

Alteplase in the Treatment of Complicated Parapneumonic Effusion: A Case Report

Naomi B. Bishop, MD; Steven Pon, MD; H. Michael Ushay, MD, PhD; and Bruce M. Greenwald, MD

ABSTRACT. The treatment of complex parapneumonic effusions in children remains controversial, with some advocating less invasive, strictly medical management and others supporting a more aggressive approach of thoracotomy with or without decortication. Recent advances, including video-assisted thoracoscopic surgery and intrapleural fibrinolytic therapy, offer new options for effective treatment. We report the first case of successful resolution of a complex parapneumonic effusion in a 16-month-old girl with the use of tissue plasminogen activator (alteplase), infused via a catheter in the pleural space. *Pediatrics* 2003;111:e188–e190. URL: <http://www.pediatrics.org/cgi/content/full/111/2/e188>; *parapneumonic effusion; intrapleural fibrinolytic therapy; tissue plasminogen activator; alteplase.*

ABBREVIATIONS. t-PA, tissue plasminogen activator; WBC, white blood cell; CT, computed tomography (scan).

The optimal management of complicated parapneumonic effusion in hospitalized children remains controversial. Some experts advocate bedside insertion of a thoracostomy tube, continuous pleural drainage, parenteral antibiotics, and diligent pulmonary toilet, with progression to more invasive therapies only when clinical resolution is not achieved. Others opt instead for early surgical intervention with open thoracotomy or video-assisted thoracoscopic surgery. To date, there is insufficient evidence to prove that either approach is consistently superior in all cases.

Although conservative treatment may spare the patient the discomfort of a thoracic incision and the risks of surgery and anesthesia, resolution may be slow or incomplete. Furthermore, conventional, rigid thoracostomy tubes can be uncomfortable and may require continuous narcotic analgesia. Often, the tube becomes obstructed by fibrinous debris and stops functioning altogether. The drowsy, disagreeable child cannot cooperate with the required chest physiotherapy and, if the pain is inadequately controlled, deliberately avoids full lung expansion and adequate pulmonary toilet. Furthermore, the deci-

sion to initiate surgical intervention once medical management has failed can be frustrating for both the physicians and the family.

Those who support early surgical intervention point to the potential for more rapid resolution of the pleural collection and shorter length of hospital stay. They argue that removal of the pleural "rind" enables antibiotics to reach their target more rapidly and effectively. They claim that the introduction of minimally invasive thoracoscopic surgery has greatly reduced both perioperative risk and discomfort. However, studies that purport the advantage of 1 therapy over others suffer from wide variations in the characteristics of the study samples, resulting in the comparison of apples to oranges.

Until a valid and convincing consensus can be reached, physicians continue to refine existing treatments. Perhaps adding to the confusing range of treatment options, we present here the first reported case of an early parapneumonic effusion successfully drained through a thin catheter with judicious use of recombinant tissue plasminogen activator (t-PA). Although there have been multiple case reports in which the fibrinolytics urokinase and streptokinase have been used to maintain pleural tube patency and allow for more effective drainage, we believe that there is sound theoretic basis for the previously unreported use of t-PA.

CASE REPORT

A 16-month-old, previously well girl was transferred to our institution from a nearby hospital for evaluation and management of right-sided pneumonia with a large parapneumonic effusion and complete consolidation of her right lung. She had been in her usual state of good health until approximately 2 weeks before admission, when she developed fever (39.5°C), rhinorrhea, and loose stools. The illness lasted 4 days and seemed to resolve completely. Six days before admission, she again developed fever to 40°C and a nonproductive cough. Two days later, she was seen in an outpatient facility and received a diagnosis of having a viral syndrome. On the day before transfer to our institution, she was noted to have persistently high fever, tachypnea, poor oral intake, and mild dehydration. She was admitted to the referring hospital for hydration and was started on intravenous cefuroxime after a chest radiograph revealed complete opacification of the right lung (Fig 1). Her white blood cell (WBC) count was 12 500/mm³ with 61% neutrophils. Blood and urine cultures were obtained, and computed tomography (CT) scan of the chest (Fig 2) demonstrated a large parapneumonic effusion, with complete consolidation of the right lung. She was transferred to our hospital for additional evaluation and management.

On arrival, the patient appeared well-developed and well-nourished (10.3 kg, 25th–50th percentile), and appropriately hydrated. Her respiratory rate was 41 breaths per minute, and her oxygen saturation by pulse oximetry was 96% while receiving 1 L/min oxygen by nasal canula. Her physical examination was

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Fig 1. Admission radiograph shows complete opacification of the right hemithorax.

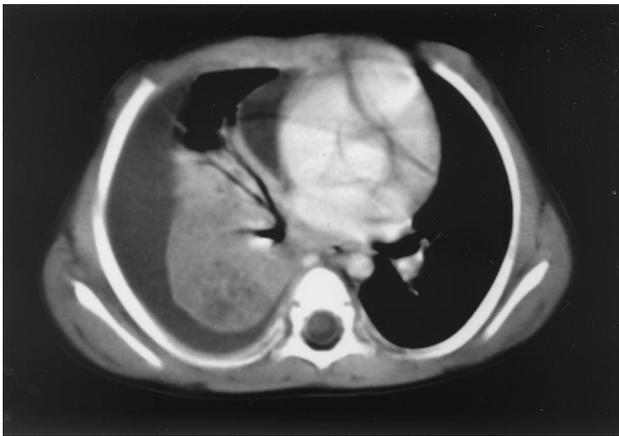


Fig 2. Chest CT scan done on admission to the referring hospital shows a large parapneumonic effusion and complete consolidation of the right lung.

significant for bronchial breath sounds on the right, which were decreased at the base. No rales were noted. Neither retractions nor nasal flaring was observed. The remainder of her physical examination was unremarkable.

Under procedural sedation, thoracentesis yielded clear, straw-colored fluid. A 16-gauge, 30-cm, flexible catheter with side holes was inserted at the sixth intercostal space, and 160 mL of fluid was aspirated. The catheter was left in place to drain at -20 cm water suction. Analysis of the fluid revealed 4100 red blood cells/ mm^3 and 1260 WBCs/ mm^3 , with a differential count of 92% neutrophils, 7% monocytes, and 1% lymphocytes. The pH was 7.14, the total protein was 3.9 g/dL, and the albumin was 2 g/dL; the serum protein and albumin were 5.6 g/dL and 2.3 g/dL, respectively. The lactate dehydrogenase was 3300 U/L in the pleural fluid and 275 U/L in the serum. The glucose was 2 mg/dL and 93 mg/dL in the fluid and serum, respectively. Gram stain of the initial aspirate contained no organisms and few WBCs. These findings were consistent with a "category 3" process with a moderate risk for poor outcome according to the American College of Chest Physicians consensus statement.¹

The patient required minimal supplemental oxygen, and she was continued on intravenous cefuroxime at a dosage of 150 mg/kg/d in 3 divided doses. On hospital day 2, the plasma WBC count increased to 27 800/ mm^3 with 61% neutrophils and 18% bands. Blood cultures from the referring hospital remained negative, as was the skin test for tuberculosis. The patient's fever persisted despite antipyretics. Vancomycin was added after 48

hours to broaden antibiotic coverage. There was minimal improvement in aeration of the right lung on chest radiograph, and pleural fluid drainage decreased to <10 mL/d within 48 hours of catheter placement.

On the fourth hospital day, the drainage decreased. The tube was flushed with a small volume of saline (1–2 mL) to ensure patency, but no additional drainage ensued. A 2-mg dose (the published dose for clearance of thrombi from central venous catheters) of recombinant t-PA (Activase; Genentech, South San Francisco, CA) was infused via the catheter directly into the pleural space, and the pleural tube was clamped for 4 hours. The catheter was then reopened to suction, and >200 mL of pleural fluid drained during the subsequent 24 hours. Alteplase infusion was repeated (4 times during the following 6 days) until there was no more fluid drainage. Besides some mild discomfort during infusion, relieved by acetaminophen, the patient experienced no appreciable side effects. A repeat chest CT scan on day 10 revealed near-complete resolution of the effusion and improvement in parenchymal disease (Fig 3). The patient became afebrile on day 9 and no longer required supplemental oxygen. She continued on chest physiotherapy and completed a 10-day course of vancomycin. She was discharged from the hospital on oral cefuroxime axetil for an additional 7 days and was referred to the pulmonary clinic for follow-up in 6 weeks. A chest radiograph at that time (Fig 4) showed clear lungs and no evidence of effusion. Her young age precluded follow-up pulmonary function testing.

DISCUSSION

Although the pathophysiology and evolution of parapneumonic effusions have been well-described,^{2,3} the most effective treatment for both children and adults remains controversial. Until recently, the literature was clearly divided into 2 schools of thought: one supporting conservative, minimally invasive medical treatment, with or without thoracostomy tube drainage, and the other advocating a more aggressive, invasive approach with early operative thoracotomy and decortication. There have been no randomized, controlled studies in children or adults to show clear benefit from either approach in terms of outcome, morbidity, and length of hospital stay. Current practice trends favor a stepwise approach, starting with less invasive measures and stepping up therapy only in cases refractory to medical management.⁴ Although this strategy may help to avoid the risks associated with general anesthesia and surgery, the time to resolution of symptoms (fever and dyspnea) can be prolonged.

During the past 5 years, new therapeutic modalities for the treatment of parapneumonic effusions

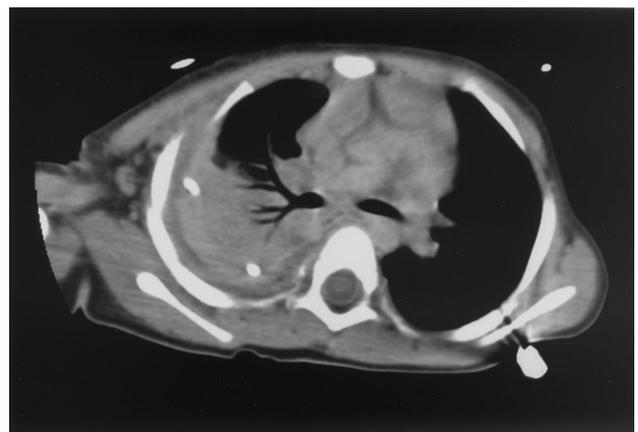


Fig 3. Repeat chest CT scan done on hospital day 10 shows resolution of the effusion and improvement in parenchymal disease.

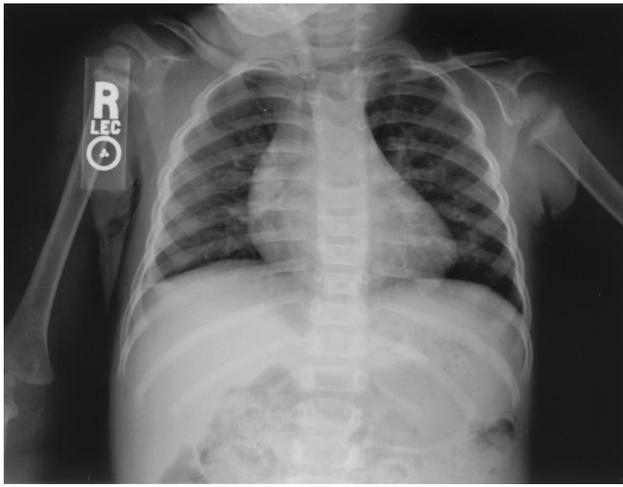


Fig 4. Follow-up chest radiograph done 6 weeks after discharge shows clear lung fields and no evidence of effusion.

(eg, thoracostomy tube placement with intrapleural fibrinolytic therapy using streptokinase or urokinase and video-assisted thoracoscopic surgery) that seem to combine the benefits of less invasive therapies with the promise of more rapid recovery have been developed.⁵⁻⁷ Several recent case series have documented the successful resolution of parapneumonic effusions, mainly in adults, using intrapleural urokinase and standard, large-sized thoracostomy tubes to facilitate pleural drainage, but consensus on standard dosing and duration of treatment are lacking. Furthermore, current recommendations urge against the use of this fibrinolytic derived from infant kidneys.⁸ Recent studies suggest that t-PA may be a more appropriate therapeutic agent. The pathogenesis of fibrin deposition in exudative pleural effusions includes alterations in the balance of procoagulant and fibrinolytic activity. This may be secondary to a decreased level of endogenous t-PA in pleural fluid⁹ or because of inhibition of plasminogen and plasmin by plasminogen activator inhibitors-1 and-2 and other mediators.^{10,11} As far as we are aware, our report is the first documented case of safe and successful treatment of a complex parapneumonic effusion in a child with the use of recombinant t-PA delivered via a small-gauge catheter. The use of a softer, smaller gauge catheter facilitates delivery of the t-PA to its intended target and minimizes the pain and morbidity associated with thoracostomy.

In 1997, an American College of Chest Physicians panel convened to draft a consensus statement regarding the standard of care for treatment of parapneumonic effusions in adults, based on a detailed review of the current literature. They were able to

stratify patients into 4 groups on the basis of their risk for poor outcome¹ but could offer only broad recommendations for therapy and were unable to arrive at formal therapeutic guidelines based on existing evidence. They concluded that the majority of current data were “methodologically flawed” and that no single therapy was proved to be superior. Clearly, more research in this area is needed before practice guidelines can be established in adults, and they will need to be applied with caution to our pediatric population.

Our review of the literature reveals only a few case reports in which urokinase fibrinolytic therapy was used in the management of complicated pleural effusions in children,¹² and as far as we can tell, ours is the first case in which t-PA (alteplase) was used in the management of a complicated parapneumonic effusion in a pediatric patient. Given the ease of application, apparent safety, and the lack of appreciable side effects, intrapleural t-PA offers a promising treatment alternative in the management of this difficult problem. A large-scale, multicenter, randomized, controlled trial would be required to document its efficacy and safety in the pediatric population.

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