Case Report

TERM NEONATE WITH RESPIRATORY DISTRESS SYNDROME SECONDARY TO CONGENITAL HYPOTHYROIDISM

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Abstract: Within the first few months of life congenital hypothyroidism presents with the characteristic symptoms of constipation, jaundice, poor feeding, hoarse cry, macroglossia, and hypotonia. These symptoms are rare at delivery, as most neonates are asymptomatic at birth. Therefore, the newborn screens are essential in detecting congenital hypothyroidism, but there are rare cases in which congenital hypothyroidism can be missed or present before the first newborn screens. This paper describes a case of respiratory distress syndrome in a term neonate as the presenting symptom of congenital hypothyroidism. Overall, clinicians should be aware that neonatal respiratory distress can be caused by congenital hypothyroidism, though more common etiologies should be ruled out following stabilization of the patient. Congenital hypothyroidism is an endocrinopathy that may present prior to the onset of symptoms at 3 months or may even present as respiratory distress syndrome prior to the results of the newborn screens. A discussion of this rare case may help physicians in the recognition and treatment of respiratory distress syndrome due to hypothyroidism.

Key words: pediatrics; neonatology; congenital hypothyroidism; respiratory distress syndrome; jaundice; newborn screen

INTRODUCTION Within the first few months of life, congenital hypothyroidism presents with the characteristic symptoms of constipation, jaundice, poor feeding, a hoarse cry, macroglossia, and hypotonia [1,2]. These symptoms are rare immediately upon delivery, as most neonates with congenital hypothyroidism are asymptomatic at birth [3]. Therefore, the standard newborn screens have become essential in detecting congenital hypothyroidism, especially since the condition is a preventable cause of intellectual disability [3]. There are rare cases in which congenital hypothyroidism can be missed or present before the first newborn screen [2]. This paper presents a case of respiratory distress syndrome as the presenting symptom of congenital hypothyroidism.

CASE PRESENTATION A late term male (40 weeks and 3 days gestational age) was born to a gravida 3, para 3 female by repeat cesarean section with maternal complications of obesity, excessive weight gain during pregnancy, and positive Group B Streptococcus (GBS) screen. The mother had a negative screen for gestational diabetes. The birth weight and length were 3800 g (80th percentile) and 51.5 cm (32nd percentile), respectively. The neonate presented with respiratory distress upon delivery with tachypnea (82 breaths per minute) marked by nasal flaring and grunting. Physical exam revealed equal breath sounds bilaterally but with decreased aeration in bases and mild substernal retractions. Following positive pressure ventilation and oxygen in the delivery room, the patient was admitted to the transitional nursery on a nasal cannula but continued to require increasing oxygen. A chest x-ray (CXR) on day of life 1 (DOL1) revealed hypoexpanded lungs with moderate reticulogranularity and streaky perihilar densities (see Figure 1). The patient was transferred to the NICU on continuous nasal positive airway pressure, but capillary blood gases showed respiratory acidosis. As respiratory...
distress progressed, the neonate required rapid sequence endotracheal intubation, synchronized intermittent mandatory ventilation, and surfactant (9.5 mL of intratracheal poractant alfa) (see Figure 2). A peripheral IV was started for fluids and IV antibiotics (380 mg ampicillin, 7.6 mL gentamicin) due to suspicion of GBS sepsis.

On DOL2, blood cultures returned negative and antibiotics were discontinued; the neonate was extubated to a high flow nasal cannula. On DOL4, an echocardiogram was unremarkable other than a small patent foramen ovale. On DOL5, phototherapy was initiated due to elevated bilirubin. On DOL7, a pediatric endocrine consult was called due to continued transient tachypnea, jaundice, and an abnormal newborn screen. Other symptoms included poor suck, hypotonia, and inability to palpate the thyroid. Laboratory studies revealed abnormally increased TSH and decreased T4 and free T4 which was diagnostic of congenital hypothyroidism. On DOL8, the patient started levothyroxine (PO 50 mcg) and was stable on room air. On DOL11, an ultrasound revealed a small but poorly visualized thyroid. By DOL13, continued administration of levothyroxine led to resolution of persistent oxygen requirements, hypotonia, and poor feedings. Following discontinuation of phototherapy on DOL13, the patient was discharged with an outpatient pediatric endocrinology follow-up.

DISCUSSION The etiologies of neonatal respiratory distress can be broadly categorized following birth as: airway obstruction, such as choanal atresia; pulmonary pathologies, such as transient tachypnea of the newborn; and cardiac anomalies, such as congenital heart defects [4]. These are some of the abnormalities that can present at delivery. In contrast, neonatal respiratory distress due to surfactant deficiency is termed respiratory distress syndrome. This is a disease of prematurity or in a term neonate can be seen with maternal diabetes or surfactant component deficiencies. Maternal diabetes leads to fetal hyperinsulinemia opposing the cortisol necessary for proper lung maturation and surfactant production, while prematurity leads to birth with underdeveloped lungs that are unable to produce enough surfactant [4]. This case is unusual in that the neonate presented at birth with respiratory distress syndrome despite being at term and having a nondiabetic mother [4]. In this case the respiratory distress syndrome was due to a lack of surfactant secondary to hypothyroidism. This is a rare presentation of congenital hypothyroidism, and thus may complicate diagnosis for clinicians.

As congenital hypothyroidism is ideally caught early by newborn screenings, the impact of thyroid hormone is best elucidated in neonates who did not receive said screenings. These neonates are typically asymptomatic until they are three months old, presenting with failure to thrive, feeding difficulties, hyperbilirubinemia with jaundice, poor weight gain, and lethargy [5]. Thyroid hormone is known to play a vital role in proper fetal bone and brain development [6].
However, the role that this hormone plays with regards to lung development, alveolar maturation, and surfactant production is still under study [6]. Animal models have shown that hypothyroidism can lead to lung hypoplasia, while other studies have demonstrated a link between thyroid hormone and epithelial cell differentiation in the lung [6]. Interestingly, the NKX2-1 gene (also known as the TTF1 gene), is known to regulate surfactant protein B in epithelial lung cells [7], and a mutation in this gene has been associated with numerous cases of respiratory distress at birth, secondary to hypothyroidism [8]. These exceedingly rare cases are collectively referred to as “brain-lung-thyroid” syndrome as they present with the triad of chooreathetosis, congenital hypothyroidism, and respiratory distress [8]. A 2016 case report discussed one such case involving a term male infant who was eutrophic at birth but developed respiratory distress on DOL6 and required noninvasive ventilation support and oxygen therapy [9]. Genetic studies later determined he had NKX2-1 gene mutations [9]. There have also been reported cases of this triad in patients with intact NKX2-1 genes, and with one case a finding of 14q13.3 deletion that was adjacent to the gene [8]. Other genetic causes of thyroid dysgenesis also include PAX8 and FOXE1, and a disruption of these genes may lead to neonatal hypothyroidism [10]. While consensus guidelines recommend genotyping to assess the cause of hypothyroidism in neonatal patients [11], the NKX2-1 gene was not specifically tested in this case due to lack of availability.

Respiratory distress typically presents as symptoms of increased work of breathing, such as tachypnea or grunting. Other signs of respiratory distress include nasal flaring and retractions [4]. Following appropriate stabilization of the newborn, CXR can be used to determine the etiology of the respiratory distress. In this case, there was low clinical suspicion for respiratory distress syndrome because the newborn was born at term without any maternal history of diabetes. However, the CXR demonstrated hypo-inflation due to a lack of surfactant, which was consistent with the diagnosis of respiratory distress syndrome. In this case, thyroid testing revealed the underlying etiology to be congenital hypothyroidism. In cases such as these, the lack of surfactant will require treatment with both surfactant administration and levothyroxine supplementation. A similar 2009 case report described a term boy born with normal APGAR scores who developed respiratory distress on DOL2, which required a week of positive pressure ventilation and 100% oxygen using a 0.2 L/min nasal cannula. This neonate was diagnosed with congenital hypothyroidism when an x-ray at 3 months performed for respiratory failure revealed interstitial lung disease in addition to a thyroid ultrasound that demonstrated athyreosis [6]. This case is similar to the case presented here, in that the respiratory distress was attributed to congenital hypothyroidism. However, the CXR and surfactant levels were not found to be consistent with respiratory distress syndrome and instead yielded a diagnosis of interstitial lung disease.

Overall, clinicians should be aware of neonatal respiratory distress caused by congenital hypothyroidism, though more common etiologies should be ruled out following stabilization of the patient. Congenital hypothyroidism is an endocrinopathy that may present prior to the onset of symptoms at 3 months or may even present as respiratory distress prior to the results of the newborn screens. Having high clinical suspicion of congenital hypothyroidism in the setting of respiratory distress is crucial, because patients with congenital hypothyroidism require monitoring throughout their lives. If available, genotyping is recommended to determine the etiology of the hypothyroidism. A discussion of this rare case may help physicians in the recognition and treatment of respiratory distress syndrome due to hypothyroidism.

REFERENCES
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