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Case report

Pediatric bronchiolitis obliterans after Stevens-Johnson syndrome: A multidisciplinary case report

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Abstract. Bronchiolitis obliterans (BO) is a rare and severe obstructive pulmonary disease marked by irreversible small airway fibrosis. In pediatric populations, BO secondary to Stevens-Johnson syndrome (SJS) poses significant diagnostic and therapeutic challenges due to overlapping symptoms with asthma. This case report describes a 5-year-old boy who developed BO following SJS triggered by antiepileptic medication and meropenem. Initial treatment targeting asthma proved ineffective, leading to further investigations. High-resolution computed tomography (HRCT) revealed mosaic attenuation patterns, and bronchoscopy showed white plaques and subcutaneous emphysema, confirming BO. Multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii infections exacerbated airway damage, complicating management. Despite a multidisciplinary approach with anti-inflammatory therapy, antibiotics, oxygen support, and nutritional interventions, the patient ultimately succumbed to respiratory failure. This case highlights the importance of early recognition, advanced imaging, and collaborative management in BO, particularly in resource-limited settings. It underscores the need for standardized diagnostic protocols and tailored therapeutic strategies to improve outcomes in similar cases. (www.actabiomedica.it)

Key words: bronchiolitis obliterans, stevens-johnson syndrome, pediatrics, case reports, diagnosis

Introduction

Bronchiolitis obliterans (BO), a rare and severe chronic obstructive pulmonary disease, is characterized by irreversible small airway fibrosis caused by inflammation. First described in 1901, BO presents significant diagnostic and therapeutic challenges, especially in pediatric populations. Despite its rarity, BO imposes substantial clinical and economic burdens, emphasizing the need for improved diagnostic and management strategies. Commonly associated with post-infectious etiologies or transplant rejection, BO can also result from Stevens-Johnson syndrome (SJS), a severe mucocutaneous reaction often triggered by drugs or infections (1). The global incidence of BO in the pediatric population is estimated to range from 1.5 to 3.6 per 100,000 children. However, the prevalence of BO secondary to SJS remains extremely rare, with only a limited number of cases documented in the literature. This rarity contributes to the diagnostic delay and therapeutic uncertainty, particularly in children presenting with overlapping respiratory symptoms. SJS-related BO is a rare but critical complication resulting from respiratory epithelial injury and fibrotic remodeling. Pediatric BO cases associated with SJS are often misdiagnosed as asthma due to overlapping symptoms, including persistent wheezing and hypoxemia. However, BO's chronic and progressive nature

typically results in poorer outcomes (2). The pathogenesis involves immune dysregulation, with pro-inflammatory cytokines like IL-6 and TNF-α playing key roles in fibrotic progression. Secondary infections, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, exacerbate this condition (3). High-resolution computed tomography (HRCT) and bronchoscopy are critical diagnostic tools, although invasive lung biopsy remains the gold standard. Emerging imaging modalities, including dual-energy CT, offer promise for non-invasive diagnosis, especially in resource-limited settings. This case report highlights the challenges of diagnosing and managing BO secondary to SJS in a 5-year-old boy, emphasizing early recognition, multidisciplinary management, and long-term follow-up. We present this case due to its clinical rarity, diagnostic complexity, and its potential implication on improving prognosis through early identification and targeted intervention. The findings underline the importance of tailored approaches for rare pediatric diseases and the need for standardized protocols to improve outcomes and reduce disease burden (4).

Case report

A 5-year-old boy was admitted with progressive respiratory distress, recurrent wheezing, and persistent cough following a previous hospitalization for SJS. The SJS episode was triggered by an adverse reaction to phenytoin and meropenem, leading to febrile seizures and severe systemic symptoms. The initial presentation included high fever, malaise, and a diffuse erythematous maculopapular rash, which rapidly progressed to extensive epidermal detachment. The patient exhibited widespread mucocutaneous lesions with hemorrhagic crusting, severe conjunctivitis with ocular discharge, painful oral ulcerations, and erosions involving the nasopharyngeal and genital mucosa. The necrotic epidermal detachment covered more than 10% of the body surface, and the patient experienced significant skin pain prior to the appearance of cutaneous lesions. The patient was managed in the pediatric intensive care unit (PICU) for 14 days. Invasive mechanical ventilation was required for 10 days, followed by 4 days of non-invasive ventilation (NIV) as respiratory symptoms persisted despite resolution of acute mucocutaneous lesions. During this phase, the patient received oxygen via high-flow nasal cannula (HFNC) and supportive care for systemic inflammation and sepsis. Upon admission to the respiratory unit, the patient exhibited severe respiratory distress characterized by tachypnea, wheezing, nasal flaring, subcostal retractions, and oxygen desaturation (SpO2 < 90%) despite HFNC oxygen support. Physical examination revealed subcutaneous emphysema extending from the thoracic region to the neck and upper abdomen, suggestive of air trapping and alveolar rupture. Fixed airway obstruction was suspected based on persistent wheezing unresponsive to bronchodilators and consistent auscultation findings. Spirometry could not be performed due to the patient's critical clinical condition. Laboratory tests at admission showed anemia (Hb 10.6 g/dL), thrombocytosis (663,000/mm^3), and mild electrolyte imbalances including hyponatremia (Na 133 mmol/L), hypokalemia (K 3.4 mmol/L), and hypochloremia (Cl 88 mmol/L). Blood gas analysis demonstrated pH 7.37, pCO_2 67 mmHg, pO_2 29 mmHg, HCO_3^- 38.7 mmol/L, base excess 13.4, and oxygen saturation 96%, indicating mixed respiratory and metabolic derangement. These findings supported the need for escalation in respiratory support.

Initial chest CT scans showed tracheal wall defects and pneumomediastinum without evidence of bronchiectasis (Figure 1). Bronchoscopy findings included white plaques resembling stomatitis in the distal intermediate lobe of the right lung and secondary carina, with slightly edematous but non-hyperemic mucosa and no visible tracheal defects (Figure 2). Histological examination of bronchoalveolar lavage fluid (BALF) confirmed the presence of multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii, both contributing to epithelial injury and fibrotic remodeling. A second HRCT scan was performed on day 17 of hospitalization due to ongoing hypoxemia and worsening subcutaneous emphysema. The imaging showed mosaic attenuation patterns and air trapping, consistent with BO (Figure 3). These findings, combined with the lack of clinical response to asthma treatment, confirmed the diagnosis of BO. The patient

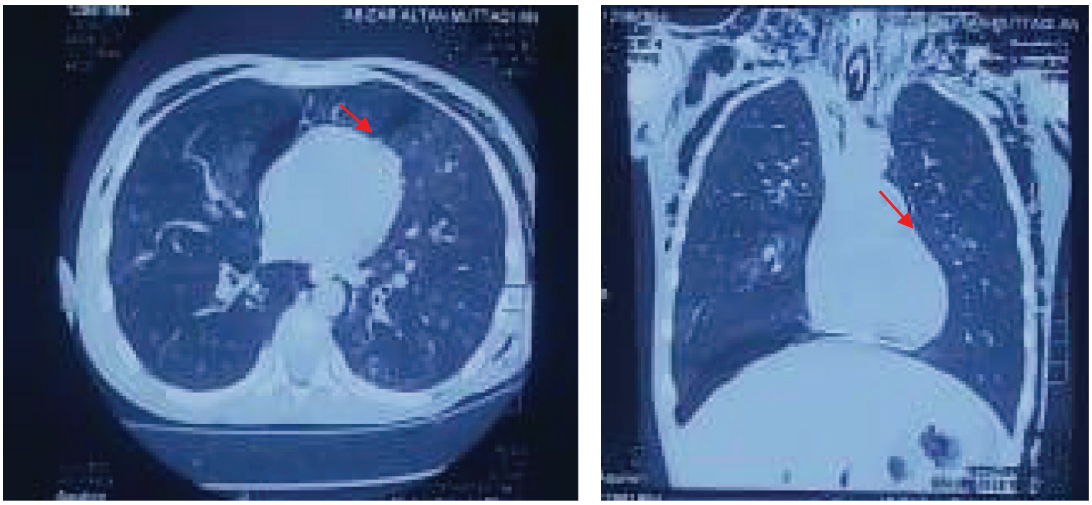

Figure 1. The Chest CT Scan of patient; (left) transverse plane; (right) coronal plane. Arrows indicate pneumomediastinum and tracheal wall discontinuity.

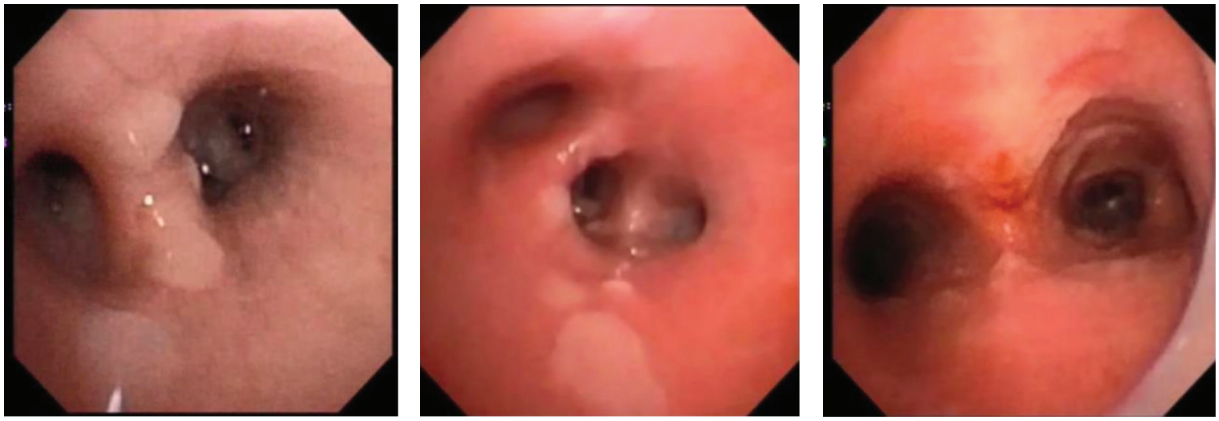

Figure 2. Bronchoscopy. (left). Lower Lobe of Right Bronchus. (middle). Tr. Intermedius. (right). Carina.

received systemic corticosteroids (intravenous dexamethasone, 9 mg loading dose followed by 3 mg every 8 hours for three days), nebulized salbutamol 2.5 mg every 6 hours, ipratropium bromide every 6 hours, and budesonide 500 mcg every 8 hours. Although meropenem had previously triggered SJS in this patient, it was cautiously reintroduced in combination with amikacin (15 mg/kg/day IV) and ciprofloxacin (10 mg/kg/dose every 12 hours IV), based on sensitivity testing and the life-threatening nature of the infections. All antibiotics were monitored for adverse reactions and adjusted according to serial cultures and clinical status. Nutritional support was initiated due to moderate malnutrition (BMI below the 3rd percentile), including total parenteral nutrition (TPN) and a high-calorie enteral diet. Respiratory physiotherapy was provided to enhance mucus clearance and prevent atelectasis. The patient showed intermittent clinical improvement, but oxygen dependence persisted. Despite multidisciplinary care, including pulmonologists, intensivists, infectious disease specialists, and nutritionists, the patient's respiratory condition deteriorated. He was

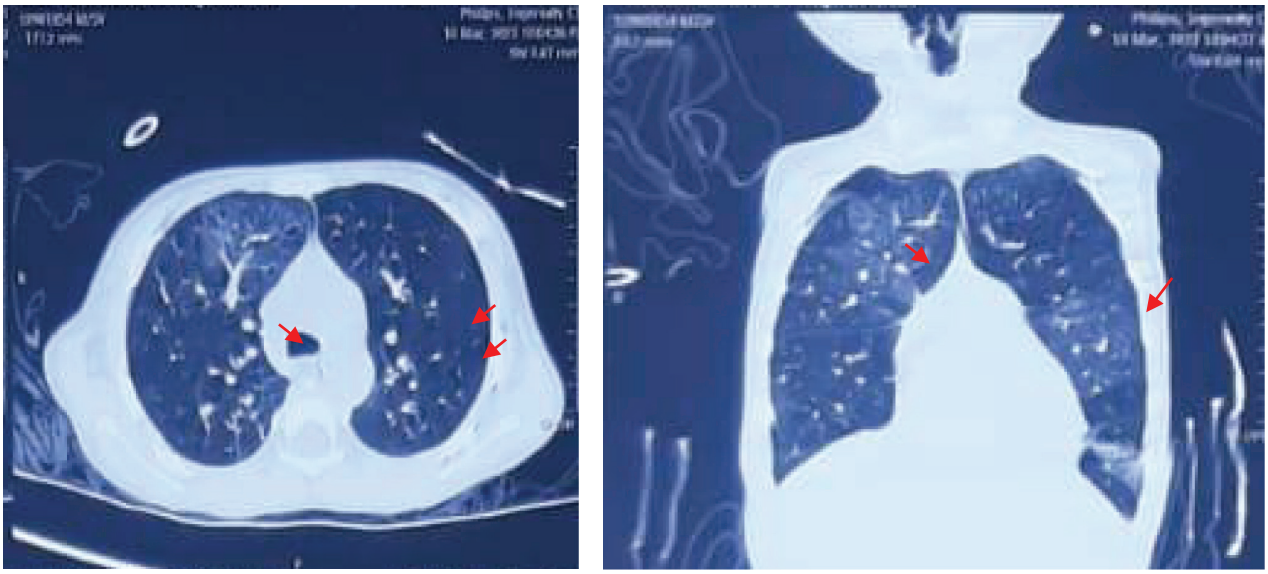

Figure 3. The Chest HRCT of the patient (left) transverse plane; (right) coronal plane. Arrows indicate mosaic attenuation patterns.

discharged on continuous low-flow oxygen therapy but readmitted two weeks later with worsening respiratory distress and severe hypoxemia. The patient ultimately succumbed to respiratory failure on hospital day 31. This case illustrates the diagnostic challenges and poor prognosis associated with BO secondary to SJS in pediatric patients, and emphasizes the importance of early suspicion, timely imaging, and collaborative management in improving outcomes.

Discussion

BO is a rare, severe obstructive pulmonary disease characterized by chronic inflammation and fibrosis of the small airways, leading to irreversible narrowing or obliteration of the bronchiolar lumen. Despite its rarity, BO imposes significant clinical and economic burdens, particularly in pediatric populations, emphasizing the need for improved understanding of its pathogenesis, early detection, and effective therapeutic strategies. Diagnosing and managing BO in children is especially challenging due to overlapping clinical features with asthma and its association with rare conditions like SJS (1,3). The pathogenesis of BO involves an inflammatory cascade triggered by epithelial injury, such as in SJS. In this case, SJS likely initiated airway remodeling, with subsequent infections exacerbating the condition. Pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α are known to mediate fibroblast activation and extracellular matrix deposition, leading to fibrosis. Severe infections with *Pseudomonas aeruginosa* and *Acinetobacter baumannii* further aggravated airway damage through oxidative stress and sustained inflammation (2,4,5). In pediatric patients, BO often mimics asthma, with symptoms like wheezing, dyspnea, and hypoxemia. However, the chronic nature of BO and its lack of response to bronchodilators often serve as critical differentiators. Clinicians should consider BO when there is no clinical improvement after 2–3 weeks of optimized asthma therapy, especially in the presence of atypical features such as persistent oxygen dependence and subcutaneous emphysema. In this case, persistent respiratory symptoms, subcutaneous emphysema, and unresponsiveness to asthma therapy prompted further investigation (6). HRCT played a pivotal role in diagnosis, revealing mosaic attenuation and air trapping, hallmark findings of BO. Bronchoscopy findings of inflammatory plaques supported the diagnosis. However, lung biopsy, the gold

standard for BO diagnosis, was not performed due to its invasiveness and the patient's critical condition. Emerging non-invasive modalities like dual-energy CT and quantitative CT densitometry show promise in improving diagnostic accuracy, particularly in resource-limited settings where lung biopsy may not be feasible (7–9). A key challenge in diagnosing BO is its clinical overlap with asthma. Both conditions present with airway obstruction, but BO involves irreversible obstruction due to fibrosis, unlike the reversible nature of asthma. In this case, the presence of subcutaneous emphysema and the patient's poor response to bronchodilators were red flags indicating an alternative diagnosis. This case emphasizes the importance of early differentiation, not only to avoid unnecessary asthma therapy escalation but also to initiate targeted interventions earlier, potentially preventing irreversible airway remodeling (8,10,11). Management of BO lacks standardized protocols, with care focusing on supportive therapies, controlling inflammation, and addressing underlying conditions. In this case, a multidisciplinary team of pulmonologists, intensivists, and infectious disease specialists played a central role in care. Supportive measures included oxygen therapy to address hypoxemia and respiratory physiotherapy to enhance airway clearance. Nutritional support was prioritized due to increased caloric demands and the patient's malnutrition (8,12). Anti-inflammatory therapies, such as corticosteroids, were used to control airway inflammation. Steroids are most beneficial during the early inflammatory stage of BO, when fibrosis has not yet matured. While corticosteroids may be effective in the early stages of BO, their benefits in advanced cases remain limited, as seen in this patient. In this case, the limited response to corticosteroids may be attributed not only to advanced fibrotic changes but also to the compounding effects of secondary infections, which promoted ongoing inflammation despite immunosuppressive therapy. Azithromycin, a macrolide with anti-inflammatory properties, was considered but complicated by concurrent multidrug-resistant infections. These infections, caused by *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, significantly worsened the patient's condition, requiring aggressive antimicrobial therapy. This underscores the importance of robust infection control measures in hospital settings (11,13–16). The role of multidisciplinary care in this case was integral, enabling comprehensive management of the patient's complex condition. Collaboration among specialists allowed for optimization of ventilatory support, targeted antimicrobial therapies, and diagnostic precision. Shifting the focus from asthma-related treatments to BO-specific management was a critical turning point facilitated by multidisciplinary discussions (3,17). Prognosis in BO is highly variable and influenced by underlying etiology and timing of diagnosis. BO secondary to SJS is often severe, with long-term morbidity due to chronic airway obstruction and remodeling. Delayed diagnosis, repeated intubations, and severe infections with multidrug-resistant pathogens in this case compounded the disease's severity, ultimately resulting in respiratory failure. This highlights the importance of early suspicion in high-risk populations, including children with recent SJS exposure, even when respiratory symptoms mimic common conditions like asthma. Continuous follow-up and vigilant monitoring are essential to address complications and adapt management strategies in such patients (12,18,19). This case highlights the critical importance of early recognition and intervention in high-risk pediatric populations, particularly those with prior severe conditions like SJS. Advanced imaging tools, such as HRCT and bronchoscopy, played a central role in diagnosis, but limitations in early detection remain a significant challenge. Emerging technologies, including dual-energy CT, offer opportunities to refine diagnostic algorithms and reduce reliance on invasive procedures (7,9). This report also illustrates an important clinical limitation: the absence of spirometry and lung biopsy, which are commonly used for diagnostic confirmation of BO. These limitations, dictated by the patient's unstable clinical status, required clinicians to rely heavily on imaging and clinical judgment. Further, the inability to assess reversibility through objective lung function tests restricted the differentiation from severe asthma early in the disease course. Lastly, this case underscores the need for further research into the pathogenesis of BO and the development of standardized diagnostic and therapeutic protocols. Identifying reliable biomarkers and creating

evidence-based guidelines is essential, particularly in resource-limited settings where access to advanced diagnostics is restricted. A streamlined, multidisciplinary approach is critical to improving outcomes and reducing the disease burden of BO (8,20). BO secondary to SJS presents significant diagnostic and therapeutic challenges, particularly in pediatric populations. Early recognition through advanced imaging and a multidisciplinary approach is crucial to improving outcomes. This case underscores the need for vigilant monitoring, personalized management strategies, and the development of standardized protocols to address BO's progressive nature. Comprehensive care and timely interventions are essential to mitigate complications and enhance the quality of life in affected children.

Ethic Approval: This study was approved by Dr. Soetomo General Academic Hospital, and informed consent was obtained from the patient's legal guardian.

Conflict of Interest: The authors declare no conflicts of interest related to this manuscript. There are no commercial associations, including consultancies, stock ownership, equity interests, or patent/licensing arrangements, that could pose a conflict of interest in connection with the submitted article.

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References

1. Carpenter L, Weinman J, Aleksanyan Y, et al. Stevens Johnson syndrome in children: consider monitoring for bronchiolitis obliterans. J Pediatr. 2021. doi: 10.1016/j.jpeds.2021.05.036
2. Seccombe E, Ardern-Jones M, Walker W, et al. Bronchiolitis obliterans as a long-term sequela of Stevens-Johnson syndrome and toxic epidermal necrolysis in children. Clin Exp Dermatol. 2019;44(8):889–902
3. Kavaliunaite E, Aurora P. Diagnosing and managing bronchiolitis obliterans in children. Expert Rev Respir Med. 2019; 13:481–8
4. Façanha ALBP, Reis RC, Prado RCP, et al. Bronchiolitis obliterans due to toxic epidermal necrolysis-a serious condition with a good therapeutic response. J Bras Pneumol. 2021; 47(4):e20210020
5. Chen X, Liu F, Zheng B, et al. Exhausted and apoptotic BALF T cells in proinflammatory airway milieu at acute phase of severe mycoplasma pneumoniae pneumonia in children. Front Immunol. 2022;12:760488
6. Colom AJ, Teper AM. Post-infectious bronchiolitis obliterans. Pediatr Pulmonol. 2019;54(2):212–9
7. Yu X, Ma Y, Gao Y, et al. Epidemiology of adenovirus pneumonia and risk factors for bronchiolitis obliterans in children during an outbreak in Jilin, China. Front Pediatr. 2021;9:722885
8. Chen I, Hsu JS, Chen YW, et al. Post-infectious bronchiolitis obliterans: HRCT, DECT, pulmonary scintigraphy images, and clinical follow-up in eight children. Front Pediatr. 2020;8. doi: 10.3389/fped.2020.622065
9. Lee H, Kim S, Lee JW, et al. Quantitative CT lung densitometry as an obstructive marker for the diagnosis of bronchiolitis obliterans in children. PLoS One. 2022;17. doi: 10.1371/journal.pone.0271135
10. Chung H, Jang Y. Bronchial hyperresponsiveness observed in children with post-infectious bronchiolitis obliterans: a long-term follow-up study. J Allergy Clin Immunol. 2019;143. doi: 10.1016/j.jaci.2018.12.660
11. Fujita Y, Miyamoto K, Imataka G, et al. Post-infectious bronchiolitis obliterans misdiagnosed as bronchial asthma in a pediatric patient. Tohoku J Exp Med. 2021;254(4):257–60
12. Griese M, Kurland G, Niemitz M, et al. Post-infectious bronchiolitis obliterans in children: diagnostic workup and therapeutic options: a workshop report. 2020
13. Mitani K, Hida S, Fujino H, et al. Rare case of Stevens-Johnson syndrome with bronchiolitis obliterans as a chronic complication. BMJ Case Rep. 2022;15(4):e249224
14. Cui Z, Zhou X, Luo F, et al. Worldwide bronchiolitis obliterans research: a bibliometric analysis of the published literature between 2002 and 2022. Medicine (Baltimore). 2023;102(28):e34263
15. Parulekar AD, Kao CC. Detection, classification, and management of rejection after lung transplantation. J Thorac Dis. 2019;11(Suppl 14):S1732
16. Cheng Q, Zhang H, Shang Y, et al. Clinical features and risk factors analysis of bronchitis obliterans due to refractory mycoplasma pneumoniae pneumonia in children: a nomogram prediction model. BMC Infect Dis. 2021;21. doi: 10.1186/s12879-021-06783-4
17. Ghosh S, Deshwal H, Haraf R, et al. Pulmonary manifestations of inflammatory bowel disease and treatment strategies. Chest Pulmonol. 2023;1(3):100018
18. Lee EY. Pediatric interstitial (diffuse) lung disease. In: Cleveland RH, Lee EY, editors. Imaging in pediatric

pulmonology. Cham: Springer International Publishing; 2020. p. 145–97
19. Liu D, Liu J, Zhang L, et al. Risk factors for post-infectious bronchiolitis obliterans in children: a systematic review and meta-analysis. Front Pediatr. 2022;10. doi: 10.3389/fped.2022.881908
20. Wang Z. Role of transforming growth factor-β in airway remodelling in bronchiolitis obliterans. Growth Factors. 2023; 41(4):192–209

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