A Rare Cause of Interstitial Lung Disease in an Infant Patient: Neuroendocrine Cell Hyperplasia

Tahir Tok1*, Muhammed Burak Selver1, Amet Yasin Guney1 and Sevgi Pekcan2

1Department of Pediatrics, Necmettin Erbakan University, Turkey
2Department of Pediatric Pulmonology, Necmettin Erbakan University, Turkey

Abstract

Infancy Neuroendocrine Cell Hyperplasia (NEHI), previously known as persistent tachypnea in infancy, is a rare lung disease first described in 2005. Etiology is unknown, but genetic mechanisms are said to play a role. NEHI typically occurs in healthy male infants during the first months of life with persistent tachypnea, wheezing and hypoxemia. In addition to these chronic clinical features; hyperinflation as a characteristic chest Computed Tomography (CT) finding, at right middle lobe and medial lingula ground glass opacity findings and lung biopsy findings showing the prominence of bombesin-positive neuroendocrine cells in the distal airways. NEHI can be diagnosed based on High-Resolution CT (HRCT) and clinical findings. Lung biopsy may still be needed if the clinical diagnosis still does not improve. Lung symptoms and hypoxemia tend to improve over time, but may last for years. The actual incidence and prevalence is still unknown. We present a 3-month-old case diagnosed as NEHI by clinical and tomography.

Keywords: Neuroendocrine cell hyperplasia; Interstitial lung disease; Children

Introduction

Infantile Neuroendocrine Cell Hyperplasia (NEHI) is a rare childhood interstitial lung disease, primarily diagnosed in infants and young children. Although etiologic causes have not been fully elucidated, genetic causes are thought to play a role. In the literature, a heterozygous mutation in NKX2-1 (also called thyroid transcription factor 1 [TTF1]) has been described in an individual with four adult family members with a history of NEHI and childhood lung disease [1,2]. Although lung biopsies taken in the pathogenesis of the disease are characterized by prominent pulmonary neuroendocrine cells in the distal airways, it is not yet fully clarified whether these cells are directly involved in the pathogenesis of NEHI or only as a marker of the disease. It shows that there is a relationship between the presence of neuroendocrine cells and the severity of small airway obstruction in NEHI cases [3]. In this case, we present the case of NEHI, a rare interstitial lung disease in children who were brought to the outpatient clinics with recurrent symptoms of respiratory symptoms such as wheezing, tachypnea, and cyanosis.

Case Presentation

Three month old girl is sick. She had complaints of cough, wheezing and rapid breathing from birth. She was admitted to the pediatric thoracic outpatient clinic because of increased complaints. Her wheezing never improved, and her rapid breathing increased compared to her previous state. Her medical history, 3720 g was born. It was learned that there was no hospitalization in the intensive care unit but there were many hospitalizations due to respiratory distress. There was no trait in the family history. In physical examination; Height: 56 cm 25 to 50 p, weight: 6.5 kg 75 to 90 p, pulse 130/min, respiratory rate 63/min, and blood pressure 100/75 mmHg and oxygen saturation were measured as 89%. The respiratory sounds of the patient were bilateral and equal. There was wheezing. There was subcostal suprasternal withdrawal. There was wheezing. The other system examination was normal. ECHO was normal. There was no pulmonary hypertension. Hb: 14.1 g/dL, white blood cell: 11600/mm3, platelet: 377.000/mm3, sedimentation: 13 mm/h, C-reactive protein: 4.7 mg/L, pH 7.41 in blood gas, PaCO2 32.65 mmHg, PaO2 in laboratory tests: 104 mmHg, HCO3: 23 mmHg. Skin prick test was negative. F2 milk specific IgE was negative. The TORCH panel was negative. Complete urinalysis, normal stool examination and microscopy were normal. Immunoglobulin values were normal for age. Phagocytic system burst test was...
normal. Ferritin and B₁₂ came normal. Anti-Hbs: 12.1 arrived. The presence of patchy areas and infiltrations on postero-anterior and lateral chest radiographs (Figure 1A and 1B) and thoracic computed tomography revealed patchy areas on the upper lobes, right middle lobe and lingula medial, ground-glass appearance, and air traps (Figure 2A and 2B). The patient was admitted to the pediatric chest diseases department with a preliminary diagnosis of interstitial lung disease. Free flow oxygen and inhaler anti-biotherapy were started. Oxygen saturation was 93% to 94% during the follow-up and only oxygen was needed at night. The respiratory rate was 40/min. NKX2-1, SFTPC genes analysis is normal.

Discussion

Interstitial Lung Disease (chILD) in children is a heterogeneous group of diseases that may pose a clinical challenge to pediatric pulmonologists. Among these, infantile Neuroendocrine Cell Hyperplasia (NEHI) is a common lung disease that is common in the first years of life and resolves spontaneously over time [4]. The clinical findings of NEHI are indistinguishable from other interstitial lung diseases, so they are diagnosed by accurate and non-invasive method because of the typical radiological appearance in chest Computed Tomography (CT) without lung biopsy. Bombesin staining is pathognomonic in diagnosis. NEHI is commonly associated with iStent ‘persistent tachypnea of infancy’. NEHI has been associated with surfactant disorders (NKX2-1, SFTPC) or other familial forms or ILD. NEHI is an interstitial disease of infancy, characterized by tachypnea from the first months of life, with a good prognosis and a rational diagnostic approach critical for a particular early diagnosis. Initially, clinical suspicions can be confirmed with reasonable accuracy by a CT scan of the chest. NEHI, first recognized in 2005, is a common childhood lung disease of unknown etiology. NEHI relates to distal airway hyperplasia of neuroendocrine epithelial cells that produce vasoactive substances, particularly bombesin. NEHI typically affects infants born at birth and presenting with nonspecific symptoms such as tachypnea, retraction, hypoxemia, and wheezing from the first months to the first few years [5]. Although it is a relatively rare disease, the prevalence and incidence of NEHI is unknown. NEHI is a rare disease, but rarely reported familial cases suggest that it may have a genetic component. However, no mutations have been identified to date [6]. The long-term outcome is generally positive. Clinical response to corticosteroids is rare. In the diagnosis of NEHI, anteroposterior and lateral chest radiographs and thorax computed tomography are used, but definitive diagnosis is made by bombesin staining in lung biopsy. The most appropriate CT method is the volumetric scan if the inspiratory phase is followed by thin-section high-resolution CT in the expiratory phase. It is also necessary to evaluate the contrast agent pulmonary vascular structures. Computed tomography of the thorax shows the appearance of patches in the upper lobes, right middle lobe and medial lingula, ground glass opacities and air jails. The basis of treatment is symptomatic treatment. Most of the cases resolve spontaneously. Many causes of tachypnea, dyspnea and hypoxia in infancy during and after respiratory system and infancy [7]. As a result, NEHI should be brought to mind by the pediatricians among the various causes of acute respiratory failure in children. In case of persistence and failure of hypoxia and tachypnea in a normal term newborn, childhood interstitial lung diseases and NEHI which has a better course should be kept in mind. If the patient with child is thought to have a good clinical presentation and normal growth, biopsy may not be necessary even if the tomographic findings are abnormal. The need for oxygen is considered by some centers as biopsy needs. In our patient, we did not perform a biopsy because the oxygen requirement did not remain outside the attacks of infection over time.
References


