Review Article

Can Post-Infectious Bronchiolitis Obliterans (PIBO) be Misdiagnosed as Persistent Pneumonia?

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Abstract

Post-infectious bronchiolitis obliterans (PIBO) is a rare but severe chronic airway disease in children. It usually follows a severe viral lower respiratory tract infection in early life. Persistent inflammation and fibrotic remodeling of the small airways lead to narrowing, air trapping, and progressive loss of lung function. In recent years, reports from countries with high childhood infection burdens, particularly in Asia and Western countries, have drawn more attention to this condition. However, PIBO often remains under-recognized because its symptoms resemble asthma or other chronic lung diseases. This review summarizes available evidence on the epidemiology, risk factors, pathogenesis, clinical features, diagnosis, and management of PIBO in children. Literature was reviewed from published pediatric studies and case series across different regions. Several studies highlight hypoxemia and prolonged mechanical ventilation as strong predictors of disease. Recurrent viral infections, bacterial co-infections, and environmental exposures appear to increase vulnerability. The pathogenesis involves epithelial injury with neutrophil-driven inflammation and fibrosis, eventually producing fixed airway obstruction. Clinically, affected children present with a chronic cough, wheeze, tachypnea, and persistent hypoxemia that do not respond to bronchodilators. High-resolution computed tomography (HRCT) is considered the most reliable imaging tool, frequently showing mosaic attenuation, bronchiectasis or air trapping. Lung function testing usually confirms irreversible obstruction. Management remains largely supportive. Systemic corticosteroids, azithromycin, and some immunomodulatory approaches have been tried with variable outcomes. What is clear is that earlier recognition and intervention can help slow progression. More collaborative research is still needed before consistent pediatric guidelines can be developed.

Keywords: Post-Infectious Bronchiolitis Obliterans (PIBO); Misdiagnosed; Persistent Pneumonia.

Introduction

Bronchiolitis Obliterans (BO) is a rare lung disease characterized by inflammation and fibrosis of the small airways. This leads to airway narrowing and obliteration. There are three main types of BO: Post-Infectious Bronchiolitis Obliterans (PIBO), bronchiolitis obliterans post-lung transplantation (Graft Versus Host Disease-GVHD), and post-hematopoietic stem cell transplantation (HSCT).[1]

Postinfectious bronchiolitis obliterans (PIBO) is a permanent obstructive lung condition marked by inflammation beneath the airway lining and fibrotic constriction of the small airways. It typically develops following a lower respiratory tract infection in childhood, particularly in the early years of life.[2]

Globally, the incidence and prevalence of BO vary, with higher rates reported in children in developing countries following viral infections like adenovirus, rhinovirus, measle, RSV, Influenze, parainfluenza, mycoplasma pneumoniae.[3] In Bangladesh, while comprehensive data is scarce, PIBO appears to be an underdiagnosed condition. However, the high burden of respiratory infections in children makes it a condition of growing concern.[4] Although the precise incidence of PIBO in children remains unclear, studies have estimated the prevalence of BO to be 0.6% based on findings from 2,897 autopsies and 244 lung biopsies conducted at a single center, where BO was diagnosed.[5]

Understanding BO is crucial because its chronic nature often leads to long-term respiratory complications and

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reduced quality of life. Early diagnosis and management can potentially prevent disease progression and improve outcomes.[6]

Risk factors

Hypoxemia is considered the most critical risk factor for PIBO, followed by early prolonged mechanical ventilation. Recurrent viral infections, such as adenovirus, respiratory syncytial virus (RSV), and influenza in early childhood, along with bacterial co-infections, further increase the risk. Delayed treatment, exposure to environmental toxins, and immune suppression from chronic illnesses are also contributing factors. The use of glucocorticoids, gamma globulin, a history of recurrent wheezing, and being male may also play a role in PIBO development.[7,8]

Pathogenesis

The pathogenesis of postinfectious bronchiolitis obliterans (PIBO) begins with epithelial damage caused by infections in the lower respiratory tract, such as those from viruses or mycoplasma. This damage triggers the release of interleukin-8 (IL-8) and other inflammatory mediators from epithelial cells, attracting neutrophils and inflammatory cells to the small airways. These cells secrete matrix metalloproteinases (MMPs) and profibrotic cytokines, which degrade the matrix, lead to collagen accumulation, stimulate fibroblast growth, and eventually cause fibrosis around the bronchioles. CD8+ T cells play a key role in continued epithelial damage and chronic inflammation following infection, while Th17 cells promote tissue remodeling by releasing IL-17, which drives IL-8 production and contributes to airway neutrophilia.[9,10]

Clinical feature

Clinical features of PIBO in children include persistent cough, wheezing, and shortness of breath, often unresponsive to bronchodilators. These symptoms may follow a severe lower respiratory tract infection. Other signs include crackles on lung auscultation and hypoxemia, which can progress to chronic lung dysfunction.[11,12]

PIBO typically presents without a history of asthma, with the disease duration ranging from 7 to 31 months. Diagnosis is based on clinical criteria, including symptoms such as persistent tachypnea, cough, wheezing, exercise intolerance, and hypoxemia lasting for over 6 weeks following severe bronchiolitis or pneumonia.[13,14]

Investigation

Chest radiology identifies abnormalities in 92% of PIBO cases, typically displaying signs such as hyperinflation, patchy ground-glass opacities, bronchial wall thickening, atelectasis, and bronchiectasis. In contrast, High-Resolution Computed Tomography (HRCT) reveals abnormalities in 100% of cases, including patchy ground-glass densities, mosaic and vascular attenuation, air trapping, bronchial wall thickening, bronchiectasis, and mucus plugging. These detailed imaging characteristics position HRCT as the most reliable diagnostic tool for detecting PIBO providing greater diagnostic accuracy than conventional chest X-rays.[15,16]

Lung function tests in PIBO patients typically reveal characteristic patterns. Spirometry often shows a fixed obstructive flow-volume curve, with reduced forced expiratory volume (FEV1), a lower Tiffeneau index (FEV1/VC), and decreased end-expiratory flow (MEF25). Body plethysmography indicates hyperinflation and air trapping, evidenced by an elevated residual volume (RV) and an increased functional residual capacity (RV/TLC). These findings reflect irreversible airway obstruction commonly seen in PIBO, making such tests crucial for diagnosing and assessing disease severity in affected individuals.[1,2,3]

Spirometry primarily evaluates obstruction in the larger airways but is generally less sensitive in detecting small airway obstruction. For better assessment of small airway conditions, such as in cystic fibrosis, primary ciliary dyskinesia, and chronic obstructive pulmonary disease, the Multiple Breath Washout test can be employed if available. In pediatric patients, the Forced Oscillation Technique (FOT) offers an advantage over spirometry, as it does not require complex respiratory maneuvers. Instead, small amplitude pressure oscillations are applied during normal breathing, making it a more suitable option for assessing lung function in children.[17,18,19]

When resources permit, the Multiple Breath Washout test can be utilized to pinpoint small airway issues commonly seen in conditions like cystic fibrosis, primary ciliary dyskinesia, and chronic obstructive pulmonary disease[20,21]. For children, the Forced Oscillation Technique (FOT) offers a significant advantage over traditional s pirometry, as it does not necessitate specific respiratory maneuvers. Instead, it employs small amplitude pressure oscillations during normal breathing, making it easier and more effective for evaluating lung function in pediatric patients.

Treatment

Bronchoscopy combined with bronchoalveolar lavage (BAL) is widely accepted as a necessary procedure to exclude ongoing infections caused by viral, fungal, or bacterial agents prior to initiating systemic anti-inflammatory therapy. This approach ensures that any underlying infections are identified and addressed, optimizing treatment outcomes and preventing complications associated with inappropriate anti-inflammatory use.[22]

As Post Infectious Bronchiolitis Obliterans (PIBO) is an uncommon, chronic, and irreversible obstructive lung condition, treatment approaches remain somewhat undefined and vary in different medical centers. Generally, management of PIBO involves a combination of optimal supportive care and anti-inflammatory therapies aimed at inhibiting lymphocyte activation and proliferation. Addressing inflammation is crucial, as it significantly contributes to the disease process and can impact overall lung function and patient quality of life. This multifaceted treatment strategy is essential for improving outcomes and managing symptoms in individuals affected by PIBO.[23]

Conclusion

In conclusion, Post Infectious Bronchiolitis Obliterans (PIBO) is a significant cause of chronic respiratory distress in children, often following severe viral infections. It should be suspected in cases where symptoms such as persistent cough, wheezing, tachypnea, and hypoxemia persist for more than six weeks post-infection, unresponsive to conventional treatments. Exclusion of other conditions such as asthma, tuberculosis, cystic fibrosis, primary immunodeficiency, and primary ciliary dyskinesia is essential for diagnosis. Early recognition and appropriate management of PIBO are crucial for preventing long-term lung damage and improving patient outcomes.

Radiological imaging, particularly Chest X-ray (CXR) and High-Resolution Computed Tomography (HRCT), plays a crucial role in diagnosing Post-Infectious Bronchiolitis Obliterans (PIBO). These imaging modalities reveal key features such as hyperinflation, ground-glass opacities, bronchial wall thickening, mosaic attenuation, air trapping, bronchiectasis, and mucus plugging. HRCT is especially valuable in detecting the extent of lung damage and differentiating PIBO from other chronic lung conditions. Early and accurate radiological assessment is essential for guiding treatment and managing the long-term consequences of PIBO effectively.

Supportive treatment for Post-Infectious Bronchiolitis Obliterans (PIBO) includes supplemental oxygen therapy for hypoxemia, nutritional support to maintain growth, immunizations against influenza and pneumonia, and airway clearance techniques to manage mucus plugging. Anti-inflammatory treatments play a key role and may involve systemic corticosteroids, azithromycin, and combination therapy like FAM (Furosemide, Azithromycin, Methylprednisolone). Immunoglobulin substitution and steroid-sparing agents are also considered in select cases to reduce inflammation and improve lung function. These interventions aim to alleviate symptoms, prevent complications, and enhance long-term respiratory outcomes in PIBO patients.

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