CASE REPORT

Neuroendocrine hyperplasia of infancy; a rare form of childhood interstitial lung disease: a case report

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Abstract

Interstitial lung disease in infancy is rare. In this case report, we discuss the case of a six-week-old male infant who presented with persistent tachypnoea, retraction and mild hypoxaemia corrected by low-dose supplemental oxygen since the age of 2 weeks. Birth history was unremarkable. Routine workup was done which turned out to be non-contributory. The child received multiple rounds of antibiotics along with bronchodilators and corticosteroids. There was no evidence of severe gastroesophageal reflux. Computed tomography of chest showed ground glass appearance, which was especially prominent in the right middle lobe and lingula ,and accompanied with air trapping. He was managed with mild respiratory supportive care, without positive pressure ventilation and nutritional management. He was discharged home, with instructions for in clinic follow up. A distinctive topographical picture and typical clinical symptoms were consistent with neuroendocrine hyperplasia of infancy (NEHI), which has a favourable prognosis. A high index of suspicion may enable a timely diagnosis. Adequate long-term respiratory and nutritional management without lung biopsy improves the outcome

Keywords: Interstitial Lung Disease, Childhood, Respiratory distress, Infants, computerized tomograpghy.

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Introduction

Diffuse lung disease or Interstitial Lung disease (ILD) in children is rare, with a reported prevalence range of 0.13 to 16.2 / 100,000 children[1]. ILD in infants (younger than 2 years age) is quite distinct from ILD in older children and adults. American Thoracic Society (ATS) published a new classification of ILDs in infants for evaluation, treatment, monitoring and prognosis[2,3]. Neuroendocrine Hyperplasia of Infancy (NEHI) is a rare form of ILD in infants, which was first described in 2005 by Deterding et al.[4]. It was previously described by the same author as "Persistent Tachypnoea of Infancy", based on clinical features of persistent tachypnoea, retraction and hypoxaemia. A histological diagnosis, based on lung biopsy, revealed near-normal morphology with standard stain and positive bombesin stain. This confirmed the presence of increased neuroendocrine cells in distal airways[2]. We report a case of an infant presenting with prolonged respiratory distress with hypoxaemia and failure to thrive, who then underwent radiologic evaluation. High Resolution of Chest Tomography (HRCT) supported the diagnosis of NEHI. However, given the paucity of such a rare disease, we present a review of the literature and discuss this case with regard to the current diagnosis and management strategies . Our aim is to raise awareness among physicians and help in diagnosing and treating such cases.

Case Report

A 6-week old, male infant was referred for persistent respiratory problems of retraction, tachypnoea and hypoxaemia for almost four weeks, along with failure to gain weight due to decreased oral feeding to Paediatric High Dependency Unit of Liaquat National Hospital and Medical College, Karachi in April 2022. The birth history was uneventful with no early neonatal complications. He had then been discharged home on breast-feeding, with anticipatory guidance for newborn care. At age of 2 weeks, he developed cough and laboured breathing. He was admitted in NICU, with a possible diagnosis of acute lower respiratory tract infection. All diagnostic work-up [complete blood count, nasal secretion for respiratory viral panel including COVID -19 PCR, ABG, blood cultures echocardiography and multiple chest X-rays] were done and were non-contributory, except mild hypoxaemia (PaO2 38 mm of Hg) on arterial blood gas [Normal value of PaO2 60-100 mm Hg]. His condition remained stable on minimal oxygen support (1 liter/min oxygen by nasal prong). Finally, HRCT was done and revealed "Diffuse ground glass appearance". He was admitted in April, 2022 to the Paediatric High Dependency Unit of Laiquat National Hospital, Karachi with tachypnoea

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(55 breaths / min), mild subcostal recessions, and hypoxaemia (85% on room air) which resolved on 1.0 l/min oxygen by nasal prongs. There was no wheezing but few crackles were heard on chest auscultation. The rest of the clinical examination was unremarkable. He had no vomiting or significant regurgitation but there was difficulty in feeding- most likely attributed to respiratory symptoms. Chest X-ray showed mild hyperinflation, with few perihilar streaks. HRCT was discussed with radiologist, who confirmed ground glass opacities- especially prominent in right middle lobe and lingula- and significant air trapping on film. There were similar findings on the repeat HRCT (Figure). This case was discussed with an international paediatric pulmonologist. NEHI was diagnosed based on the presence of a combination of classical clinical and tomographic findings. The infant's parents were counselled about this diagnosis having a good favourable outcome and need of long-term supplemental oxygen and adequate nutritional support. Consequently, they agreed to continue the care plan. The infant was discharged home with the above mentioned plan. On his one-month follow-up, there was an overall clinical improvement, . He was more active and had a social smile. His respiratory symptoms improved significantly and is now receiving only 0.5lit/min on oxygen by nasal prongs, through oxygen concentrator, and is experiencing appropriate weight gain.

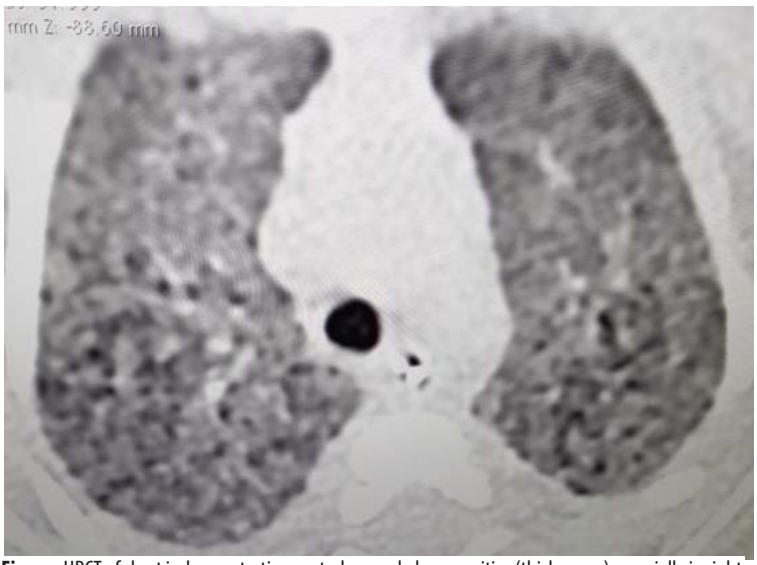

Figure: HRCT of chest is demonstrating central ground glass opacities (thick arrow) especially in right middle lobe and lingula as well as multiple hyper lucent areas (thin arrow) indicating air trapping.

Discussion

Our case report is a typical case of NEHI, as described in the cohorts of American and European patients[4,5]. However, the interstitial lung disease is rare in infancy. In the last decade, NEHI is the most common form of ILD in infants in the published medical literature[6]. The exact aetiology and pathogenesis of this illness is not known. However, it is presumed that it reflects pulmonary immaturity, evident by presence of neuroendocrine cells (NEC) in the distal airway. It is more common in the male gender;with the most common presenting age being 3-6 months; and is triggered by acute respiratory tract infection, followed by prolonged mild to moderate respiratory distress and failure to thrive-which is common[2]. However, our patient presented earlier than the mean age of presentation. Recently, Liptzin et al described a composite score of clinical features to make a clinical diagnosis of NEHI and 93% of patients had NEHI clinical score of ≥7/10 (95% CI, 0.86 - 0.97) in their multicentre cohort of NEHI cases[5]. Our patient also had a NEHI clinical score of 7 with early presentation. HRCT has an important role in the diagnosis of NEHI in children in a report of imaging from a multicentre study. The geographical ground glass opacities, involving more than four lobes, especially in the right middle lobe and lingula, as well as presence ofmosaic pattern of air trapping are pathognomonic for NEHI. This can be useful in differentiating NEHI from other types of ILDs in children. It is considered as a potential novel imaging biomarker of NEHI[7]. ATS guidelines support the clinical diagnosis of NEHI based on the constellation of clinical-tomographic features in such infants, and obviate the need of invasive procedures[2]. The major limitation of this case report is the lack of longitudinal follow-up.

The favourable prognosis of this disease is based on the long-term positive outcome with the patient eventually being symptom-free by the age of 2-3 years,as reported in a few longitudinal follow-up studies[8]. However, most of the infants (70%) had failure to thrive due to decreased intake, secondary to respiratory distress in the initial phase of illness, like in our case[9]. The adequate nutritional support, with supplemental oxygen, for optimal calorie intake due to high requirements and respiratory support to minimize working of breathing with correction of hypoxaemia gradually improves the clinical condition respectively.

Conclusion

A high index of suspicion in an infant with prolonged respiratory signs and symptoms with characteristics

tomographic findings without need of invasive procedures support the clinical diagnosis of NeuroEndocrine Hyperplasia of Infancy.

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Parent's Consent: Father gave the written consent for publishing this case.

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Conflict of Interest: None.

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