Case Report / Olgu Sunumu

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# Massive Pulmonary Hemorrhage As A Complication of Intrapleural Streptokinase Therapy

## İntraplevral Streptokinaz Tedavisinin Bir Komplikasyonu Olarak Masif Pulmoner Hemoraji

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## Abstract

Intrapleural streptokinase therapy (IST) is commonly used to manage pediatric parapneumonic effusion. Although considered safe, rare complications, such as pulmonary hemorrhage, have been reported, particularly in high-dose IST administration in patients with coexisting coagulopathy or trauma. We report a case of massive pulmonary hemorrhage following IST in a 14-month-old child with left parapneumonic effusion. He initially presented to the hospital with community-acquired pneumonia, and intravenous antibiotic therapy was initiated. Subsequently, he developed left complex parapneumonic effusion, with worsening respiratory distress requiring non-invasive ventilation. Chest tubes were inserted using the blind method and were complicated by traumatic insertion. Four hours after IST, the patient developed severe respiratory distress with profuse bleeding from the oronasal cavity. He required intubation and was ventilated for four days. There was no coagulopathy. Respiratory support was gradually weaned off, and the patient was discharged well after a six-week course of antibiotics. Healthcare providers should be vigilant regarding the risk of pulmonary hemorrhage, particularly in high-risk patients. Ultrasound-guided chest tube insertion, patient assessment before IST, and close monitoring during and after therapy may help minimize this adverse event. Further research is warranted to better understand the safety profile of IST in children.

**Keywords:** Intrapleural fibrinolytic, pediatric intensive care, pediatric respiratory

## Öz

İntraplevral streptokinaz tedavisi (IST), pediyatrik parapnömonik efüzyonu yönetmek için yaygın olarak kullanılmaktadır. Güvenli olduğu düşünülse de özellikle koagülopati veya travmanın eşlik ettiği hastalarda yüksek doz IST uygulamasında pulmoner hemoraji gibi nadir komplikasyonlar bildirilmiştir. Bu yazıda, sol parapnömonik efüzyonu olan 14 aylık bir çocukta IST'yi takiben gelişen masif pulmoner hemoraji olgusu sunulmuştur. Hasta başlangıçta toplum kökenli pnömoni ile hastaneye başvurdu ve intravenöz antibiyotik tedavisi başlandı. Daha sonra hastada sol kompleks parapnömonik efüzyon gelişti ve solunum sıkıntısı kötüleşerek non-invaziv ventilasyon gerektirdi. Göğüs tüpleri kör yöntem kullanılarak yerleştirildi ve travmatik yerleştirme nedeniyle komplike oldu. IST'den dört saat sonra, hastada oronazal boşluktan bol miktarda kanama ile birlikte ciddi solunum sıkıntısı gelişti. Entübasyon gerekti ve dört gün boyunca ventile edildi. Koagülopati yoktu. Solunum desteği kademeli olarak kesildi ve hasta altı haftalık bir antibiyotik tedavisinin ardından taburcu edildi. Sağlık hizmeti sağlayıcıları, özellikle yüksek riskli hastalarda pulmoner hemoraji riski konusunda dikkatli olmalıdır. Ultrason kılavuzluğunda göğüs tüpü yerleştirilmesi, IST öncesi hastanın değerlendirilmesi ve tedavi sırasında ve sonrasında yakın izlem ile bu advers olay sıklığı en az seviyeye indirilebilir. Çocuklarda IST'nin güvenlik profilini daha iyi anlamak için daha fazla araştırma yapılması gerekmektedir.

**Anahtar Kelimeler:** İntraplevral fibrinolitik, pediyatrik yoğun bakım, pediyatrik solunum

## Introduction

Parapneumonic pleural effusion is a common complication of bacterial pneumonia in children in developing countries.[1] Approximately 25% of these patients develop empyema thoracis.[2] Empyema thoracis is defined as the collection of pus in the pleural cavity.[2] The progression of parapneumonic pleural effusion into empyema thoracis is divided into three stages: Exudative, fibropurulent, and organized.

Despite its significant prevalence, the management of empyema thoracis among children remains challenging for clinicians.[3] Intrapleural fibrinolytic therapy, such as

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streptokinase, urokinase, and alteplase, have been reported to be beneficial for dissolving fibrinous clots, preventing fluid sequestration, and improving drainage of the pleural fluid.[3,4] However, no universal guidelines have been established to provide definitive criteria and optimal timing for intrapleural streptokinase therapy (IST).[5] The safety and efficacy profiles of this therapy have been established in the adult population, but data in the pediatric population is limited.[1] We report a case of massive pulmonary hemorrhage that complicated intrapleural fibrinolytic therapy. The educational objectives of this case report are to highlight a crucial gap in our understanding of the safety and efficacy of such interventions, particularly in the pediatric population. This finding emphasizes the need for further studies on the safety profile of intrapleural streptokinase.

Our case report serves as a valuable reference for clinicians navigating the complexities of pediatric care in resource-constrained settings and promoting a more nuanced understanding of the risks associated with intrapleural fibrinolytic therapy. Our institution does not require ethical approval for reporting individual cases. Written consent from the parent or guardian was obtained prior to submission.

## Case Report

H was born at 31 weeks of gestation with a birth weight of 1.42 kg via emergency lower segment caesarian section for severe pre-eclampsia. He was admitted to the neonatal intensive care unit (ICU) due to prematurity with moderate respiratory distress syndrome. He was initially ventilated for 3 h and required oxygen support for a total of 5 days throughout his hospital stay. He was discharged on day 31 of life at a corrected age of 35 weeks 3 days.

Subsequently, he had two episodes of pneumonia at the age of 5 and 11 months, for which he required a short hospital stay, with the highest oxygen requirement being high-flow nasal cannula during the second admission. He tested positive for respiratory syncytial virus during the first episode of pneumonia at 5 months of age.

At 14 months of age, he presented to the hospital with a 2-day history of cough, runny nose, and rapid breathing. He was diagnosed with community-acquired pneumonia, and intravenous antibiotic therapy was initiated. He required low oxygen supplementation and was discharged after 3 days with oral antibiotics. However, he presented again after 1 day of discharge with acute respiratory distress. At the time of presentation, he required nasal prong oxygen and was started on intravenous cefuroxime for partially treated pneumonia. The chest radiograph on admission showed consolidation over the right lower zone.

On day 5 of admission, he developed worsening respiratory distress requiring non-invasive ventilation. Repeat chest radiography revealed a pleural effusion on the left side. This was confirmed on ultrasound thorax on the next day, which showed minimal complex left pleural effusion with thickened pleura. Thus, a chest tube was inserted using intrapleural streptokinase.

Chest tubes were inserted using the blind method and were complicated by multiple traumatic attempts. After several hours, the chest tube was dislodged, and a second chest tube with intrapleural streptokinase was inserted on the subsequent day. Four hours later, he developed profuse bleeding from the nasal and oral cavities and severe respiratory distress. He was intubated and transferred to the ICU for close monitoring.

In the ICU, he developed further episodes of pulmonary hemorrhage associated with anemia necessitating packed-cell transfusion. His coagulation profile was normal. Platelet levels were mildly high at $622x10^9$/L. No other evidence of bleeding disorders or secondary infection was observed. Repeat ultrasound thorax showed a left pleural effusion with echogenic moving debris/sediment within, with a depth of 1.7 cm and thickened pleura. The chest tube was removed after 4 days, and the patient was ventilated for the same duration. Respiratory support was gradually weaned over 11 days. Blood cultures were negative. Investigations for pulmonary tuberculosis were negative. He completed intravenous crystallized penicillin and ceftriaxone for a total of 14 days and subsequently completed oral cefuroxime for another month. He was discharged home after 16 days of admission with metered dose inhaler fluticasone and salbutamol.

## Discussion

The use of IST for the management of parapneumonic effusion has a longstanding history that dates back to its introduction by Tillett and Sherry.[6] Numerous studies have since explored the efficacy and potential risks associated with various fibrinolytic therapies. The primary rationale for employing fibrinolytic in parapneumonic effusion is their ability to disrupt pleural septations and loculations that impede drainage, consequently facilitating improved drainage, hastening recovery, and mitigating the need for surgical interventions, such as thoracotomies or video-assisted thoracoscopic surgeries.[7]

The use of intrapleural fibrinolytic in pediatric cases was first documented in 1993 by Handman and Reuman[8] who utilized urokinase. Subsequent studies have reported a high success rate among pediatric patients,[3] demonstrating increased pleural fluid drainage and shorter hospital stays.[9] However, the use of fibrinolytic therapy is not without its inherent

risks, including therapy failure and pulmonary hemorrhage. In adults, identified risk factors for pulmonary hemorrhage include traumatic chest tube insertion, coagulopathy, concurrent administration of systemic anticoagulants[10,11] and the presence of other medical comorbidities.[11]

Limited case reports exist regarding pulmonary hemorrhage in children subjected to fibrinolytic therapy. Anevlavis et al.[12] reported a 6-year-old boy with no significant risk factors who developed pulmonary hemorrhage after alteplase therapy. In a study involving 73 pediatric and adolescent cases,[13] two patients developed pulmonary hemorrhage, which was thought to be related to the necrotic pulmonary process itself rather than the administration of alteplase.

Despite advancements, universal guidelines specifying definitive criteria and optimal timing for intrapleural streptokinase in pediatric populations have not been established,[5] and the existing basic guidelines for managing parapneumonic effusions have shown low adherence.[14] To enhance current intrapleural fibrinolytic practices and minimize adverse effects, specific prerequisites must be met, including ultrasound-guided chest tube insertion and proper training for safe chest tube insertion.[14,15] The British Thoracic Society guidelines[15] recommend that chest drains be inserted by adequately trained personnel to reduce the risk of complications, emphasizing the operator's skill in correctly identifying the safe triangle location.

Rahman et al.[14] demonstrated significant benefits of t-PA and the addition of DNase, including improved fluid drainage in patients with pleural infection and reduced frequency of surgical referral and duration of hospital stay. Thus, attention should be given to determining the suitable dose and duration of fibrinolytic therapy, the choice of fibrinolytic agents, and their combination with DNAse.[14] Further studies are required to determine the optimal therapy.

Close monitoring during and after treatment is crucial, particularly for patients with identified risk factors. Assessing suitable and low-risk candidates is imperative, necessitating a thorough pre-procedure evaluation to ensure the absence of pre-existing thrombocytopenia and coagulopathy. The British Thoracic Society guidelines recommend correcting any coagulopathy or platelet defect before drain insertion and advocating routine pre-procedure checks of platelet count and prothrombin time in patients with risk factors, such as those on hemodialysis, following cardiac surgery, or after chemotherapy.[15]

## Conclusion

IST remains a valuable therapy for managing pediatric parapneumonic effusion. Healthcare providers should be vigilant regarding the risk of pulmonary hemorrhage, particularly in high-risk patients. Ultrasound-guided chest tube insertion, patient assessment before IST, and close monitoring during and after therapy may help minimize this adverse event. Further research is warranted to elucidate the risk factors associated with pulmonary hemorrhage in children with IST.

### Ethics

**Informed Consent:** Written consent from the parent or guardian was obtained prior to submission.

### Authorship Contributions

Concept: A.M.K., Design: A.W.A.R., C.Y.L., A.M.K., Data Collection or Processing: A.W.A.R., C.Y.L., A.M.K., Analysis or Interpretation: A.W.A.R., C.Y.L., A.M.K., Literature Search: A.W.A.R., C.Y.L., A.M.K., Writing: A.W.A.R., C.Y.L., A.M.K.

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