Index of Suspicion in the Nursery

1 Infant with Hypoglycemia and Midline Defects in Heart Failure

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PRESENTATION

A male infant is born at 37 weeks' gestation, with a birthweight of 2,915 g (~6th percentile on the World Health Organization growth curve, Z score = −1.53) to a 22-year-old gravida 5, para 1 woman, who has a history of 4 spontaneous abortions. After an uneventful prenatal course, the neonate is brought to our NICU 16 days after birth because of concern about dysmorphic features, poor feeding tolerance, and respiratory distress. At the transferring institution, he had received nasogastric tube feedings because of intermittent hypoglycemia and desaturations, with episodes of tachypnea during oral feeding attempts. He had been placed on nasal cannula at 13 days after birth because of his worsening respiratory condition. At the time of transfer, his oxygen saturation is good on high-flow nasal cannula and he is tolerating full enteral nasogastric feeds.

Shortly after transfer, the infant's respiratory requirements escalate, including the need for ventilator support for suspected pulmonary hypertension, which improves after initiation of milrinone and nitric oxide, and hypotension requiring fluid resuscitation and pressors. Cardiac echocardiography reveals small-to-moderate-sized secundum atrial septal defect, small-to-moderate-sized patent ductus arteriosus, mild dilation of all 4 chambers, elevated right ventricular pressure, moderate global biventricular hypokinesia, and a shortening fraction of 17% consistent with heart failure. Poor oral intake is initially managed with nasogastric feeds and the infant subsequently undergoes Nissen fundoplication and gastrostomy tube placement at 8 weeks of age.

Physical examination reveals a dysmorphic male infant with dolichocephaly, small malformed ears with a crumpled helix and triangular concha, absent uvula, left-sided iris coloboma, bilateral fifth-digit clinodactyly, intact palate, right-sided supernumerary nipple, micropenis (7 mm stretched penile length), cryptorchidism, and mild hypotonia (Figs 1–3). There is no family history of genetic disorders. Chromosomal microarray (CMA) and CHD7 testing are performed.

Newborn screening reveals low thyroxine (T_4), which triggers further endocrine studies. Given the low T_4 concentration, initial episodes of hypoglycemia at the referring institution, microphallus, and absent uvula, magnetic resonance imaging of the brain is performed, which is revealing. Other laboratory findings include normal random human growth hormone level and failed adrenocorticotropic hormone stimulation test. Testosterone and antimullerian hormone levels are low. He is started on treatment with hydrocortisone, somatropin, and levothyroxine.

He is discharged from the hospital with a gastrostomy tube because of oral motor dysfunction and with multiple medications. Echocardiography before

AUTHOR DISCLOSURE Drs Bhatia, Coon, and Huff have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

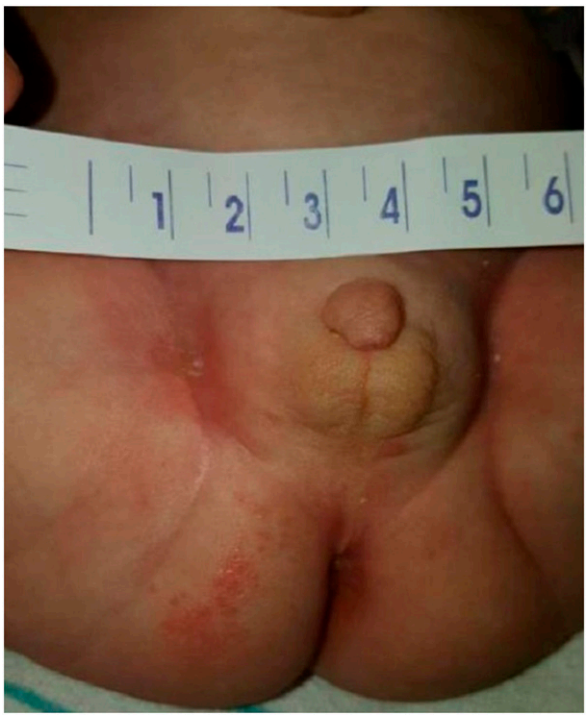

Figure 1. Micropenis measuring 7 mm stretched penile length.

discharge reveals biventricular hypertrophy and a dilated, globular left ventricle. He fails his hearing screen at discharge.

DISCUSSION

We present an interesting case of clinical CHARGE syndrome (coloboma, heart defects, choanal atresia, growth restriction, genital abnormalities, and ear abnormalities) with negative results on CHD7 testing. CMA revealed 15q24 microdeletion. Microdeletion of chromosome 15q24 is a rare condition that was first described less than 20 years ago. It has reportedly been associated with growth restriction, intellectual disability, and distinct facial features, as well as congenital malformations. (1)

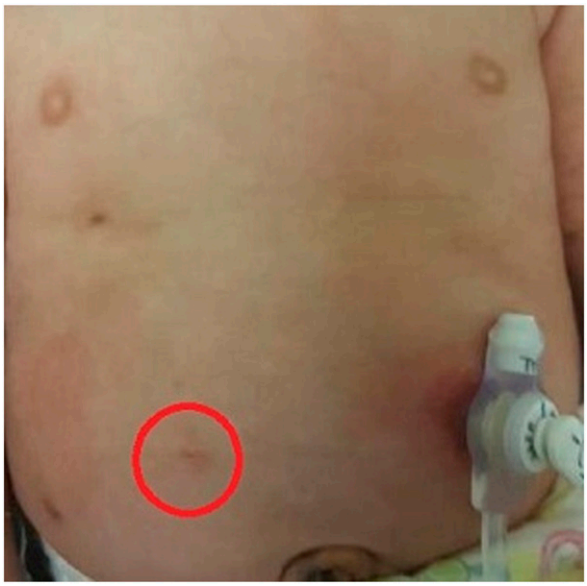

Figure 2. Supernumerary nipple over abdomen.

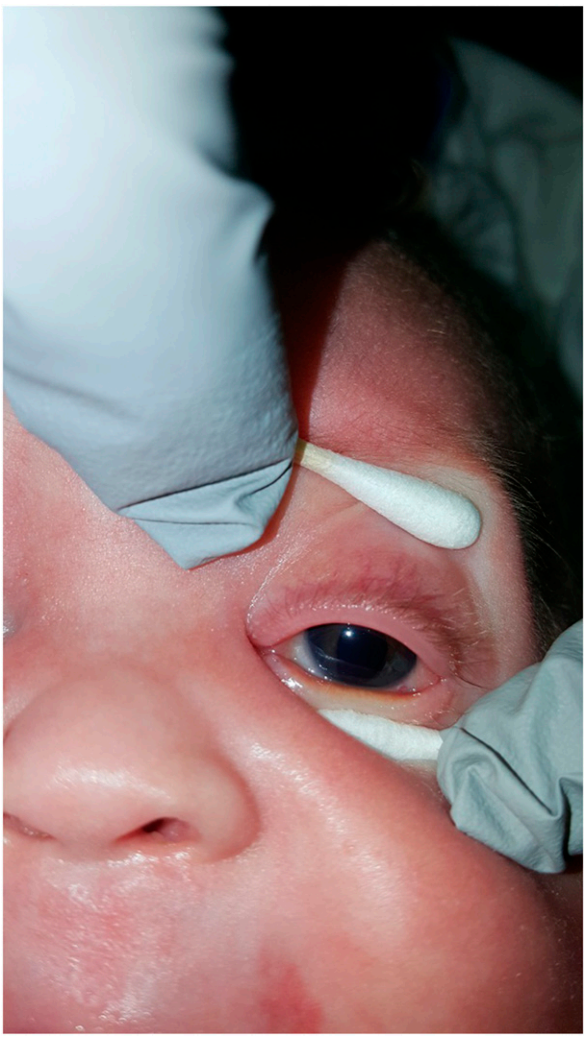

Figure 3. Left eye coloboma.

The features associated with this microdeletion are similar to those seen in other well-described conditions such as 22q11.2 deletion, Noonan syndrome, and Prader-Willi syndrome, which are in the differential diagnosis.

We describe a novel presentation of 15q24 deletion associated with cardiomyopathy and hypopituitarism. The phenotypic spectrum of 15q24 is limited by the few reported cases in the literature. To our knowledge, 15q24 deletion has been associated with structural cardiac anomalies such as

tetralogy of Fallot and ventricular septal defects. (2) This case represents possible myocardial dysfunction associated with deletion of this gene sequence, leading to cardiac failure requiring vasopressor support in the first few weeks after birth.

The infant in this case had a constellation of midline defects that prompted a search for further midline anomalies, which led to the discovery of his hypopituitarism. Neonatal hypopituitarism is usually a delayed diagnosis, which leads to subsequent delay in starting growth hormone. However, in cases such as this, where multiple midline defects occur, it can be useful to perform imaging to determine the presence of pituitary abnormalities and initiate hormone replacement sooner rather than later.

Lessons for the Clinician

- CHARGE syndrome with additional anomalies should warrant further genetic inquiry.
- Cardiomyopathy without significant structural anomalies and hypopituitarism are potentially associated with 15q24 microdeletion.
- It can be useful to perform brain imaging in a patient with multiple midline defects to assess for pituitary abnormalities.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Recognize the diagnostic implications of single vs. multiple anomalies.
- Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for an infant with a condition affecting myocardial performance.

References

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NeoReviews 2020;21;e616
DOI: 10.1542/neo.21-9-e616

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AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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