Challenge Cases

Tachypnea Since Birth with Worsening Cough in a Term Female

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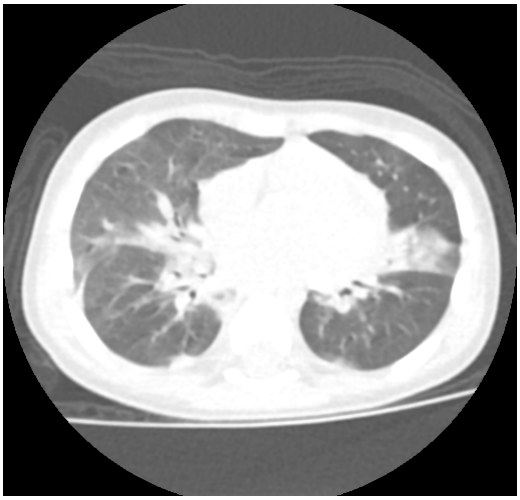
A 6-month-old term female is brought to the emergency department due to one day of cough that prevented her from sleeping. On history, family notes that she has been tachypneic since birth with respiratory rates 60s – 80s, but they have been reassured by her pediatrician that this may be normal. She underwent treatment for community—acquired pneumonia four weeks prior to admission but has not had other bacterial infections. She is up to date on her immunizations. She had one fever recorded by family in the past week, for which she received acetaminophen. She recently started in daycare. She has generally gained weight well since birth, although her pediatrician has had some concerns in the past several weeks. Parents note that she sometimes coughs with feeds. She has previously been seen in Pulmonology clinic, where she had a negative sweat chloride test and was started on a trial of albuterol without significant benefit.

In the emergency department, vital signs include temperature 97.8, pulse 147, respiratory rate 55, BP 86/39, and saturations 86% on room air in all extremities. Weight is 6.71kg, which is the 20th percentile for her age. Her exam is within normal limits except for diffuse crackles throughout all lung fields, tachypnea, and mild subcostal retractions. Her chest x-ray demonstrates a normal cardiomediastinal silhouette and peribronchial thickening; echocardiogram revealed normal anatomy. Pharyngeal function study revealed transient and mild laryngeal penetration with formula. She underwent high-resolution chest CT, with results shown below.



Q: What Do You Do Next?

A. Initiate short course of oral steroids and scheduled albuterol.

B. Arrange for supplemental oxygen at home.

C. Begin antibiotics for community—acquired pneumonia.

D. Empirically thicken formula feeds with rice cereal.

Answer: B

Discussion

The patient's history of tachypnea since birth with diffuse crackles on exam is concerning for interstitial lung disease, a collective term for multiple rare disorders characterized by diffusely altered lung structure, especially in the interstitial region.[1] Several of these disorders present nonspecifically with tachypnea, retractions, crackles, cough, hypoxemia, and failure to thrive in infancy. The differential diagnosis usually includes cystic fibrosis, congenital heart disease, immunodeficiency, chronic aspiration, pulmonary infection, and primary ciliary dyskinesia, which must be ruled out. While the gold standard for diagnosis of interstitial lung disease is lung biopsy, this patient's CT findings are concerning for a specific diagnosis, neuroendocrine cell hyperplasia of infancy (NEHI). Classic findings on CT include ground-glass opacification, predominantly in the right middle lobe and lingual, and air trapping; CT is reported to be at least 78% sensitive and 100% specific for the diagnosis of NEHI.[2] Some cases are thought to be familial,[3] and one genetic mutation associated with familial NEHI has been identified to date.[4] If available, infant pulmonary function testing demonstrating airflow obstruction and air trapping can also suggest a diagnosis of NEHI.[5] To further support the diagnosis in this case, our patient underwent genetic testing for other interstitial lung diseases, which were negative, and flexible bronchoscopy with ciliary biopsy, which revealed normal ciliary morphology.

There are limited data on the treatment of interstitial lung disease, and management is largely supportive. Supplemental oxygen is necessary for patients with hypoxemia; some patients may also require ventilatory or nutritional support. Two small longitudinal cohort studies of patients with NEHI demonstrated clinical improvement over time, with complete disease resolution in some patients.[6,7] The pathogenesis remains unclear. Lung biopsy reveals a proliferation of neuroendocrine cells in otherwise normal lung architecture without significant inflammation. Although a subset of infants with NEHI goes on to develop asthma in follow-up, treatment with corticosteroids during infancy did not affect the duration or severity of their respiratory symptoms.[7]

Although these conditions are rare, interstitial lung disease should be considered in any infant presenting with tachypnea, retractions, and hypoxemia, especially when symptoms have been present since birth. High-resolution CT scan can be diagnostic in certain conditions and may help avoid unnecessary invasive testing and therapeutics.

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References

1. Kuo CS and Young LR. "Interstitial lung disease in children." Curr Opin Pediatr 2014;26(3):320-327.
2. Brody AS, Guillerman RP, Hay TC, Wagner BD, Young LR, Deutsch GH, Fan LL, Deterding RR. "Neuroendocrine cell hyperplasia of infancy: diagnosis with high-resolution CT." AJR Am J Roentgenol. 2010;194(1):238-244.
3. Popler J, Gower WA, Mogayzel PJ, Nogee LM, Langston C, Wilson AC, Hay TC, Deterding RR. "Familial Neuroendocrine Cell Hyperplasia of Infancy." Pediatr Pulmonol. 2010;45;749-755.
4. Young LR, Deutsch GH, Bokulic RE, Brody AS, Nogee LM. "A mutation in TTF1/NKX2.1 is associated with familial neuroendocrine cell hyperplasia of infancy." Chest. 2013;144(4):1199-1206.
5. Kerby GS, Wagner BD, Popler J, Hay TC, Kopecky C, Wilcox SL, Quinones RR, Giller RH, Accurso FJ, Deterding RR."Abnormal infant pulmonary function in young children with neuroendocrine cell hyperplasia of infancy." Pediatr Pulmonol. 2013;48:1008-1015.
6. Gomes VCC, Silva MCC, Filho JHM, Daltro P, Ramos SG, Brody AS, Marchiori E. "Diagnostic criteria and follow-up in neuroendocrine cell hyperplasia of infancy: a case series." J Bras Pneumol. 2013;39(5):569-578.
7. Lukkarinen H, Pelkonen A, Lohi J, Malmstrom K, Malmberg LP, Kajosaari M, Lindahl H, Fohr A, Ruuskanen O, Makela MJ. "Neuroendocrine cell hyperplasia of infancy: a prospective follow-up of nine children." Arch Dis Child. 2013;98:141-144.