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ASSESSMENT OF VOLUME STATUS AND APPROPRIATE FLUID REPLENISHMENT IN THE SETTING OF NEPHROTIC SYNDROME

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☐ **Abstract—Background: When the permeability of the glomerular filtration barrier increases, leading to proteinuria, nephrotic syndrome (NS) occurs. First episodes or relapses of NS can be concurrent with acute gastroenteritis (AGE) infections. This condition can cause further deterioration of the hypovolemic state, as intravascular water is lost through both AGE-related vomiting/diarrhea and NS-related fluid shifting into the interstitium. In this case report, we wish to raise the issues about the difficult management of children presenting with both NS and AGE. Case Report: We report two cases characterized by concurrence of NS and AGE. Despite our intervention, case #1 required dialysis, whereas in the case #2 we restored the patient's liquid homeostasis. Why Should an Emergency Physician Be Aware of This?: No guidelines helping general physicians in the management of children presenting with both NS and AGE are available in the literature. However, it is common for these patients to seek the first line of treatment at emergency departments. In these patients, restoring the liquid homeostasis is a challenge, but some key points can help the physicians with first-line management: 1) carefully evaluate the signs of hypovolemia (edematous state can be misleading); 2) bear in mind that—in hypovolemic, severely hypoalbuminemic (serum albumin levels < 2 g/dL) NS children—initial fluid administration should be followed by a 20% albumin infusion if oligoanuria persists; intravenous 4.5% albumin may be a valid alternative as a first-line therapy instead of crystalloid and 20% albumin; and 3) pay attention when using furosemide; it should only be administered after albumin infusion or after hypovolemia correction.**

☐ **Keywords—nephrotic syndrome; hypovolemic shock; hypoalbuminemia; furosemide; dehydration**

INTRODUCTION

Nephrotic syndrome (NS) is a kidney disease characterized by an increased permeability of the glomerular filtration barrier leading to proteinuria, hypoalbuminemia, edema, and hyperlipidemia, and it has an incidence of 1–3 per 100,000 children < 16 years of age per year (1,2). Acute and life-threatening complications can occur in NS-affected children, such as hypovolemia/hypotension, invasive bacterial infection, and thrombosis (1,2). Acute gastroenteritis (AGE) is a major cause of illness worldwide, with 3–5 billion cases and nearly 2 million deaths occurring each year in children under 5 years of age, mostly in the developing world (3,4). Dehydration, metabolic acidosis, and electrolyte disturbance are the most important and dangerous AGE-related complications (4). Careful management with oral or intravenous

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fluids can help to prevent them (4). NS may start or relapse during AGE in childhood (5,6). Moreover, infections could represent a risk factor for acute kidney injury (AKI) in patients with NS (7). It is common for patients presenting with both NS and AGE to seek medical treatment at emergency units. Both evaluating and treating the hypovolemic state of a patient losing water through both AGE-related vomiting/diarrhea and NS-related fluid shifting into the interstitium is a challenge for emergency physicians. Also, the timing of albumin and furosemide administration is a difficult choice. No indications or guidelines are available in the literature. In this case report, we want to raise the issues about the difficult management of children presenting with both NS and AGE and give to the emergency physicians some elements helping in the first-line management of these patients.

CASE #1

A 9-year-old girl affected by steroid- and cyclosporine-dependent NS, receiving cyclosporine alone (4 mg/kg/day) during the last 3 years, presented with both NS relapse and AGE infection. She showed incoercible vomiting (not responsive to two doses of sublingual ondansetron) and diarrhea (up to 10 discharges/day) for 4 days and NS relapse for 2 days prior to coming to our unit. At the AGE onset, renal function was normal (creatinine 0.6 mg/dL). She was receiving prednisone (60 mg/m^2/day) since the NS relapsed. Physical examination revealed drowsiness, tachycardia (118 beats/min), cold hands and feet, and refill time of about 2 s. She reported only one, low-quantity micturition during the last 18 h, and presented weight gain of 0.8 kg in absence of peripheral edema (the weight 1 week prior was 35.2 kg; at our observation it was 36 kg). Blood pressure was 90/50 mm Hg. Blood tests showed creatinine 4.1 mg/dL, sodium 139 mEq/L, potassium 6.1 mEq/L, urea 150 mg/dL, and albumin 1.8 g/dL. Echo-color Doppler sonography excluded renal vein thrombosis, and low-dose aspirin was started to prevent it. As NS- and AGE-related hypovolemia was evident, we administered i.v. 20 mL/kg 0.9% NaCl in 1 h followed by 2.5 mL/kg 20% albumin in 3 h and then 1 mg/kg of furosemide as a bolus. Despite our treatment, 6 h after admission she had passed only 66 mL (0.22 mL/kg/h) of urine, and levels of creatinine, potassium, and urea were 4.45 mg/dL, 6.4 mEq/L and 250 mg/dL, respectively. Therefore, despite hypovolemia correction, the acute renal failure seemed unresponsive to medical treatment and required dialysis. Renal function was restored after 15 days.

CASE #2

A 3-year-old boy presented with AGE-related incoercible vomiting and diarrhea (up to 8 discharges/day, for 1 day), which had been preceded by gradual peripheral edema and weight gain of 1 kg (his weight 1 month prior was 10.7 kg; at our observation it was 11.710 kg). Oral rehydration was difficult due to vomiting. The amount of the previous urine volume was unknown. He appeared abnormally sleepy with sunken eyes, and showed pallor, peripheral edema with the fovea sign, bilateral hydrocele, and a refill time of 3 s. Blood pressure was 75/40 mm Hg. Blood tests and urinalysis showed low sodium levels (125 mEq/L), hyperlipidemia (cholesterol 406 mg/dL and triglycerides 530 mg/dL), hypoalbuminemia (1.50 g/dL), and proteinuria (urinary protein/urinary creatinine ratio: 11.8; n.v. < 0.25). Creatinine and urea levels were 0.27 and 34 mg/dL, respectively. The clinical and biochemical evidence was suggestive of a first episode of NS concurrent with AGE. Firstly, i.v. 20 mL/kg 0.9% NaCl in 20 min was administered, with apparent improvement in the patient's general condition. Sixty mg/m^2/day prednisone and 3 mg/kg/day aspirin were started. Secondly, i.v. 0.9% NaCl (900 mL/24 h) was continued over the following 4 days to restore and maintain the euvolemic state. Each day (including the first day), he received a 3-h i.v. 2.5 mL/kg/die 20% albumin followed by a 1-mg/kg furosemide bolus. Saline administration was suspended during the albumin infusion.

After 4 days of therapy, the hypovolemic state and the AGE-related vomiting and diarrhea resolved. The weight was 11.4 kg. Intravenous therapy was stopped and daily oral corticosteroid therapy continued. The serum creatinine values always appeared in the normal range.

DISCUSSION

The rehydration of a patient with concomitant AGE and NS who is then not able to retain fluids in the vessels due to hypoalbuminemia, raises issues among clinicians because the conventional rehydration schemes alone are not sufficient to restore the euvolemic state. In this situation, the intravascular volume is further depleted and the dehydration can become severe. Abnormal skin turgor represents one of the most useful predictors of 5% or more dehydration, but in a patient with NS, the edematous state can partially complicate the dehydration evaluation (8). Therefore, a careful detection of all the signs of dehydration is fundamental, and a proper and timely treatment could reduce the risk of a possible evolution to AKI (7).

In case #1, the peripheral edema was not marked, despite the relapsing NS, because the vomiting-related hypovolemia limited fluid shift into the interstitium. The delay (4 days after the onset of symptoms) in coming to the emergency department (ED) possibly led to acute renal failure. Nephrotoxic medication exposure has been identified as a risk factor for AKI in NS patients;