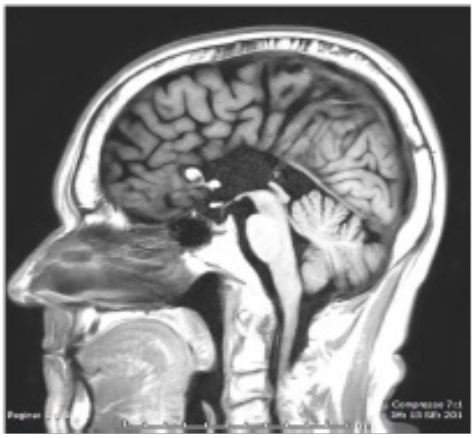

Figure 1: Sagittal view of MRI head of our Shapiro 's patient showing the Corpus Callosum's absence.

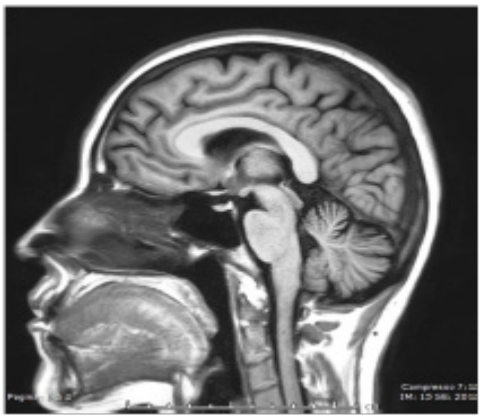

Figure 2: Normal sagittal view of MRI head.

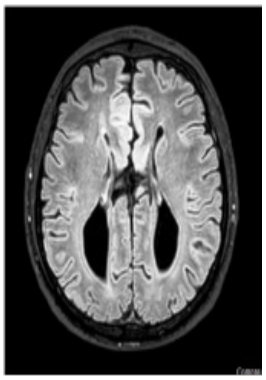

Figure 3: Axial view of MRI head of our patient showing again the "C.C." absence.

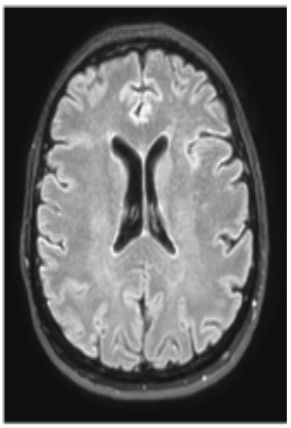

Figure 4: Normal Axial view of MRI head.

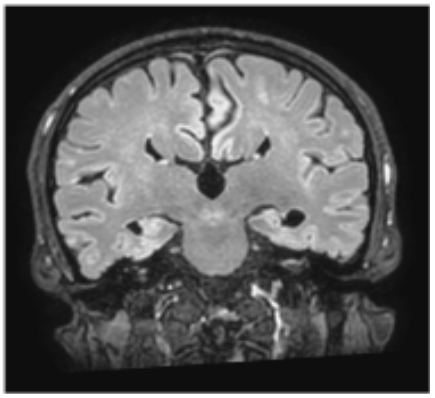

Figure 5: Coronal view oh MRI head of the Shapiro's case showing the two lateral ventricles forming a "Viking Helmet" like structure due to the absence of the corpus callosum.

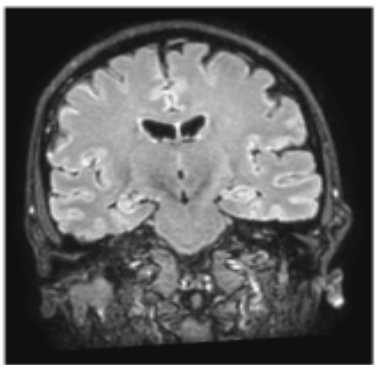

Figure 6: Normal Coronal view of MRI Head.

A renal ultrasound check showed normal kidneys, mild prostatic hypertrophy and as an accessory finding slight pleural effusion on the right side. The encephalic CT scan done at the admission did not show bone fractures rhymes related to post-syncopal accidental trauma.

A neurological consultation denoted ideo-motor slowdown linked to an evident prostration state with marked diffuse sweating in the absence of focal neurological signs. Together with hydration, it recommended a gradual resumption of oral clonidine therapy up to a dosage of 150 mg x 2 per day (discontinued before owing to systolic hypotension).

Because of the high amount of fluids to be administered and the limited availability of the peripheral venous tree, it was necessary to place a peripherally inserted central venous catheter in an ultrasound-guided way (P.I.C.C. type). This was followed by a chest X-ray to check the correct place of the device into the cardiac right chamber.

To check the daily water balance, a bladder catheter was placed on and every fluid loss during the hyperhidrosis crises (from three to five per day) in sweating crises was recorded.

The initial intravenous hydration of about a liter and a half per day allowed the diuresis to resume (from zero fifty-hundred cc per day and after until to one liter per day) with improving blood pressure, renal blood exams and serum electrolytes.

Consequently, a reduction of fluid infusions and an oral hydration trial were applied. But the improvement was followed by another severe hyperhidrosis crisis with hypothermia (Figure nr.1), massive fluid loss with new severe mucus-cutaneous dehydration, recurrent hyponatremia (serum Natrium from 133 down to 124 mEq/l) (Figure. nr. 2), daily diuresis reduction, acute renal failure (serum creatinine increased from 1.0 mg/dl to 5.0 mg/dl, serum urea increased from 40 mg/dl to 97 mg/dl) (Figure nr. 3), metabolic acidosis (pH 7.23, bicarbonates soft reduction to 23 meq/l), plasma osmolality tightly the standard (296 mOsm / kg).

Therefore, intravenous hydration was increased again (flow rate of 100-200 ml per hour), monitoring systemic blood pressure and daily diuresis rate. The clonidine (an alfa-2-adrenoceptor that plays a stabilizing role on hypothalamic thermoregulation) was gradually recovered (starting from 25 mg/day to 37.5 mg/day on full maximum dose on discharge) after observing a better systolic pressure trend.

After an alternating phase of excessive sweating/rehydration over two weeks of hospitalization, the patient presented a progressive reduction of the hyperhidrosis crises and improved the clinical status as the laboratory exams and was discharged at his own home.

After seven days of home assisted hydration (really done?) he was hospitalized again for mucus-cutaneous dehydration, mild hyponatremia (123 mEq/l), systemic arterial hypotension (70 mmHg), acute renal failure (serum creatinine up to 3.7 mg/dl from discharge value of 1.7 mg/dl, serum urea up to 81 mg/dl from previous one of 62 mg/dl), metabolic acidosis (pH 7.159, bicarbonates 16.9 Meq/l) and severe asthenia.

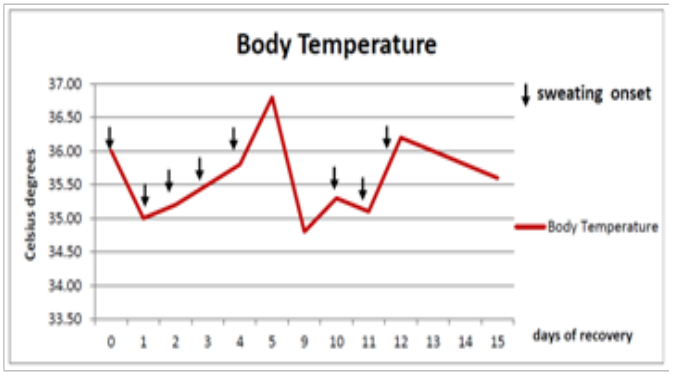

Figure nr. 1: Recurrent Hypothermia and sweating attacks.

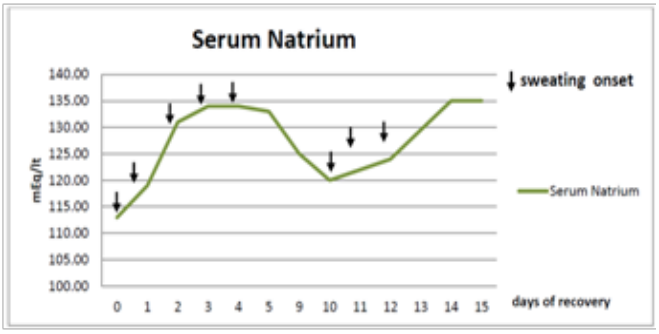

Figure nr. 2: Hyponatremia and sweating attacks.

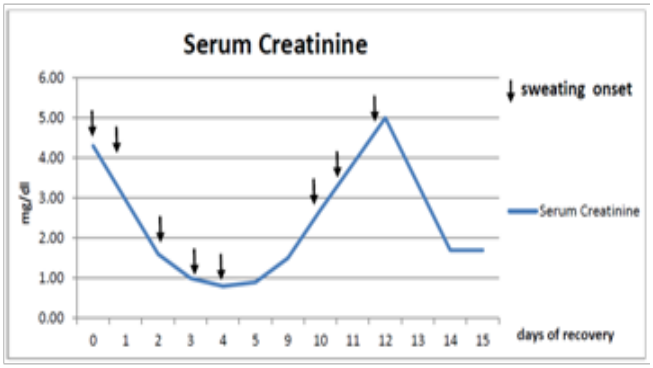

Figure nr. 3: AKI and sweating attacks

4. Discussion

Shapiro syndrome is neurological disease characterized by the absence of the "Corpus Callosum" that is a hemispheric inter-associative nervous bundle. It connects the right cerebral hemisphere with the left one. It plays a crucial role, in addition to hypothalamus body's thermoregulation, ensuring a continuous flow of information between the two cerebral hemispheres (dominant/non-dominant) and its absence can lead to severe relapsing hyperhidrosis

crises and rapidly fatal mucus-cutaneous dehydration if not corrected [6].

In this patient the diagnosis of Shapiro syndrome was formulated at the age of twenty and thereafter the nature and frequency of hyperhidrosis attacks have varied over time and have led to hospitalization in most severe cases of muco-skin dehydration and psychic-motor slowdown. The nature and frequency of the sweating attacks is random and asynchronous and any trigger can determine it [7].

This condition is a difficult psychological element for the patient himself. He was not able to plan his life or his own occurrences because of the hidden but real frightful risk of sudden hyperhidrosis crises appearing.

The Shapiro syndrome invalidates the quality of life itself and could lead the patients to an anxious-depressive syndrome to the point that he can refuse or forget the oral home daily drugs in the chronicle period.

Some drugs as clonidine (an alpha-2 adrenoceptor drug effective on prophylaxis and treatment of hyperhidrosis) can have a prophylactic role against hyperhidrosis crises (others reported are mirtazapine, carbamazepine, alprazolam, amitriptyline, sodium valproate) [8, 9].

Closely in cases of hypothermia, hyperhidrosis and related severe systemic hypotension you have to stop the clonidine because of the hypotensive hearth failure risk.

Once excluded the other causes of hyperhidrosis and the Shapiro's syndrome is diagnosed it is necessary to give a large and constant fluid infusion in order to avoid severe muco-cutaneous dehydration, hyponatremia, acute renal failure and also metabolic acidosis (apart from neurological symptoms) [10].

In the case of severe systemic hypotension it is necessary to stop the clonidine (an alpha -2 adrenoceptor drug effective on prophylaxis and treatment of hyperhidrosis.

Severe hyponatremia and related hypocloraemia are often consensual to the excess of fluid waste during the hyperhidrosis crisis (up to four, five, six liters of sweating per day). Plasma osmolality values can be normal as done by the kidney that balances the fluids leak by increasing the reabsorption of free water [11].

But if the fluids loss is extreme and uncontrolled it can induce acute renal failure with oligo-anuria and it is necessary hospitalize the patient quickly and give him an adequate intravenous hydration (from one hundred to two-hundred ml per hr of saline (0.9% concentration) or bicarbonate solution (based on blood gas venous sampling) in order to pursue a weakly negative water balance.

Among the laboratory exams alterations reported in the literature dysthyroidism can be present and was found in our case [3].

The improvement of the clinical-laboratory parameters should not correspond to an immediate interruption of intravenous fluids as the risk of dehydration recurrence is very high.

In this case it is likely that the patient, also affected by an anxious depressive syndrome, just feeling better at home he can have discontinued chronically oral drug therapy and this may have triggered hyperhidrosis crises again.

Shapiro's syndrome is very rare but it can determine a severe hyponatremia following intense mucus-cutaneous dehydration but also an acute pre-renal renal failure in patients with normal glomerular filtration rate. It depends on type and quantity of crises' fluids loss.

The kidney attempt to compensate the loss of excess fluids is not infinite and in severe cases can lead to the need for urgent replacement hemodialysis treatment.

To avoid this, it is necessary to immediately carry out abundant and continuous intravenous re-hydration considering not only the liquids leak with sweat but also the "insensible perspiration" and residual diuresis (it can be lost from four to six or more of sweating liquids per day).

In addition to the high quantity of saline solution infusion (0.9 % concentration, infuse to one hundred to two hundred ml per hour) it is useful to give saline bicarbonate solution in cases of associated metabolic acidosis [12].

It is important since the first sweating to immediately start abundant intravenous hydration and it may also help giving home oral support therapy and to verify the patient's therapeutic adhesion to it, especially in young people or cases of associated psychiatric or neurological disease (anxious-depressive syndrome or other's inherited neurological forms). In them, the clinical improvement or disappearance of sweating crises may correspond to an early suspension of support therapy and subsequent recurrence of the crises themselves [13, 14].

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