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Case Report

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Neuroendocrine Cell Hyperplasia of Infancy (NEHI Syndrome) in an Immunocompetent Infant

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Abstract

Neuroendocrine cell hyperplasia of infancy (NEHISyndrome)is a rare lung disease that typically presents in otherwise healthy infants during the first months to year of life with persistent tachypnea, crackles and hypoxemia. Patients may present after apparent viral upper respiratory infections but in most cases the respiratory symptoms predate the acute illness. Other infants present because of failure to thrive.We report the atypical presentation of NEHI Syndrome in an immunocompetent 3-month-old Caucasian male.

Keywords: NEHI Syndrome; Respiratoryinfections

Introduction

Neuroendocrine cell hyperplasia of infancy (NEHI), previously known as persistent tachypnea of infancy, is a rare lung disease first described in 2005. The etiology is unknown but genetic mechanisms may play a role. A heterozygous mutation in NKX2-1 (also called thyroid transcription factor 1 [TTF1]) was identified in an individual with confirmed NEHI as well as 4 adult's family members with history of childhood lung disease.[1].

NEHI presents in otherwise healthy infants with chronic tachypnea and retractions, with tachypnea being the most consistently reported clinical feature. Chronic subglottic, intercostal and subcostal retractions are also common symptoms. On physical examination, inspiratory crackles are the most prominent finding but are not universally present [2]. Other common findings is chest wall deformity with increased anteroposterior diameter of the chest and wheezing[3].

Many infants with NEHI have difficulty gaining weight or failure to thrive. A decline in growth trajectory has been reported to precede diagnosis of NEHI. Gastroesophageal reflux is a common comorbid condition [4]. We report a case of a 3-month-old immunocompetent caucasian male diagnosed with NEHI syndrome.

Case report

A 3-month-old male presented to the emergency department (ED) following a short episode of pallor and flaccidity. The patient has a significant past medical history for intra-uterine growth r estriction(IUGR),bronchopulmonary dysplasia(BPD), oxygen dependent, laryngomalacia, gastroesophageal reflux disease (GERD), cow's milk protein allergy (CMPA), and failure to thrive (FTT). At presentation parents reported cough, congestion and decreased oral intake over two days.A head CT scan was performed demonstrating no acute intracranial anomalies. EKG showed no abnormalities and CXR revealed bronchovascular interstitial thickening compatible with reactive airways disease.

Laboratory workup included CBC and BMP, which were both within normal limits.In the course of the patient's ED stay, he presented two cyanotic episodes with the first one accompanied by flaccidity and O2 saturation between 60-70% on room air, which resolved with sternal rub. He was given Ativan for suspected seizure-like activity and started on 2L through nasal cannula. The

patient was transferred to another Pediatric ICU for neurology evaluation.

On admission, vital signs were within normal limits. A respiratory viral panel was performed, which was positive for coronavirus.oxygen saturation dropped to 70% and he was placed on 1L through nasal cannula. EEG was normal and CT angiography showed an aberrant right subclavian artery without airway narrowing and perihilar infiltrates. During the fourth day of hospital stay, the patient presented two episodes of desaturations down to 30% and was placed on NPO, IV fluids, caffeine and ND tube for feeds later repositioned to NG. A PSG was done, reporting no central apneas or OSA events. On the seventh day of hospital stay, one apnea episode presented requiring positive pressure ventilation.

The patient's regular O2 settings were reinstalled at the twelfth day of hospital stay and after two days, he was transferred to the pediatrics floor. However, on day eighteenth, he presented another drop in O_2 saturation down to 30% and was taken to the PICU. Over four days O2 requirements increased to 2L and he developed runny, yellow stools.

After 30 days of hospital stay, the patient was transferred to a facility specialized in aerodigestive disorders.An immunologic workup was done showing normal results. An outpatient CT scan of the thorax revealed bilateral perihilar interstitial infiltrates and perihilar and upper lobe ground-glass changes.

Discussion

Childhood interstitial lung disease (chILD) is a heterogeneous group of rare disorders characterized by abnormal imaging findings, impaired gas exchange; and is associated with substantial morbidity and mortality. Neuroendocrine cell hyperplasia (NEHI) is a unique sub-group, which is more prevalent in infants and children younger than 2 years of age, and typically manifests with chronic tachypnea, retractions, hypoxemia and failure to thrive

The classic presentation of chronic tachypnea and retractions of insidious onset in the first few months of lifeare not always exhibited. For infants beyond the neonatal period with interstitial lung disease (ILD) with hypothyroidism and/or neurologic abnormalities (e.g. hypotonia or choreoathetosis) or those with severe disease, a family history of ILD, it is recommended to get genetic testing for NKX2.1 (i.e., TTF-1) mutations or deletions.All patients with diffuse lung disease (DLD) should also be evaluated for immunodeficiency because infections can cause DLD [5].

The first step in evaluating an infant with chronic tachypnea is to exclude more common causes of the symptoms such as acute or chronic infection asthma, immunodeficiency, cystic fibrosis, and congenital heart disease. In infants with NEHI, chest radiographs may be normal or reveal hyperinflation and perihilar opacities, which are findings also consistent with viral infection[3, 6, 7].

Screening for immunodeficiency as well as evaluation of acid base status to exclude metabolic acidosis as a cause of tachypnea is recommended. Thyroid function testing should also be considered, particularly in infants with low muscle tone or failure to thrive because of the possible association of ILD with hypothyroidism in infants with mutations in the NKX2-1 (thyroid transcription factor 1).HRCT findings in infants with NEHI and distinctive and specific and can be used to establish a confident diagnosis without lung biopsy in the appropriate clinical context. Findings include well demarcate geographic ground glass opacities centrally and in the right middle lobe and lingula. Air trapping is often demonstrated when expiratory images are performed. [8, 9].

Bronchoscopy does not specifically diagnose NEHI, cytologic analysis of fluid from bronchoalveolar lavage in NEHI patients is generally macrophage predominant, without an excess of neutrophils or lymphocytes.Lung biopsy (via video assisted thoracoscopic surgery [VATS]) is the gold standard for NEHI diagnosis, although it is increasingly accepted to make the diagnosis based on typical findings in chest HRCT rather than lung biopsy. [10] The primary histopathologic abnormality in NEHI is increased neuroendocrine cells, which are identified based on immunopositivity to bombesin and serotonin [7].

The mainstay of treatment is largely supportive and preventive care. Supplemental oxygen has been required for the vast majority of cases. Treatment of comorbidities such as gastroesophageal reflux is recommended [3, 7, 11].

Respiratory symptoms and hypoxemia generally improve over the course of years.No deaths or need for lung transplantation have been reported. CT abnormalities may persist for years in some cases [7, 4].

The present case highlights the importance of considering NEHI Syndromeas the cause of pulmonary disease in a patient with marked hypoxemia and nonspecific findings on chest imaging studies even in the absence of documented immunodeficiency.

References

1. Nevel RJ, Garnett ET, Worrell JA, Morton RL, Nogee LM, et al. (2016) PersistentLungDisease in Adultswith NKX2.1 Mutation and FamilialNeuroendocrineCellHyperplasia of Infancy. Ann Am ThoracSoc 13:1299.
2. O'Connor MG, Wurth M, Young LR (2015) RareBecomes More Common: RecognizingNeuroendocrineCellHyperplasia of Infancy in EverydayPulmonaryConsultations. Ann Am ThoracSoc 12:1730-1732.
3. Gomes VC, Silva MC, MaiaFilho JH, Daltro P, Ramos SG, et al. (2013) Diagnosticcriteria and follow-up in neuroendocrinecellhyperplasia of infancy: a case series.J BrasPneumol 39:569-578.
4. Nevel RJ, Garnett ET, Schaudies DA, Young LR (2018) Growthtrajectories and oxygen use in neuroendocrinecellhyperplasia of infancy. PediatrPulmonol 53:656.
5. Kurland G, Deterding RR, Hagood JS, Young LR, Brody AS, et al. (2013) Anofficial American ThoracicSocietyclinicalpracticeguideline: classification, evaluation, and management of childhoodinterstitial lungdisease in infancy.American ThoracicSocietyCommitteeonChildhoodInterstitialLungDisease (chILD) and thechILDResearch Network. Am J RespirCritCareMed. 188:376-394.
6. Lukkarinen H, Pelkonen A, Lohi J, Malmström K, Malmberg LP, et al. (2013) Neuroendocrinecellhyperplasia of infancy: a prospectivefollow-up of ninechildren.ArchDisChild 98:141-144.
7. Deterding RR, Pye C, Fan LL, Langston C (2005) Persistenttachypnea of infancyisassociatedwithneuroendocrinecellhyperplasia.PediatrPulmonol 40:157-165.

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8. Young LR, Deutsch GH, Bokulic RE, Brody AS, Nogee LM (2013) A mutation in TTF1/NKX2.1 isassociatedwithfamilialneuroendocrinecell-hyperplasia of infancy.Chest 144:1199-206.

9. Brody AS, Guillerman RP, Hay TC, Wagner BD, Young LR, et al. (2010) Neuroendocrinecellhyperplasia of infancy: diagnosis withhigh-resolution CT. AJR Am J Roentgenol194:238.

10. Popler J, Wagner BD, Tarro HL, Accurso FJ, Deterding RR (2013) Bronchoalveolarlavage fluid cytokineprofiles in neuroendocrinecellhyperplasia of infancy and follicularbronchiolitis.Orphanet J RareDis8:175.

11. Hayes D Jr, Wilson KC, Krivchenia K, Hawkins SMM, Balfour-Lynn IM, et al. (2019) Home OxygenTherapyforChildren. AnOfficial American ThoracicSocietyClinicalPracticeGuideline.Am J RespirCritCareMed 199:e5.

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