CASE REPORT

Early Recognition and Management of Nephrogenic Diabetes Insipidus in Preterm Newborn: A Vital Case Study

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ABSTRACT

Diabetes insipidus (DI) is a rare but critical condition in neonates, often challenging to diagnose due to subtle symptoms, especially in preterm and very low birth weight (VLBW) infants. We present a case of a preterm twin male diagnosed with nephrogenic diabetes insipidus (NDI) after developing polyuria and severe hypernatremia. Initial desmopressin challenge confirmed NDI, requiring careful fluid and electrolyte management. He later presented with Pyomeningitis and hydrocephalus, necessitating neurosurgical and nephrology interventions. Treatment with hydrochlorothiazide led to stabilization. This case underscores the importance of early recognition and tailored management of neonatal DI to prevent long-term neurodevelopmental complications. A high index of suspicion for DI is crucial in neonates with persistent polyuria and hypernatremia.

Key Words: *Neonatal diabetes insipidus, Nephrogenic diabetes insipidus, Preterm infants, Hypernatremia, polyuria*

INTRODUCTION

Diabetes Insipidus (DI) presents a diagnostic challenge in neonates due to subtle symptoms that are often overlooked, leading to increased mortality and morbidity. It encompasses central and nephrogenic types, with congenital cases often linked to genetic mutations. Congenital nephrogenic diabetes insipidus (NDI) presents with polyuria and polydipsia due to impaired urine concentration despite normal or increased ADH levels, potentially leading to growth delay and irreversible cognitive deficits if left untreated.[1] Timely detection and prompt intervention are vital to prevent complications like developmental delays and intellectual impairment.[2]

Differentiating between central diabetes insipidus (CDI) and nephrogenic diabetes insipidus (NDI) is crucial as treatment strategies vary. However, water deprivation tests are not applicable in neonates. Determining the optimal desmopressin dose poses a challenge, with varying approaches reported in the literature, ranging from 1 to 10 µg/kg/day, due to the potential for significant serum sodium fluctuations even with small doses.[3,4]

CASE REPORT

Our index patient was a twin 2 male, delivered at 34 weeks of gestation and underwent a stormy neonatal course compared to his sibling. Twin 1 was born with good Apgar scores and was discharged soon after birth. Twin 2 presented with a delayed cry and poor Apgar scores at birth necessitating immediate resuscitation and mechanical ventilation. Initial blood investigations revealed elevated hemoglobin, total leukocyte count, platelet count, raised C-reactive protein, and abnormal coagulation profile suggesting early onset sepsis. Electrolytes at presentation were

within normal limits. His cranial imaging indicated periventricular white matter abnormalities indicative of asphyxia, and echocardiography detected a small patent ductus arteriosus with mild pulmonary hypertension, which was resolved subsequently. He was managed with broad-spectrum antibiotics, vitamin K, multiple blood transfusions, and nutritional support.

On the ninth day of life, the patient manifested symptoms of polyuria and dehydration, alongside laboratory evidence of hypernatremia (Na=170 mEq/l). His blood glucose, serum calcium, potassium, and renal function tests were all normal. His serum osmolality was 309 mOsm/kg with urine osmolality of 180 mOsm/kg confirming the diagnosis of diabetes insipidus. She underwent a desmopressin challenge test at 14th day of life showing no response **(table 1)** confirming the diagnosis of nephrogenic diabetes insipidus. The patient was offered treatment but they got leave against medical advice and lost follow-up.

TABLE 1: Desmopressin challenge test results

Day of Life	**14th DOL**		
Desmopressin Dose (mcg)	**0.3 µg/kg**		
Parameter	**Before desmo-pressin**	**1 hour after**	**4 hours after**
Weight (g)	**1200**	**1100**	**1000**
Urine Output (ml/hr)	100	88	95
Blood Sodium (mEq/L)	175	166	150
Blood Osmolarity (mosm/kg)	309	314	320
Urine Osmolarity (mosm/kg)	250	295	268

Findings indicate a lack of response to desmopressin, consistent with nephrogenic diabetes insipidus (NDI).

At 4 months of age, the patient presented again with symptoms of fever and fits and was confirmed to have pyomeningitis (CSF proven) with moderate hydrocephalus. He was started on antibiotics and neurosurgical consultation was taken and acetazolamide for mild to moderate hydrocephalus on cranial ultrasound. A nephrology consultation was taken for NDI and hydrochlorothiazide was started along with correction of hypernatremia and replacement of extra-urinary losses to prevent dehydration. He was discharged on hydrochlorothiazide and acetazolamide **(table 2).**

TABLE 2: Comparison of Serum Electrolytes and Urine Output Before and After Thiazide Treatment

Parameter	**Before treatment**	**After thiazide treatment**
Serum Sodium (mEq/L)	151	137
Serum Potassium (mEq/L)	6.4	4.8
Serum Chloride (mmol/L)	118	105
Serum Bicarbonate (mmol/L)	17	21
Serum Osmolality (mOsm/kg)	329	285
Urine Osmolality (mOsm/kg)	114	214
Urine Output (ml/kg/hr)	11	4.3

Currently, he is 14 months of age with a weight of 6.5 kg. His latest Na is 146 mEq/L with serum osmolarity of 280 mOsm/kg on tab hydrochlorothiazide.

DISCUSSION

Diabetes Insipidus (DI) is a rare disease that presents with symptoms of polyuria and polydipsia due to impaired urinary concentrating ability. The disease has different manifestations in the neonatal period and childhood.[5,6] There are two types of DI: central DI (CDI), which occurs due to deficiency of antidiuretic hormone (ADH), and nephrogenic DI (NDI), which is due to inadequate response to ADH.[5] It is important to differentiate between the two types of diabetes insipidus as both conditions have different treatment plans.[7]

Diagnosing DI in premature infants is challenging because newborns cannot express thirst, and signs of irritability may go unnoticed. Therefore, the most crucial indicator of DI in infants is excessive urination. Moreover, severe fluid loss leading to dehydration is often difficult to clinically detect in preterm infants and can result in shock.[8] Though neonatal DI is infrequent, it should be contemplated in scenarios involving resistant hypernatremia coupled with fever, polyuria, and shock. Maintaining a vigilant mindset is essential to facilitate early detection. Furthermore, it is crucial to note that diabetes insipidus (DI) can exhibit transient characteristics.[9]

Nephrogenic DI (NDI) is of two types: congenital and acquired. About 90-95% of inherited NDI is X-linked and caused by V2 receptor gene mutation.

However, 5-10% of congenital NDI cases have aquaporin-2 gene mutations with autosomal dominant/recessive inheritance.[10,11] Acquired (secondary) NDI results from drug toxicity, electrolyte imbalances such as hypercalcemia or hypocalcemia, and renal tubular/medullary damage. Congenital NDI treatment includes adequate fluid intake and diuretics, while secondary NDI is managed by treating the underlying condition.[7]

In patients with congenital NDI, symptoms usually appear in infancy and include excessive urination, fluid intake, hypernatremia, hyperthermia, irritability, and poor weight gain.[10,11] Repeated episodes of dehydration in early life can lead to developmental delays and intellectual impairment, although this has become less common with improved fluid management. Enuresis (bedwetting) is also common due to the large urine volumes. Excessive water consumption often leads to reduced appetite and poor food intake, resulting in growth abnormalities. Social problems like hyperactivity and short-term memory issues may also be observed.[12] In contrast, patients with acquired (secondary) NDI typically present later in life, primarily with hypernatremia and polyuria. Developmental delay and social abnormalities are less common in this group.

This case emphasizes the importance of early identification and management of neonatal diabetes insipidus, especially in preterm infants, highlighting the challenges in diagnosis and the need for prompt recognition of key symptoms. It underscores the significance of distinguishing between central and nephrogenic DI for tailored treatment and addresses the potential long-term implications of untreated DI, advocating for comprehensive care and vigilant monitoring to optimize outcomes.

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Authors' contribution

NA: Study design, methodology development, data collection, and manuscript writing.
SA: Literature review, referencing, and overall quality assurance of the manuscript.
SH: Proposed topic and guidance in conceptual development.

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.