Cardiology in the Young

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A late diagnosis of Pseudohypoaldosteronism type I in an infant with hypoplastic left heart syndrome presenting with failure to thrive

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Brief Report

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Abstract

Pseudohypoaldosteronism type I is caused by a peripheral resistance to aldosterone and can present with electrolyte abnormalities, poor growth, or dehydration. Although a rare disease, several case reports have been published regarding Pseudohypoaldosteronism type I in neonates and infants. We report a case of failure to thrive and hyponatremia in an infant with hypoplastic left heart syndrome who was subsequently found to have Pseudohypoaldosteronism type I.

Background

Pseudohypoaldosteronism type I is caused by a peripheral resistance to aldosterone and can present with electrolyte abnormalities, poor growth, or dehydration.[1] Although a rare disease, several case reports have been published regarding Pseudohypoaldosteronism type I in neonates and infants.[1–5] However, to our knowledge, no cases have been reported in neonates or infants with CHD. We report a case of failure to thrive and hyponatraemia in an infant with hypoplastic left heart syndrome who was subsequently found to have Pseudohypoaldosteronism type I.

Case

A Hispanic female with prenatally diagnosed hypoplastic left heart syndrome (mitral atresia, aortic atresia) had undergone a Norwood procedure with Sano shunt at 5 days of age. Her postoperative course was notable for oropharyngeal dysphagia and poor weight gain despite caloric fortification of feeds. After hospital discharge, she was followed closely by our institution's home surveillance monitoring programme which included daily weight and oxygen saturation measurements. Despite parent adherence to the formula mixing instructions and prescribed feeding schedule, she struggled with weight gain, averaging only 17 g per day following hospital discharge (Fig 1).

At 2 months of age, she was re-admitted to the hospital for further evaluation of poor weight gain, emesis, diarrhoea, and decreased oxygen saturation levels. The echocardiogram on re-admission revealed moderate tricuspid regurgitation, mildly decreased right ventricular function, and anatomic suggestion of distal shunt narrowing (all stable from prior studies). The comprehensive metabolic panel revealed hyponatraemia with sodium of 123 mmol/L, hyperkalaemia with potassium of 6.6 mmol/L, acidaemia with bicarbonate level of 18 mmol/L, mildly elevated blood urea nitrogen of 20 mg/dl, and creatinine of 0.5 mg/dl. She was initially observed without any changes to her home feeding or medication regimens to determine whether issues such as gastrointestinal losses or incorrect formula mixing were responsible for her laboratory abnormalities. On day two of hospitalisation, she was noted to appear ill and given persistent electrolyte derangements (sodium of 124 mmol/L, potassium of 6.8 mmol/L, and bicarbonate level of 18 mmol/L); she was transferred to the Cardiac Intensive Care Unit. Paediatric Nephrology was consulted given the concern for possible adrenal insufficiency, renal tubular acidosis, or disturbances in the aldosterone pathway. On the third day of hospitalisation, she was started on sodium chloride supplementation. Her aldosterone level was found to be elevated at 2384 ng/dl (normal range 7–99 ng/dl) and her cortisol level was in normal range at 146 mcg/dl, consistent with Pseudohypoaldosteronism type I. Her sodium levels normalised, and the acidaemia resolved with titration of sodium chloride supplementation (Table 1). She was discharged home on hospital day 16 on 1 g tablet of sodium chloride supplementation twice daily. Since discharge, her weight gain has improved significantly and underwent an uneventful bidirectional Glenn operation.

Table 1. Electrolyte trends during interstage hospitalisation

Electrolytes	DOH #1	DOH #2	DOH #3	DOH #4	DOH #5	DOH #7	Normal range
Sodium (mmol/L)	123	124	133	133	133	140	135–145
Potassium (mmol/L)	6.6	6.8	4.4	3.7	4.4	3.7	3.5–5.1
Chloride (mmol/L)	91	93	101	100	101	107	98–108
Bicarbonate (mmol/L)	18	19	22	23	24	23	20–28
Calcium (mg/dl)	10.6	10.7	9.9	9.7	9.8	9.2	8.5–11
Blood urea nitrogen (mg/dl)	20	14	6	4	4	4	3.4–16.8
Creatinine (mg/dl)	0.5	0.3	0.3	0.3	0.3	0.3	0.2–0.6

DOH, day of hospitalisation.

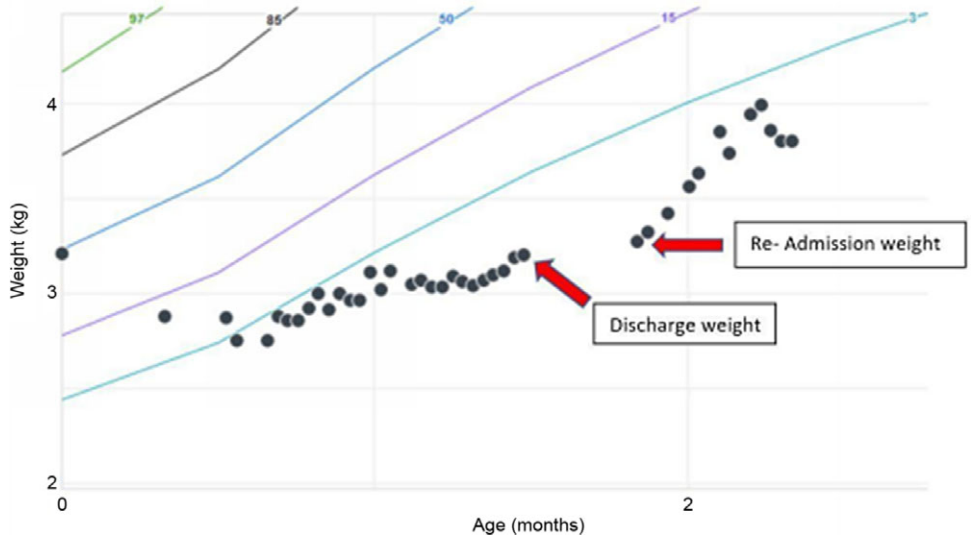

Figure 1. Growth curve from birth to 2.5 months of age. Source: World Health Organization (2006).

Discussion

Pseudohypoaldosteronism type I is caused by a resistance to aldosterone at the end organ level and can present with electrolyte changes, poor growth, and/or dehydration.[1] Patients typically present in infancy with dehydration, failure to thrive, salt-wasting, hypotension, hyperkalaemia, and metabolic acidosis despite increased aldosterone levels.[2] Initial presentation can often be mistaken for congenital adrenal hyperplasia given similar electrolyte derangements of hyponatraemia, hyperkalaemia, and acidosis; however, differentiation is critical as Pseudohypoaldosteronism type I does not respond to corticosteroids and should be suspected with lack of improvement with treatment.[1] Laboratory workup should include serum aldosterone levels to exclude congenital adrenal hyperplasia as well as renin level, spot urine sodium and potassium levels.[1]

Multiple forms of Pseudohypoaldosteronism type I exist which are distinguished by severity, genes involved, and inheritance pattern. The renal form is more common and typically milder in presentation, following an autosomal dominant inheritance pattern with mutation involving the mineralocorticoid receptor resulting in the inability of aldosterone to bind to the receptor. The systemic form can have a more severe presentation and is inherited in an autosomal recessive pattern. This mutation causes a defective sodium transport channel affecting the lung, kidney, colon, sweat, and salivary gland.[3] Treatment of Pseudohypoaldosteronism type I includes rehydration, replacement of sodium, and when indicated, treatment of hyperkalaemia and acidosis. Most patients improve with sodium supplementation and resume normal growth.[6] Genetic testing has been considered in our patient but has not yet been pursued.

While common presentations of Pseudohypoaldosteronism type I include neonatal growth failure and hyponatraemia,[3] the diagnosis may be opaque in infants who have undergone the Norwood operation given the underlying increased risk for both conditions. Growth failure is a well described, common morbidity in infants who have undergone the Norwood operation due to multiple possible aetiologies including increased metabolic rate, catabolic state related to surgical stress, cyanosis, genetic syndromes, gastrointestinal complications, and oral-motor dysfunction which may influence feeding and nutrition.[7] Hyponatraemia is also common in this population due to the frequent use of diuretics. In retrospect, our patient displayed clinical details that should have raised suspicion for atypical growth failure and hyponatraemia. Despite adequate caloric intake and close weight monitoring with our interstage team, she continued to have poor weight gain. She also did not develop mild contraction alkalosis as is typically seen with loop diuretics and in retrospect had slightly elevated potassium

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levels after her Norwood procedure. Loop diuretic use may have also potentially blunted more severe hyperkalaemia. Failure to recognise these clinical details may have contributed to a delay in diagnosis of Pseudohypoaldosteronism type I.

Conclusion

While hyponatraemia and failure to thrive are common problems in infants with complex CHD, a broad differential diagnosis should be considered. Although Pseudohypoaldosteronism type I is a rare disease, it should be included in the differential diagnosis for hyponatraemia and failure to thrive when other concurrent features such as unexplained hyperkalaemia and metabolic acidosis persist and other more common aetiologies such as poor cardiac output have been thoroughly evaluated. While this was likely a coincidental association, Pseudohypoaldosteronism type I could potentially be underrecognised in infants with complex CHD as electrolyte derangements and poor weight gain are often attributed to medication use and underlying cardiac physiology.

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Conflicts of interest. None.

References

1. Saravanapandian N, Paul S, Matthai J. Pseudohypoaldosteronism type 1: a rare cause of severe dyselectrolytemia and cardiovascular collapse in neonates. J Clin Neonatol 2012; 1: 224–226.
2. Bangash AS, Ali NF, Sami S, Iqbal M. Pseudohypoaldosteronism type-I: a rare cause of hyperkalemia in neonates. J Pak Med Assoc 2014; 64: 484–486.
3. Amin N, Alvi NS, Barth JH, Field HP, et al. Pseudohypoaldosteronism type 1: clinical features and management in infancy. Endocrinol Diabetes Metab Case Rep 2013; 2013: 130010.
4. De Clerck M, Vande Walle J, Dhont E, Dehoorne J, Keenswijk W. An infant presenting with failure to thrive and hyperkalaemia owing to transient pseudohypoaldosteronism: case report. Paediatr Int Child Health 2018; 38: 277–280.
5. Yakubov R, Ayman A, Kremer AK, van den Akker M. One-month-old girl presenting with pseudohypoaldosteronism leading to the diagnosis of CDK13-related disorder: a case report and review of the literature. J Med Case Rep. 2019; 13: 386.
6. Nur N, Lang C, Hodax JK, Quintos JB. Systemic pseudohypoaldosteronism type i: a case report and review of the literature. Case Rep Pediatr 2017; 2017: 7939854.
7. Hehir DA, Rudd N, Slicker J, et al. Normal interstage growth after the Norwood operation associated with interstage home monitoring. Pediatr Cardiol 2012; 33: 1315–1322.

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