

Hyponatremia — an Unusual Presentation of Respiratory Syncytial Virus Infection

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Citation

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Abstract

Respiratory syncytial virus (RSV) bronchiolitis is the most common cause of admission to the pediatric ward and Pediatric Intensive Care Unit (PICU) for respiratory distress and respiratory failure in infancy. There has been an increasing emphasis on the importance of extra pulmonary manifestations of RSV infection that include hyponatremia, hepatitis, seizures, arrhythmias, and cardiorespiratory failure. Physicians should consider this diagnosis in all newborns especially the preterm infants born after 35 weeks of gestation, and who do not qualify for the monoclonal antibody (Palivizumab) prophylaxis against RSV. Such patients can deteriorate rapidly, if extra pulmonary manifestations of RSV infection are not recognized and managed in a timely fashion. We report a case of RSV Bronchiolitis in a 32 days old preterm infant (ex-35 weeker) who presented with hypoglycemia, hyponatremia, respiratory failure and shock of unknown etiology.

INTRODUCTION

Respiratory syncytial virus (RSV) bronchiolitis is the most common cause of admission to the pediatric ward and Pediatric Intensive Care Unit (PICU) for respiratory distress and respiratory failure in infancy. There has been an increasing emphasis on the importance of extra pulmonary manifestations of RSV infection that include hyponatremia, hepatitis, seizures, arrhythmias, and cardiorespiratory failure. Physicians should consider this diagnosis in all newborns especially the preterm infants born after 35 weeks of gestation, and who do not qualify for the monoclonal antibody (Palivizumab) prophylaxis against RSV. Such patients can deteriorate rapidly, if extra pulmonary manifestations of RSV infection are not recognized and managed in a timely fashion. We report a case of RSV Bronchiolitis in a 32 days old preterm infant (ex-35 weeker) who presented with hypoglycemia, hyponatremia, respiratory failure and shock of unknown etiology.

CASE REPORT

A 32 days old female was admitted for respiratory distress, hypothermia, hyponatremia, hypoglycemia and anemia of unknown etiology. She was born at 35 weeks of gestation (twin B) via Cesarean section for premature rupture of membrane. Her birth weight was 2.1kg and 2.15kg at three days of life. The patient did not require NICU stay. There were no respiratory or feeding problems. There were also no

comorbid conditions after birth. The baby was tolerating the premixed Enfamil.

The patient was doing fine until five days ago when she developed cold, cough and gagging during feeding. Her physical examination was normal except nasal congestion at other hospital. The patient improved after nasal suction and was discharged home after getting normal results of blood test and Chest x-ray.

After the discharge from the hospital, the patient was feeding poorly, drinking only one ounce of formula every three hours. Her urine output gradually decreased and became more lethargic and sleepy. The patient was brought to our emergency department by EMS for generalized limp after drinking one ounce of formula. Her past medical and surgical history was unremarkable.

In the emergency department, her vital signs were pulse rate of 150 beats per minute, respiratory rate of 40 breaths per minute, temperature of 90.8° F, and blood pressure of 95/35 mm of Hg. Initial oxygen saturation was 85 percent on room air which improved to 94 percent with 100 percent oxygen by non-rebreather face mask. The physical examination was remarkable for thick nasal secretion and severe respiratory distress (subcostal and intercostal retractions, and bibasilar crackles). The patient didn't appear to be dehydrated or edematous on physical examination. There were no episodes

of apnea or seizure noted.

The patient had a complete sepsis work up including complete blood count, electrolytes, urinalysis, cultures (blood, urine and cerebrospinal fluid), and chest x-ray, and treated with 100 percent oxygen, intravenous antibiotics, intravenous fluids, and intravenous 10 percent Dextrose push times three (10ml/kg) to treat hypoglycemia (initial finger stick glucose- 28 mg/dl). The patient was placed in the overhead radiant warmer and transferred to Pediatric Intensive Care Unit for further management. In the PICU, the respiratory status worsened and the patient was placed on BiPAP (bi-level positive airway pressure). The arterial blood gas showed respiratory acidosis (pH of 7.21, pCO₂ of 75 mm of Hg, pO₂ of 65mm of Hg, and bicarbonate of 30mmol/L) and the patient was intubated and connected to a mechanical ventilator (Table 1). An ABG was attempted earlier in the ED but it couldn't be obtained.

Her initial electrolytes showed hyponatremia (121mmol/L) with potassium of 5.8mmol/L (Table 2). The hyponatremia was managed by giving normal saline (isotonic crystalloid) boluses and then starting the patient on D5W ½NS (normal saline). The sodium chloride concentration of intravenous fluids was gradually decreased with increasing serum sodium levels. Patient was gradually weaned to 1/3NS and then 1/4NS with subsequent discontinuation of IV fluids after normal sodium levels had been reached. Initial serum osmolality was 594mOsm/kg serum H₂O but this sample was drawn after 3 D10W pushes for hypoglycemia so this may not be an accurate value. The urine specific gravity was 1.005 but this urine sample was also obtained after multiple boluses of normal saline IV fluids so this value did not reflect the actual hydration status of the patient at the initial presentation. The corrected sodium for hyperglycemia (254mmol/L) was 123mmol/L which is still considered hyponatremia. This shows that it was actually not factitious hyponatremia. The exact diagnosis could not be established as the baby was too sick. But some of the possible diagnoses will be discussed in detail in the following sections.

The diagnosis of adrenal failure was considered and the patient was treated with intravenous hydrocortisone sodium succinate times two. SIADH associated with pulmonary RSV infection was also considered especially since the hyponatremia resolved after the initial intravenous fluid resuscitation. The lab studies done in our patient were unfortunately performed after administration of the IV normal saline and dextrose boluses so they didn't support the diagnosis of SIADH in our case. The patient was also

transfused with packed RBC for severe anemia (Hemoglobin of 7.8g/dL and Hematocrit of 21.7g/dL). The chest x-ray showed right perihilar infiltrate.

During the episodes of hypoglycemia, the levels of growth hormone, insulin and cortisol were normal. The rest of blood tests including liver functions, urinalysis, urine electrolytes, cerebrospinal fluid and head sonogram were also normal. The nasopharyngeal viral culture was positive for respiratory syncytial virus (RSV). The bacterial cultures of blood, urine and cerebrospinal fluid were negative.

The patient was extubated on the second day but continued to have thick nasal secretions requiring frequent nasal suction and intermittent oxygenation by nasal cannula. The patient was discharged to home on the sixth day.

RSV bronchiolitis is the most common cause of admission to the hospital due to respiratory failure in infancy (1). RSV is a negative-sense, single-stranded RNA virus of the family Paramyxoviridae, that includes common respiratory viruses like measles and mumps (2).

The Center for Disease Control considers RSV to be the “most common cause of bronchiolitis and pneumonia in children under 1 year of age in the United States” (2). Other RSV symptoms common among infants include listlessness, poor or diminished appetite, and fever (3). The extra pulmonary manifestations of RSV include cardiovascular failure requiring inotrope support, myocardial damage as evident from elevated cardiac troponin levels (35–54 percent of ventilated infants), cardiac arrhythmias such as supraventricular tachycardia and ventricular tachycardia, central apnea (16–21 percent of admissions), focal and generalized seizures, focal neurological abnormalities, hyponatremia (33 percent) and hepatitis. The physicians should consider this diagnosis in all preterm infants who present with respiratory distress and who do not meet the criteria to receive Palivizumab (monoclonal antibody) prophylaxis. Palivizumab (Synagis) is recommended for high risk infants born between 32 and 35 weeks of gestation (4). It can be effective in preventing hospitalization for some infants.

The hyponatremia is caused by increased secretion of Anti Diuretic Hormone (7, 11, 12) and use of electrolyte-free water (5, 6). It should be treated with appropriate intravenous fluids (1). Syndrome of inappropriate antidiuretic hormone secretion usually results from CNS processes that disturb the posterior pituitary gland resulting

in over secretion of ADH, or peripheral tumors that secrete ADH or ADH-like substances (8, 9). The exact mechanism behind the development of hypervolemia with pulmonary infections is not fully understood. Hyponatremia (a serum sodium value of less than 136 mmol/l) was found in 33% of infants requiring ICU care with RSV infection; 11% of the patients had a serum sodium level of less than 130 mmol/l [7]. In a less specifically chosen population of children, including patients with milder disease, only 0.6% of patients had a serum sodium level of less than 130 mmol/l [8]. The association of hyponatremia with RSV infection was first investigated in a study of four infants admitted to the ward with hyponatremia and bronchiolitis during an outbreak of RSV. One patient presented with focal seizures and hyponatremia and was found to be positive for RSV. Antidiuretic hormone (ADH) levels were elevated in all four infants. Synacthen test was performed for one, which showed normal cortisol release [9]. Additional studies showed that ADH levels were considerably higher in patients with bronchiolitis than in patients with upper respiratory tract infections or apneas with RSV. The highest levels were specifically found in patients receiving mechanical ventilation [10]. Elevated ADH levels were associated with increased arterial partial pressure of CO₂ and hyperinflation on a chest X-ray. Hyponatremia and hyponatremic seizures have also been associated with the application of hypotonic fluids at 100 to 150 ml/kg per day [7].

There are several other theories that have tried to explain the finding of hyponatremia in pulmonary diseases. One theory deals with pulmonary infection leading to hypercapnia. This can reduce the renal blood flow and, as a result, increase water and sodium retention with the final effect of edema and hyponatremia (14). In addition, lung hyperinflation can lead to pulmonary hypovolemia which decreases left atrial filling pressure. The baroreceptors in the left atrium sense this decrease in filling pressure and this subsequently leads to an increase in ADH production (14). Another study found that plasma arginine vasopressin values were significantly higher during pneumonia compared with values after recovery despite comparable plasma sodium concentrations, both beforehand and after water load (15). A positive correlation between plasma arginine vasopressin and minimum urine osmolality was found during pneumonia (15). Thus, impairment in renal water excretion seemed to be due to resetting of the vasopressin osmostat and could not be ascribed to any recognized nonosmotic stimulus for vasopressin secretion (15). A recently approved vasopressin

receptor antagonist offers a new option for the management of SIADH associated with respiratory illness especially pneumonia (13).

RSV and its genetic material have been isolated from cerebrospinal fluid, myocardium, liver and peripheral blood (11). In our patient, the diagnosis of adrenal failure was considered due to the clinical presentation and electrolyte abnormalities but later on, it ruled out, as urine electrolytes and blood cortisol were normal. The signs and symptoms of adrenal crisis include weakness, fever, abdominal pain, hypotension, dehydration, hypoglycemia, seizure, and shock (12). The laboratory tests, supporting the diagnosis of adrenal insufficiency, include low serum sodium, high serum potassium, low serum carbon dioxide, and low blood glucose. Urine electrolytes demonstrate high sodium and low potassium.

Figure 1

Table 1. Blood Gas Analysis

Blood Gas (time)	FiO2	PIP (cm H2O)	PEEP (cm H2O)	Mode	pH	CO2 (mmHg)	O2 (mmHg)	HCO3 (mmol/L)
Day One								
Arterial Blood Gas (8AM)	50%		5	BiPAP	7.21	75	65	30
Pt was intubated and placed on SIMV.								
Arterial Blood Gas (8:45AM)	50%	15/13	5	SIMV	7.21	80	36	27
Arterial Blood Gas (9:40AM)	45%	15/13	5	SIMV	7.37	51	111	28
Venous Blood Gas (11AM)	40%	15/13	5	SIMV	7.39	45	58	31
Day Two								
Venous Blood Gas (9AM)	Room Air	-	-	-	7.4	41	53	28

Figure 2

Table 2. Electrolyte Abnormalities on day # 1

	Na	K	Cl	HCO3	Glucose	BUN/Cr	Calcium
4:30AM	121	5.8	84	24	254	11/0.3	10.3
9:30AM	135	3.9	99	31	134	8/0.2	9.4
11:30AM	138	3.8	102	24	110	8/0.5	9.1

* IV Fluid management: Initially placed on D5W ¼ NS + 5meq/L KCL then switched to D10W ¼ NS switched to D10W 1/3NS + 10meq/L KCL at 12ml/hr. Also received a normal saline bolus.

CONCLUSION

This case was unique to us as patient presented with hypoglycemia, hyponatremia, hypothermia, respiratory failure and shock of unknown etiology. The physicians should be familiar with the signs and symptoms of extra pulmonary manifestations of RSV infections and suspect it in all preterm infants, especially those who didn't receive Palivizumab prophylaxis.

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