

**Clinical Case Seminar**

**CCS2 (1-3)**

## **A case of pleural empyema treated with intrapleuralurokinase**

**<sup>1</sup>Federica Xerra, <sup>1</sup>Immacolata Rulli, <sup>1</sup>Mauro Iannelli, <sup>1</sup>Antonella Gambadauro, <sup>1</sup>Francesca Galletta, <sup>1</sup>Monica Fusco, <sup>1</sup>Simona Allera, <sup>2</sup>Sara Manti; <sup>3</sup>Carmelo Romeo, <sup>4</sup>Francesco Monaco, <sup>1</sup>Eloisa Gitto**

<sup>1</sup>Neonatal and Pediatric Intensive Care Unit, Department of Human Pathology of the Adult and Developmental Age "Gaetano Barresi", University of Messina, Messina, Italy; <sup>2</sup>Pediatric Unit, Department of Human Pathology of the Adult and Developmental Age "Gaetano Barresi", University of Messina, Messina, Italy ; <sup>3</sup>Pediatric Surgery Unit, Department of Human Pathology of the Adult and Developmental Age "Gaetano Barresi", University of Messina, Messina, Italy; <sup>4</sup>Thoracic Surgery Unit, Department of Biomedical sciences, Dental and of Morphological and Functional Images, University of Messina, Messina, Italy

### **Abstract**

Pleural empyema, a severe complication of bacterial pneumonia, is a rare entity in the neonatal period. Treatment with systemic antibiotics and tube drainage may fail because of the thick viscous fluid, bacterial products with fibrin deposition, and multiple involvement. Intrapleural fibrinolytic therapy with urokinase is an effective and non-invasive treatment option that avoids surgical intervention, although its use in neonates has not been studied extensively. In this report, we describe the case of a 39-day-old male newborn with pneumonia and pleural empyema, treated successfully with antibiotics, chest tube drainage and intrapleuralurokinase.

**Keywords:** pleural empyema; newborn; intrapleuralurokinase

**Introducing Member:** Eloisa Gitto

**Corresponding Author:** Sara Manti – smanti@unime.it

### **Introduction**

Pleural empyema, a severe complication of bacterial pneumonia, is a rare nosological entity in the neonatal period (1-3). *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus* are the most common agents for this condition (1-3). If untreated, the parapneumonic exudate, following fibrin synthesis and deposition, can increase its density and progressively organize itself into septate collections, resulting in antibiotic treatment and pleural drainage failure. In septated parapneumonic empyema, intrapleural fibrinolytic agents represent the first-line therapy, showing the same effectiveness as thoracoscopic surgery but less invasive (1,3).

The use of intrapleural fibrinolytic agents (urokinase) represents a safe, effective and non-invasive first-line therapeutic option that, by improving the fluidity and drainage of the endopleural collection, reduces the need for a surgical approach and a prolonged hospital stay (1-4).

We describe a case of bacterial pleural empyema in a newborn who was successfully treated with intrapleuralurokinase.

## Case Report

We describe the case of M., born preterm, appropriate for gestational age(AGA), from eutocic delivery and normal course pregnancy, complicated by maternal type 1 diabetes mellitus. Non-contributory obstetric-gynecological history. Admitted to our Neonatal Intensive Care Unit at 39 days of life due to feeding difficulties, rhinorrhea and dyspnoea that arose 24 hours earlier.

Upon admission, he was afebrile, tachycardic and tachypneic, with suboptimal values of oxygen saturation (SO<sub>2</sub>) at room air (85%), last intercostal spaces recession, and significant reduction of vesicular murmur in the left hemithorax. The chest radiogram showed multiple parenchymal thickenings in the left lung. On the first day, he was placed in high flow nasal cannula (HFNC) support (8 Lt/min, FiO<sub>2</sub> 0.30) with good compensation. Laboratory findings showed neutrophilic leukocytosis (GB 42,400/mm<sup>3</sup>, N 78%) and a significant increase in inflammation indices (Pcr 43 x N, Pct 11.3 x N), thus, empiric antibiotic therapy with ampicillin, gentamicin and clindamycin was started.

Due to the worsening of dyspnoea and blood gas values (hypoxemic-hypercapnic respiratory acidosis), oro-tracheal intubation was carried out on the second day of hospitalization. Mechanical ventilation in SIPPV mode was started. A second chest X-ray documented complete opacity of the left hemithorax and contralateral deviation of mediastinal structures (Fig. 1); transthoracic ultrasound and thoracic computed tomography (CT) (Fig.2) were performed, confirming the suspicion of massive left pleural effusion.

**Fig. 1** Chest radiograph showing opacity of the left hemithorax and rightward shift of the cardio-mediastinal structures



**Fig.2** Thoracic computed tomography showing abundant pleural effusion on the left, which presents shirt distribution in its most caudal portion. The lower lobe of the ipsilateral lung appears almost completely atelectatic



Therefore, exploratory thoracentesis was performed, and subsequent pleural drainage with the aspiration of a total of 30 ml of purulent material, establishing the diagnosis of pleural empyema.

On the third day of hospitalization, due to an unchanged chest X-ray, an intrapleural instillation procedure of Urokinase 10,000 U (diluted in 10 ml of physiological solution, twice a day for a total of 4 days) was started, assisting in a progressive reduction of the purulent exudate.

Microbiological diagnostics via PCR/Filmarray on broncho-aspirate resulted positive for Methicillin-Resistant Staphylococcus Aureus (MRSA), which was confirmed by culture. Therefore, targeted

antibiotic therapy was started by replacing clindamycin with teicoplanin. On the eighth day, due to the improvement of the radiological findings, the pleural drainage tube was removed.

Upon completion of the diagnosis, further tests were carried out, all of which were negative or normal including quantiferon-TB Gold standard, serum immunoglobulin levels, lymphocyte subpopulations and genetic analysis for cystic fibrosis.

### Conclusions

Intrapleural fibrinolytic agents (chemical debridement) are currently considered a valid therapeutic option in cases of bacterial pneumonia complicated by septated parapneumonic effusion and/or frank pleural empyema. The ability to reduce the viscosity of the endopleural collection, preventing the synthesis, deposition and subsequent organization of fibrin, makes this treatment strongly recommended as first-line therapy, in combination with pleural drainage and targeted antibiotic therapy. Urokinase is to date the only fibrinolytic agent studied in randomized controlled trials in pediatric age, demonstrating its validity in terms of safety, efficacy, reduction of length of hospital stay and the risk of resorting to a thoracotomy surgical approach (1-4).

**Conflicts of Interest:** There is no potential conflict of interest, and the authors have nothing to disclose. This work was not supported by any grant. Informed consent was obtained

### References

1. Marhuenda, C., Barceló, C., Fuentes, I. (2014). Urokinase versus VATS for treatment of empyema: a randomized multicenter clinical trial. *Pediatrics*, 134(5), 1301-1307. doi:10.1542/peds.2013-3935
2. Cha, L.M., Choi, S., Kim, T., Yoon, S.W. (2016). Intrapleuralurokinase therapy in a neonate with pleural empyema. *Pediatr Int.*, 58(7), 616-619. doi:10.1111/ped.12906
3. Saeed Al-Shamrani, A. (2020). Management of Complicated Pneumonia in Children: Evidence Beyond Guidelines. *American Journal of Pediatrics*. Volume 6, Issue 3, 240-252. doi: 10.11648/j.ajp.20200603.22.
4. Diez, J.R.V., Perez, M.L.M., Malayan, G.V., Cenabre, M.V.L. (2020). Loculated empyema in a neonate successfully treated with chest tube thoracostomy and antibiotics. *Respir Med Case Rep*. doi:10.1016/j.rmcr.2020.10127



©2023 by the Author(s); licensee Accademia Peloritana dei Pericolanti (Messina, Italy). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

*Communicated Dec 15, 2022; received February 20, 2023; revised and accepted February 28 2023; published on line April 7, 2023*