

## CASE REPORT

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# The Application of Intrapleural Dornase Alfa Alone in a Pediatric Case

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**ABSTRACT** The treatment of empyema in children is controversial. In both children and adults, in addition to empyema drainage and parenteral antibiotics, it has been reported that treatments of intrapleural dornase alfa alone or in combination with fibrinolytic agents have been used successfully. Although fibrinolytic treatment seems to be less invasive, it may cause traumatic or intolerable side-effects in young children. There are some reports in the literature about the efficacy of intrapleural dornase alfa used alone in the treatment adults with empyema. To best of our knowledge, there are no data related to children. In this case report, a 6-year old girl, diagnosed with empyema, resistant to intravenous antibiotics and tube drainage, treated with intrapleural dornase alfa alone, was presented.

**Keywords:** Parapneumonic effusion; empyema; dornase alfa; intrapleural treatment

Despite the widespread use of broad spectrum antibiotics, parapneumonic effusion and empyema are still significant problems in childhood. The main aim of parapneumonic empyema treatment is to improve parenchymal infection with appropriate antibiotic treatment and drainage of the infected pleural cavity in childhood. There are various treatment approaches for childhood parapneumonic empyema, some of them are repeated thoracentesis, tube thoracostomy, fibrinolytic treatment, and decortication with video-assisted thoracoscopy or open thoracotomy.<sup>1</sup>

However, there has been no consensus on the best treatment method, yet. There are many studies in the literature related to the intrapleural application of fibrinolytic agents alone or in combination with deoxyribonuclease (DNase).<sup>2</sup> Although the efficacy of intrapleural fibrinolytic treatment has been shown, some complications such as allergic reactions and bleeding problems may occur.<sup>3</sup> DNase, which is a mucolytic agent is considered to be effective for pleural drainage by reducing intrapleural fluid viscosity.

Some studies have been reported that the combination of intrapleural fibrinolytic agents and DNase increased success of treatment, but some studies have reported no efficacy.<sup>2,4</sup>

The intrapleural application of DNase alone in adults has been reported in 10 patients of case series and in that report this treatment could be effective alone in some patients.<sup>5</sup> There is no information in literature about the intrapleural alone application of DNase in children. A 6-year old girl, diagnosed with empyema, treated successfully with alone intrapleural DNase treatment and tube thoracostomy with 10 days of antibiotic use, was presented.

## CASE REPORT

A 6-year old female was admitted to emergency department of our hospital for cough, began one week ago, and respiratory distress. The patient was diagnosed with pneumonia and treated with oral antibiotherapy (amoxicillin-clavulanate) for one week before admission to our unit. The parent's approval was re-

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ceived for this report. In the physical examination, the patient was conscious, cooperative and tachypneic (respiratory rate 52/min). There were intercostal and subcostal retractions, and no respiratory sounds in the left hemithorax. Physical examination findings of other systems were normal. The laboratory test results were: Hb: 10.9 gr/dL, WBC: 18,800/ $\mu$ L (88% neutrophil), PLT: 427,000/ $\mu$ L, C-reactive protein: 240 mg/L (0-5 mg/L). On the posteroanterior chest radiograph, total consolidation was detected in the left hemithorax and there was a mark about the level of fluid (Figure 1).

The thorax computed tomography examination of the patient revealed total atelectasis of the left lung and the presence of massive fluid of 30 mm dense content in the left hemithorax. A thorax tube was inserted. The underwater drainage was done but only a small amount of purulent fluid was obtained. There was no bacterial growth in this fluid culture. The polymerase chain reaction of nasopharyngeal swab indicated rhinovirus. The patient was treated for bacterial pneumonia and empyema with ceftriaxone and teicoplanin for 10 days, but at the end of antibiotic treatment, the left lung did not expand and the appearance of fluid continued (Figure 2). On the thorax ultrasonography examination, the septated appearance with dense fluid content persisted.

Therefore, it was planned to try the combination of intrapleural tissue plasminogen activator (TPA) and DNase, and if no response was obtained to this treatment, a surgical approach with video thoracoscopy would be applied. As TPA could not be provided, 5 mg DNase diluted with 15 mL saline was administered once a day for 3 days within the thoracic tube, then the tube was clamped and the patient was moved at frequent intervals to left and right, and Trendelenburg and anti-Trendelenburg positions. The clamp was removed after 2 hours and drainage was continued. After 3 days of treatment, the findings of the patient at rest were improved, and on direct radiographs, there was observed to be significant expansion of the lung and improvement (Figure 3).

## DISCUSSION

In the treatment of empyema and resistant pleural effusion, intrapleural treatment methods are being increasingly used in adult and pediatric patients. Dense

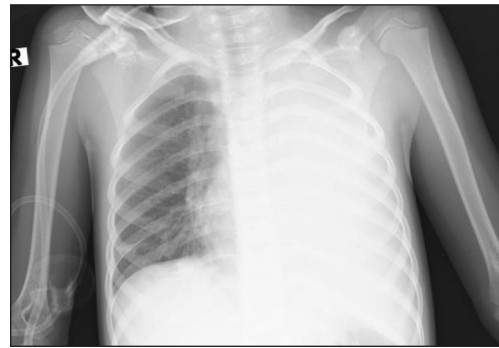


FIGURE 1: The first chest X-ray at admission.



FIGURE 2: Chest X-ray on the 10<sup>th</sup> day of treatment.



FIGURE 3: Chest X-ray after 3 days in the treatment of deoxyribonuclease.

pleural fluid of exudate texture adheres to the visceral and parietal leaves of the pleura by forming fibrins. This makes it difficult to drain the fluid remaining with the closed septa that have emerged.

Treatments reducing fluid viscosity are effective in this way. Polymerised DNase depolymerises deoxyribonucleopeptides. This effect is thought to be seen in both mammals and bacterial DNA. However, bacteriae forming a biofilm layer over the tube and in

other tissues create a barrier.<sup>6</sup> For a long time, it has been safely used in the treatment of cystic fibrosis. The current authorised indication is for administration once or twice a day via nebulisation at a dose of 2.5-5 mg. Side-effects of this usage have been reported as skin rash, hoarseness, and chest pain.<sup>7</sup> There are no reports in literature of side-effects related to intrapleural use. In the current case, no side-effects were determined related to the intrapleural DNase treatment.

There is no standard approach for pediatric cases in respect of dose and duration in the application of combined fibrinolytic and mucolytic treatments. In the “Multicenter intrapleural sepsis trial 2” protocol, it is stated that in adult studies treatment of 5 mg DNase and 10 mg TPA administered to the pleural gap for 3 consecutive days has been adopted and found to be useful.<sup>8</sup> Furthermore, to prevent hemorrhagic complications, the efficacy has also been reported of the combination of 1 mg TPA+5 mg DNase, which can keep TPA at a lower dose.<sup>9</sup> In a rat model study of experimental empyema with *Streptococcus pneumoniae*, TPA and DNase were administered to the pleural space separately and combined. The combination treatment was not seen to be superior to the administration of each agent alone.<sup>4</sup> However, in adult clinical studies, combination treatment has been reported to be superior in respect of reducing systemic inflammation symptoms, the efficacy of pleural drainage, the length of stay in hospital, and reducing the need for thoracic surgery.<sup>10</sup> Our patient didn't need surgery and totally recovered as a result of

DNase monotherapy. Therefore, we think that single DNase therapy is an effective option in pediatric empyema cases. In this regard, it may be appropriate to evaluate it in terms of effectiveness with larger case series.

## CONCLUSION

The combination therapy of TPA and DNase is commonly used in the treatment of empyema in pediatric patients. In cases where TPA is not available, DNase monotherapy may be beneficial.

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### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea/Concept:** Nazik Yener; **Design:** Hatice Albayrak; **Control/Supervision:** Nazik Yener; **Data Collection and/or Processing:** Hatice Albayrak; **Analysis and/or Interpretation:** Hatice Elif Kınık Kaya; **Literature Review:** Muhammed Udurgucu; **Writing the Article:** Muhammed Udurgucu; **Critical Review:** Nazik Yener; **References and Fundings:** Hatice Elif Kaya.

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