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Case Report

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A rare cause of unimproved respiratory distress syndrome in a preterm infant: congenital hypothyroidism

Mustafa Gürkan, Ümit Ayşe Tandırcıoğlu, Serdar Alan
Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkiye

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Corresponding Author: Ümit Ayşe Tandırcıoğlu, aysetandrcoglu@gmail.com

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ABSTRACT

In our country, congenital hypothyroidism (CH) is screened in all centres' within the scope of the national screening program. Because early diagnosis and treatment of CH prevents not only mental retardation but also the lots of morbidities. The findings of respiratory distress syndrome (RDS) and thyroid dysfunction of prematurity have a bidirectional relationship. Here we discuss the regression of RDS findings in a preterm infant with CH with hypothyroidism treatment. A 910 g female infant, born at 28 weeks' gestation from the twin pregnancy of a 27-year-old mother, was admitted to the neonatal intensive care unit (NICU) with a diagnosis of prematurity and RDS. The RDS resolved with treatment in the infant's first days. On postnatal day 7, the newborn's respiratory symptoms worsened and RDS symptoms developed again. Respiratory distress syndrome signs and symptoms did not improve despite treatment until CH was detected on postnatal day 14 and thyroid replacement therapy (levotiroksin [L-T4]) was initiated. Thyroid function improved with L-T4 treatment and the unexplained RDS findings improved without the need for additional treatment within 48 hours of L-T4 treatment.

Keywords: Respiratory distress syndrome, congenital hypothyroidism, thyroid replacement

INTRODUCTION

Thyroid hormone abnormalities in preterm infants can have several causes, including transient or permanent congenital hypothyroidism (CH), transient hypothyroxinemia of prematurity and transient hyperthyrotropinemia.[1] The findings of respiratory distress syndrome (RDS) and thyroid dysfunction of prematurity have a bidirectional relationship.[1-3] Previous studies have shown that free thyroxine (fT4) remains low during the first 5 days of life in late preterm and term infants with RDS.[1] However, it is also known that hypothyroxinemia of prematurity is associated with pulmonary dysfunction (particularly surfactant deficiency).[2]

Here we discuss the regression of RDS findings in a preterm infant with CH with hypothyroidism treatment.

CASE

A 910 g female infant, born at 28 weeks' gestation from the twin pregnancy of a 27-year-old mother, was admitted to the neonatal intensive care unit (NICU) with a diagnosis of prematurity and RDS. The infant, who received surfactant treatment for RDS on the first day of life, was referred to our hospital because of persistent respiratory distress on the 6th day of life. The history at the previous centre showed that he was extubated after surfactant treatment, his oxygen requirement decreased to 21%, but tachypnea and retractions resumed on day 5 and his oxygen requirement increased. During follow-up in our NICU, echocardiography revealed first-degree tricuspid regurgitation and mild pericardial effusion. Chest radiography showed mild reticulogranular pattern and air bronchograms (Figure 1). The patient was not administered surfactant treatment again.

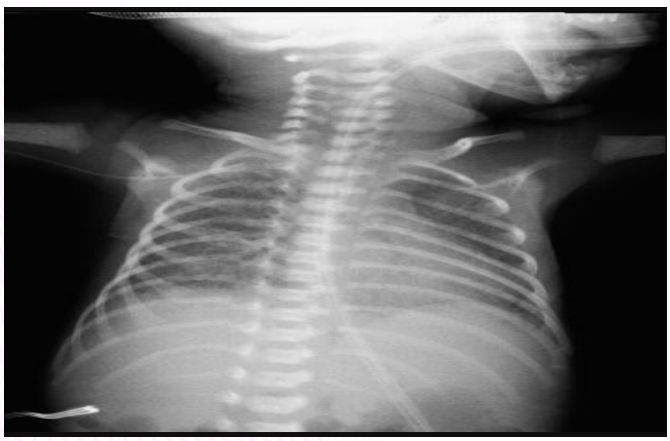

Figure 1. Reticulogranular pattern and air bronchograms

On postnatal 7th day, Thyroid stimulating hormone (TSH): 13.8 uIU/ml (0.7-7.9 uIU/ml) and fT4: 0.83 (0.84-1.76 ng/dl), the reference interval was obtained from literature data according to the gestational age of the infant.[3] On postnatal 14th day, the patient was supported by non-invasive mechanical ventilation (NIV) due to increased tachypnoea and retractions. Acute phase reactants were negative in concurrent investigations. Hemoglobin was 12.9 g/dl. Lung ultrasound showed that diffuse B-lines in the basal and apex of the right lung with no hepatisation. Control TSH value increased to 84.1 uIU/ml and fT4 value decreased to 0.57 ng/dl after seven days. CH was diagnosed and L-T4 treatment was started at a dose of 10 mcg/kg/day. This patient did not improve at the desired rate after all supportive treatments such as appropriate respiratory support, fluid electrolyte support, nutritional support, cardiac support were provided appropriately. The symptoms of respiratory distress resolved within 48 hours after L-T4 treatment without surfactant or antibiotic treatment, and the patient was weaned from NIV.

The radiological findings resolved within 72 hours (**Figure 2**). Thyroid hormone values 1 week later were as follow, TSH: 1.09 uIU/ml (0.27- 4.2), fT4: 2.43 ng/dl (0.93-1.7). The administration of oxygen was discontinued on the 62nd day, and the infant was discharged with L-T4 treatment on the 70th day. The patient, who had reached the expected developmental milestones for his age, is currently 21 months old and continues to receive L-T4 treatment at a dose of 8 mcg/kg/day.

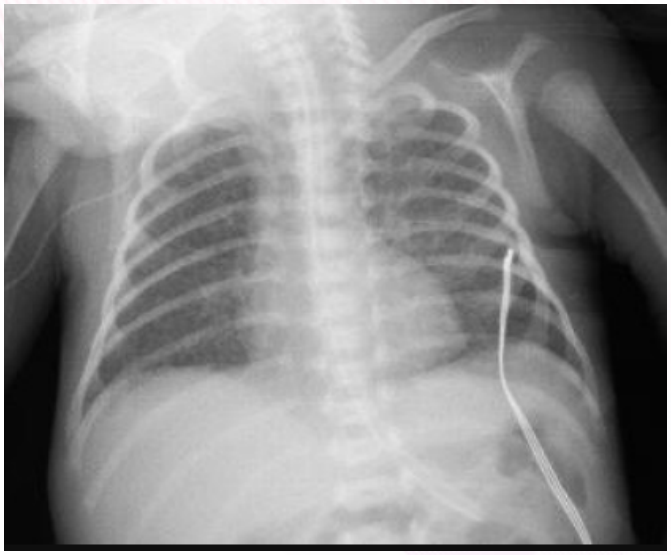

Figure 2. Resolved radiological findings

DISCUSSION

CH is one of the most important endocrine and metabolic causes of mental retardation in the neonatal period if diagnosis or treatment is delayed, and CH is diagnosed in 3500-4000 infants each year and the incidence is even higher in premature infants.[3] Although their underlying pathophysiology is multifactorial, RDS and CH have been shown to have a bidirectional clinical relationship.[1-3]

In a study by Val Abbassi et al. using fetal cord blood, preterm infants with low cord blood free T3 levels were found to be more at risk for RDS. Contrary to our case, the same study reported no difference in fT4 levels.[4]

Some studies have found TSH levels to be relatively higher in preterm infants diagnosed with RDS than in non-RDS preterm infants.[5,6] In a study conducted by Hye Rim Chung et al.[8] in premature infants with similar other characteristics, the rate of RDS was found to be 62% in the group with hypothyroidism, while this rate was found to be 40% in premature infants without hypothyroidism with statistical significance. This supports the improvement of RDS signs of the present case just after L-T4 treatment.

These studies have investigated the relationship between low thyroxine levels and short-term clinical outcomes; however, it is thought that clinical conditions such as disease severity, respiratory distress syndrome, and heart disease may alter thyroid function alone and that low thyroxine levels do not cause or predispose to such adverse outcomes.[7-10] In our case, L-T4 treatment was initiated after CH was detected in a neonate who was followed up for RDS, and the respiratory distress findings resolved within 48 hours.

In addition, a mutation in the NK2 homeobox-1 (NKX2.1) gene encoding thyroid transcription factor-1 (TTF-1), which is important for the morphogenesis and function of the lungs, thyroid, and central nervous system, causes a rare clinic for respiratory failure called brain-lung-thyroid syndrome.[11] In this case, this diagnosis was excluded because no neurological findings were observed.

According to the results of a group of patients consisting of term and late preterm infants in besides the early preterm case we presented, it has been reported that low fT4 levels are associated with increased RDS similar to our case.[12]

CONCLUSION

Our patient with RDS signs that did not improve despite surfactant treatment was diagnosed as CH and RDS signs improved dramatically with L-T4 treatment. CH should be considered in cases of recurrent and/or unresolving RDS in neonates, even if they are premature.

Also, in our country, CH is screened in all centres' within the scope of the national screening program. Because early diagnosis and treatment of CH prevents not only mental retardation but also the lots of morbidities. We would like to emphasize this with this case.

ETHICAL DECLARATIONS

Informed Consent
The patient signed a free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Mustafa Gürkan

I was born on 16.03.1997 in Giresun. I completed my medical education at Kırıkkale University Faculty of Medicine between 2016-2022. I did compulsory service in Giresun for 4 months. In January 2023, I started to work as a research assistant at Kırıkkale University Faculty of Medicine, Department of Child Health Diseases. I started my chief residency in July 2024. I am still continuing my current duty.