Rational Treatment of Empyema in Children

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Hypothesis: Efficacious and cost-effective treatment of pediatric empyema can be accomplished following a protocol based on its radiographic appearance. Therapeutic modalities include thoracostomy tube drainage (TTD) with or without fibrinolytic therapy (FT) and video-assisted thoracoscopic debridement (VATD).

Design: Retrospective case series.

Setting: Tertiary referral center.

Results: From 1995 through 1999, 31 children were treated ranging in age from 11 months to 18 years (mean age, 5.1 years). Twenty-seven (87.1%) underwent TTD; of these, 22 (81.5%) received FT with urokinase. The TTD failed in 4 children (14.8%) who required salvage VATD. Primary VATD was performed in another 4 children (12.9%). The mean length of stay was 14.6 days (TTD, 14.1 days; salvage VATD, 20.0 days; primary VATD, 11.5 days), ranging from 8.0 to 30.0 days. Complications included readmission for fever (2 patients [6.5%]) and gastrointestinal bleeding (1 patient [3.2%]). There were no anaphylactic reactions or bleeding episodes due to urokinase. Two patients (7.4%) treated with TTD and FT developed an air leak that resolved spontaneously. The mean hospital charges were $78,832 (TTD with or without FT, $75,450; salvage VATD, $107,476; primary VATD, $69,634). The procedural charges were highest for salvage VATD.

Conclusions: Most cases of pediatric empyema can be treated by TTD with or without FT. This therapy is safe and effective for children with nascent disease. Primary VATD is preferred in children with advanced disease. Cost-effectiveness could be further improved through better prediction of those patients likely to fail TTD and require salvage VATD. An algorithmic approach based on findings from computed tomography or (better) ultrasonography of the chest may be the best way to make this distinction and rationalize care.

SUBJECTS, MATERIALS, AND METHODS

SUBJECTS

We reviewed 39 patients with International Classification of Diseases, Ninth Revision hospital discharge code 510 (thoracic empyema) at our facility for 4 years ending in July 1999.21 Treatment was dictated by an algorithm (Figure) based on the radiographic appearance of the parapneumonic fluid collection. We analyzed 3 treatment groups: (1) patients who were successfully treated with thoracostomy tube drainage (TTD) with or without fibrinolytic therapy (FT) (TTD ±FT), (2) patients who required video-assisted thoracoscopic debridement (VATD) after TTD (±FT) had failed (salvage VATD), and (3) patients who were treated this way from the outset (primary VATD). The children received at least 2 weeks of intravenous antibiotics and 2 weeks of oral antibiotics.

The FT consisted of intrapleural administration of urokinase (UK) at 1 of 2 dosings: 20000 U/20 mL of isotonic sodium chloride solution for children younger than 5 years and 100000 U/40 mL isotonic sodium chloride solution for children between ages 5 and 18 years. The chest tube was clamped for 4 hours after each instillation during which time the child was repositioned hourly. After unclamping the chest tube, pleural drainage was measured and net pleural fluid volume flux (volume out−volume in) was recorded. Treatment was continued for 3 to 5 days and as long as the net flux remained notably positive (>25 mL/8-hour shift).

COST AND STATISTICAL ANALYSES

Hospital charges were obtained from itemized computer records. Stratified charges for the intensive care unit (ICU), hospital ward costs, surgical procedures, radiology studies, and pharmacy costs, as well as total charges, were analyzed. A 2-tailed t test for unpaired samples was performed to compare means between the groups.

(71.0%) had been treated with antibiotics for a mean of 7 days (range, 2-36 days).

Twenty-seven children (87.1%) were initially treated with TTD (±FT), and of these, 7 (25.9%) required placement of more than 2 chest tubes. Seventeen children (63.0%) required general anesthesia or conscious sedation for chest tube placement. Twenty-two children (63.0%) had been treated with antibiotics for a mean of 7 days (range, 2-36 days).

In 4 children (14.6%), TTD (±FT) failed and salvage VATD was necessary owing to persistent symptoms not attributable to parenchymal lung disease, associated with unchanged or worsening pleural fluid accumulation. The average time lag between TTD and VATD was 4 days (range, 2-6 days). The duration of symptoms prior to admission in this group was shorter (5 days), and the proportion receiving preadmission antibiotics was smaller (50%; n=2) compared with the TTD group (12 days, 74%; n=17). These patients became afibrile 6 days (range, 1-9 days) after undergoing VATD.

Four children (12.9%) underwent primary VATD. This group had a comparatively longer symptomatic phase prior to hospitalization (14 days), and the febrile phase after surgery was similar to that of the salvage surgery group (7 days). The average number of computed tomographic (CT) scans per patient was 2.7 (TTD, 2.8; salvage VATD, 3.5; primary VATD, 1.5).

The mean length of stay (LOS) for all patients was 14.6 days (TTD, 14.2 days; salvage VATD, 20 days; primary VATD, 11.5 days) (P=.047 for salvage VATD vs TTD; P=.02 for salvage VATD vs primary VATD) (range, 8-30 days). Nineteen patients (61.3%) required ICU admission during their hospital stay. All patients undergoing VATD received postoperative care in the ICU (means: salvage VATD, 3.5 days; primary VATD, 2 days). Eleven patients who underwent TTD successfully (47.8%) required ICU admission for a mean of 2.8 days.

CULTURES

All children received parenteral antibiotics, usually cefuroxime and clindamycin. Nineteen patients (61.3%) had positive findings from blood, sputum, or urine cultures during hospitalization, but pathogens within pleural fluid were identified in only 8 patients (25.8%). In 2 patients (6.5%) multiple species were isolated. The most common pleural isolates were Streptococcus (6) and Staphy-
lococcus aureus (4); Klebsiella and Pseudomonas were each isolated once.

**COMPLICATIONS**

There were no deaths. Two patients (6.5%; 1 TTD, 1 salvage VATD) were readmitted for recurrent fever unrelated to pleural space infection. One child (3%) had a mild upper gastrointestinal hemorrhage but did not require transfusion. There were no anaphylactic reactions or bleeding associated with UK. Two children (6%) undergoing FT developed air leaks that resolved when UK was stopped.

**COST ANALYSIS**

The mean hospital charge was $78832 (TTD, $75450; salvage VATD, $107476; primary VATD, $69634). Substratification of the TTD-only group (n=23) into patients receiving no more than 2 chest tubes (n=19) vs those receiving more than 2 tubes (n=4) revealed that the former group incurred the lowest hospital charges ($54147) and the latter group the highest charges ($176642) (P=.09). A detailed breakdown of the charges is given in the Table.

**COMMENT**

In 1982, the Mayo Clinic, Rochester, Minn, defined the goals of treating thoracic empyema: to save lives, to minimize morbidity, to reduce hospital stay, and to restore respiratory function. Therapeutic controversy arises when one considers the treatment options available and realizes the existing potential for undertreatment or overtreatment of a disease with a known continuum of pathologic severity. During the early (exudative) phase of empyema, the fluid is thin and communicates throughout the pleural space. In these patients, TTD should be adequate treatment. With disease progression into the second (fibronodular) phase, the fluid becomes gelatinous with fibrin strands, loculations, and adhesions. A more aggressive approach to debridement of the pleural cavity becomes necessary in countries where the resources are available; however, some practitioners in Third World countries report success with TTD, weeks of hospitalization, and intravenous antibiotics. Recently, reports demonstrate that VATD may cause less pain and shorten the LOS compared with prolonged TTD or thoracotomy. The last phase (organized) is characterized by increased cross linking of the fibrin, trapping bacteria in the interstices as fluid reabsorbs. The VATD or thoracotomy will be necessary; fortunately, this stage is uncommon in children.

To customize treatment strategies for empyema based on disease severity, we developed an algorithm that uses chest imaging (plain radiographs and CT scans) to stage the empyema and select appropriate treatment. Routine radiography is helpful early in the exudative phase, but only findings from CT scan with intravenous contrast can delineate the 3-dimensional nature of the sometimes complicated findings (pneumonia, pulmonary necrosis, pneumatoceles, lung abscesses, BPF, pneumothorax, or empyema) and provide a surgical road map. It also helps distinguish confounding diseases such as subdiaphragmatic abscess and malignant pleural effusion from tumor in the lung, chest wall, mediastinum, or liver. Initially we used CT findings of pleural thickening and contrast enhancement with the presence of loculations to predict advanced disease. However, chest ultrasonography is better than CT at quantifying fibrin, the main determinant of stage, and we began using it recently when experienced radiology personnel became available.

The frequency of imaging studies can be rationalized. We routinely obtain preoperative chest radiographs (2 views) and chest CT with or without chest ultrasound. A follow-up CT scan is performed prior to chest tube removal if lung findings confound the interpretation of plain chest radiographs. During the 4-day time lag to salvage VATD, we administered FT. While this will prevent disease progress, the TTD failures could have been prevented if early CT scans had documented thick pleural loculations. Long-term follow-up with 1 or 2 monthly chest radiographs should suffice to document the resolution of pneumatoceles and infection. The incidence of permanent sequelae is extremely low.

The success of FT with UK as an adjunct to TTD has been previously reported. We feel its use should be confined to a 3- to 5-day period after chest tube placement and may prevent but should not delay further the need for surgical drainage. Recently, UK was removed from most dispensars on realization that it is derived from the kidneys of dead infants. A recombinant product is awaited, but until it becomes available, VATD will be necessary more often.

One of the apparent shortcomings of our algorithm was its inability to predict 4 treatment failures in the TTD group. These patients incurred longer hospitalizations and higher costs, with a mean lapse of 4 days between TTD and salvage VATD.
salvage VATD. Donnelly and Klosterman reported the non-specificity of the CT appearance of empyema, as defined by pleural fluid analysis in 30 children with parapneumonic fluid collections, concluding that CT characteristics of such collections alone are inadequate predictors of appropriate therapy. This fact may explain the TTD failures and favor the use of chest ultrasonography.

Recognizing the limitation of our small sample size, especially in the primary VATD group, we were nonetheless surprised by the LOS and cost data that would seem to advocate primary VATD for all patients. However, when we stratified our 23 TTD patients into those treated with no more than 2 chest tubes (n=19) and those receiving more than 2 chest tubes (n=4), we noted a doubling of LOS (12 vs 25 days; P=0.049), and tripling of charges ($54,147 vs $176,642; P=0.09). In retrospect, these 4 patients might have been more expeditiously and inexpensively treated with primary VATD. The 19 patients treated with 1 or 2 chest tubes had a LOS comparable to that of the primary VATD group and incurred fewer charges ($54,140 vs $69,630; P=0.19). This suggests that for most patients presenting with early stage disease, TTD is still the most appropriate therapy.

With the exception of the occasional patient requiring thoracotomy, most children with advanced pleural space disease can be cared for with VATD. However, it is important to acknowledge the small but real potential for complications, which include bleeding, BPF, carbon dioxide embolism, and damage of the diaphragm and mediastinal structures. The operation is best performed with single-lung ventilation. This can be tricky in smaller children who either require mainstem intubation or endobronchial balloon occlusion. Thus, we reserve VATD for those patients with advanced disease at presentation or those who fail an initial, more conservative treatment approach.

The ideal management for all patients with parapneumonic fluid collections ranging from thin exudates to organized, infected fibrin is best predicted by an algorithmic analysis of their clinical and radiographic presentation. The limitations of the imaging modality chosen must be recognized and steps must be taken to identify treatment failures early. Only a randomized prospective multicenter trial will be able to define the ideal imaging modality and the role of TTD, FT, and VATD in the management of this diverse group of patients.

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REFERENCES


DISCUSSION

Eric W. Fonkalsrud, MD, Los Angeles, Calif: This study covers a short time period and has no randomized features as was just pointed out. However, it does cover several salient aspects in the current management of empyema in young children and brings up several questions for discussion. I hope I don’t bring up too many of these questions for discussion.

With the current array of sophisticated diagnostic studies available and the number of effective antibiotics, it is surprising that one hospital would encounter such a large series
of empyema in young children, the average age being 5 years, and they had 18 patients within the past year. I wonder if you believe that the recent flu epidemic is at all related to the increased frequency of empyema in this group of patients.

All patients received antibiotics before the empyema was treated surgically. How is the choice of these antibiotics made? Is thoracentesis ever recommended to obtain a culture? It is noteworthy that the antibiotics used in the present study cost more than $10000 per patient if you look at the expense analysis that was just provided. Computed tomography scans were used to evaluate patients during treatment, an average of about 2.71 CT scans per patient. Could the less expensive ultrasound be used for follow-up in some of these evaluations rather than the more expensive CT?

The importance of early drainage of the empyema with a large tube is supported by the authors since delayed drainage commonly is followed by development of a pleural peel, which requires more complex management. Could the authors tell us how large a tube is used for these small children and where in the chest it is placed? Twenty-two of the 27 children treated with a chest tube subsequently received urokinase infusions. How was this decision made, or perhaps should all patients drained by chest tube in today’s setting receive urokinase from the beginning? The dose of urokinase used by the authors was considerably less than that used by Rogers and others in previous reports treating pediatric empyema. How effective is the urokinase in spreading throughout the areas of a thickened peel between the lung and chest wall? Could you tell us what complications you encountered with the urokinase, which is somewhat controversial in the pediatric surgical literature? Is an antibiotic flush ever placed into the chest tube? How do you decide when to place a second tube? This was used in almost half of the patients in your series? Your data suggest that when more than one chest tube is used, the length of treatment and the cost go up considerably. Why wouldn’t you therefore use thoracoscopic debridement for all patients who require more than one chest tube? How do you decide when to remove the chest tube, and do you ever convert the closed chest tube to open drainage as has been used effectively so often in past years?

It is clear from this very well-presented report that specific antibiotic therapy and early tube drainage, perhaps with urokinase infusion for pediatric empyema, is the optimal treatment. For those with a thickened peel, early thoracoscopic debridement and large tube drainage would appear advisable. Could the authors tell us if there is any further role for the traditional open pleural debridement in current practice?

James B. D. Mark, MD, Stanford, Calif: I do not wish to take exception with the authors’ recommendation to make treatment decisions mainly on the radiographic and ultrasonographic appearance of the effusion, but to add another dimension, at least to emphasize another. And that is the clinical picture presented by the patient. If a tube is placed early, good culture information obtained, and appropriate antibiotic treatment instituted, most of these youngsters will improve clinically. But the radiographic appearance of the effusion may not improve as dramatically or as rapidly. My plea is to consider the patient’s clinical response to treatment before deciding to intervene further. The child’s pleura has remarkable powers of recuperation. Let me show you a few slides.

Here is the x-ray of a youngster with a big left empyema that was treated with a chest tube and drainage and appropriate antibiotics. This happened to be a staphylococcal empyema. Here we are a few days later and the radiographic appearance is no better, but the patient is considerably better. Just a few days later the tube has been removed, but we see bad things beginning to happen. The child is getting scoliosis, there is a restriction of the left side of the chest, but again the clinical situation is better. The question now is, do we do a thoracotomy for decortication, or do we continue nonoperative treatment? We decided to follow this patient clinically, and engage the patient in exercises to improve the restriction in the chest. Six weeks later we see a nice improvement, and 6 weeks following that we see the appearance of a hemithorax that all of us would be proud of if we had operated on that child. To repeat an old adage. When all else fails, examine the patient.

Jack H. Bloch, MD, Bakersfield, Calif: Most of us have grown up with the conventional wisdom that pediatric empyemas are largely staphylococcal. In the last 10 years, we have been seeing a significant change, and most of our empyemas, both in children and in adults, are becoming streptococcal pneumonias or pneumococcal pneumonias. It’s nice to think that a healthy pleura will heal itself, but with this particular organism, that doesn’t seem to happen. Most often we see the infection controlled by the pediatrician with an appropriate antibiotic, but the lung does not improve, the pneumonia doesn’t change, and on chest x-ray and later CT scan we see a Swiss cheese appearance of a fibrin material with a lot of stuff that looks like fluid but in fact is gelatinous. Nothing is removable through a chest tube. Are pneumococcal empyemas a peculiar subset of empyemas that you are dealing with in some different way? When we proceed to decorticate a lung, the traditional decortication is done open and removes both the parietal and the visceral peel. When one decorticates with a laparoscope or thoracoscope, removing the visceral peel is often very difficult. The third problem concerns the natural history of empyema in pneumococcal pneumonia. Most often what I find feeding the empyema are small ruptured lung abscesses on the diaphragmatic surface of the lower lobe since pneumococcal pneumonia tends to be a lower lobe pneumonia.

I would like to ask 4 questions. Does the organism involved in the empyema make a difference in your treatment algorithm? Second, what is the window of opportunity in the face of ongoing consolidative pneumonia in the lung and the presence of this Swiss cheese fibroglatinous empyema to determine the ideal time in which to conduct an operation when you have missed the early opportunity if it ever existed for tube drainage? Third, what in your practice is replacing urokinase since it is no longer available, and what fibrinolytic treatment regimen or algorithm are you suggesting? Often even in the small children there is a half pound of fibrinous to fibrous material in here along with the gelatin, and it would seem to me that one must take a large amount of fibrinolytic agent to be able to dissolve that. When you have a pneumococcal empyema in elderly adults, you can sometimes have 3 pounds of material in the empyema, a real challenge for fibrinolysis. Finally, how complete a visceral decortication do you try to accomplish, and what do you do about the ruptured lung abscess along the diaphragmatic surfaces?

Dr Harrison: Let me try to put some of the questions together. Dr Bloch and Dr Fonkalsrud wondered why there are so many kids. There are 2 possible explanations. One might be the virulence of the disease. Certainly we hear from our colleagues around the country that there is more empyema. In the last Journal of Pediatric Surgery, Phil Gazetta’s group in Dallas looked at 131 kids they had treated. So it may be that the virulence of the disease is getting worse. That is one factor. But the second factor is certainly our relationship with our pediatrician friends. Are they holding on to these patients longer so that we see the bad ones at the end? Or are they coming around to our view that our new surgical therapies, particularly the VATDs, is saving time and money and they are therefore sending to us earlier. Our pulmonologists are certainly coming around to that view.

The second question had to do with thoracentesis and antibiotics. I guess the answer is that most of the kids that we see have been treated with antibiotics of which we have no con-
Thoracentesis I think is always appropriate but frequently negative because they have already been treated with antibiotics, and what we are left with is the anatomic problem of debris in the pleural space.

The next question addressed the important question of how to figure out those kids who don’t need our surgical intervention—the early ones with thin exudates who can be effectively treated with a tube. The issue is CT or sonogram. There is some evidence accumulating that sonograms may be better at figuring out the nature of the fluid—how much fibrin, how thick and goopy is it? If you put even a fairly big tube in, will you get anything out? If the material is very thick, you are not going to get anything, and those kids need a surgical solution.

The next question had to do with the thrombolytic agent itself, urokinase. I think urokinase probably won’t be used at all because it is politically incorrect; it has been collected from the kidneys of infants in underdeveloped countries. Will there be another fibrinolytic that won’t have that problem? Yes, of course. There will probably be a recombinant fibrinolytic.

The next issue is the surgical technique. Let’s say that we can pick out those kids who really need surgery. We suggest in this study and others have suggested that it is best done early in the course. We need to clean out the pleural space, get the pleural surfaces together, take care of those little abscesses at the base, and get the job done. If the question is whether we should go back to the old fashioned way of making an incision in the chest, cleaning out the junk, putting in tubes, cutting them off, sending them home, I think the answer is no. The scope is pretty good, but the actual visualization is not the crucial thing. You make a couple of holes in the chest, put instruments in, pull some stuff out, then put your tube in the right place under visualization.

The real question is, when you have a kid who fits this category, do you take him to the operating room, give him general anesthesia, and get the job done or do you put in tubes and let our pediatric colleagues look after him? That question of course was not answered and could not be answered by this small retrospective nonrandomized study. But the question needs to be answered. The only way is for surgeons to roll up our sleeves and do a proper randomized trial. What stands in the way? Our own reluctance to look our patients in the eye and say, you know what? I don’t know what is the best way to treat this disease. Right now, I don’t know what the best treatment is: surgery or drainage. Would you be willing to decide this by the flip of a coin? I think we should do a proper randomized trial of early intervention with VATDs technique vs tube drainage and fibrinolytic therapy. We have the right group to do it. The usual limitation is having a critical mass of colleagues who are like minded and have suspended their prejudices enough to pull it off. I think we can do it with the group at UCSF and Stanford.