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REVIEW / DERLEME

Empyema in children

Çocuklarda ampiyem

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ABSTRACT

Empyema is the infection of the fluid in the pleural space due to different causes. The most common cause of empyema in children is parapneumonic effusion. Although its frequency has decreased significantly with the use of antibiotics, it is still a significant cause of morbidity and mortality worldwide. The main aim in the treatment of empyema is to drain the pleural cavity to provide reexpansion of the compressed lung, to treat the parenchymal infection with appropriate antibiotic therapy, and to prevent complications that may develop in the acute and chronic periods. Treatment options for this disease vary depending on the stage of the disease. Treatment success in childhood empyema detected at an early stage is high. The diagnosis and treatment of empyema in children differs from adults. Due to rapid tissue regeneration in childhood, healing can occur without the need for aggressive treatment options.

Keywords: Children, empyema, parapneumonic effusion, pleura, tube thoracostomy.

ÖZ

Ampiyem, farklı nedenlere bağlı olarak plevral aralıkta oluşan sıvının enfekte olmasıdır. Çocuklardaki ampiyemin en sık nedeni parapnömonik efüzyonlardır. Antibiyotik kullanımı ile sıklığı belirgin olarak azalmış olsa da dünya genelinde halen ciddi bir morbidite ve mortalite nedenidir. Ampiyemin tedavisinde ana amaç plevral boşluğun drenajı ile bası altındaki akciğerin re-ekspansiyonunun sağlanması, uygun antibiyotik tedavisi ile parankimal enfeksiyonun tedavi edilmesi ile akut ve kronik dönemde gelişebilecek komplikasyonların önlenmesidir. Bu hastalığın tedavi seçenekleri hangi evrede bulunduğuna göre değişmektedir. Erken evrede tespit edilen çocukluk çağı ampiyemlerindeki tedavi başarısı yüksektir. Çocuklardaki ampiyem tanı ve tedavisi erişkinlerden bazı farklılıklar göstermektedir. Çocukluklardaki hızlı doku rejenerasyonu nedeniyle agresif tedavi seçeneklerine gerek kalmadan iyileşmeler görülebilmektedir.

Anahtar sözcükler: Çocuklar, ampiyem, parapnömonik efüzyon, plevra, tüp torakostomi.

Although empyema is frequently known as purulent fluid accumulation in the pleural space, accumulation in other body cavities is also called empyema. Although it frequently develops after pneumonia, many factors can cause empyema. Interventions performed after early detection are favorable, but late cases may have a mortal course. It is thought that Hippocrates used the open drainage method for empyema in 500 BC.[1] Hawit applied the closed tube drainage method in 1876, which is the main treatment of empyema.[2] Thoracoplasty by Eastlander and Shede and decortication operations by Kuster and Fowler have been applied for empyema.[2] It is useful to sufficiently know the formation process to better understand empyema.

PLEURAL EFFUSION

Fluid accumulation in the pleural area is called pleural effusion. In the pleura adjacent to the pneumonic area, fluid in the form of protein-rich exudate begins to accumulate due to impaired permeability of mesothelial cells. The fluid, which can initially be removed by pleural lymphatics, begins to accumulate in the pleural space over time when the capacity is exceeded.[3] In the early 20th century, before the use of antibiotics, it was known that approximately 10% of patients developed empyema after pneumonia. A rapid decrease was observed in this rate due to the use of antibiotics. However, empyema is still an important health problem despite the use of broad-spectrum antibiotics all over

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the world, particularly in developing countries. The most common cause of pleural effusion in children is pneumococcal pneumonia. Parapneumonic empyema in children is a significant complication observed in approximately 0.6% of patients with bacterial pneumonia. Despite potent antibiotics and improved intensive care facilities, mortality in children with empyema is still significantly high (6-12%). In parapneumonic effusions, it is known that pleural effusion usually regresses even with treatment of pneumonia alone. However, surgical intervention is required in about 10%.[2]

Pleural effusion is divided into three types: dry (plastic) pleurisy, serofibrinous pleurisy, and empyema (purulant pleurisy). In dry pleurisy, a small amount of yellow and serous fluid is found in the pleural space, usually as a result of inflammation of the visceral pleura. It is usually encountered after acute bacterial pneumonia and upper respiratory tract infection but can also be observed in tuberculosis, collagenoses, and lung abscess. Serofibrinous pleurisy is seen in all lung, mediastinal, and abdominal infections, usually tuberculosis. It is usually unilateral. The potential for pleural adhesions is high. Empyema (purulent pleurisy), is the infected state of pleural fluid. It appears as a result of untreated pleural effusion.

Different stages are observed during the development of empyema.[4] In the pleuritis sicca stage, inflammation in the lung first affects the visceral pleura and then the parietal pleura. Pleuritic chest pain occurs when the parietal pleura is affected. With appropriate treatment, it can be terminated before pleurisy develops. In exudative stage, increased permeability as a result of pneumonia results in a sterile fluid in the pleural space. Pleural fluid is usually clear, sterile, and in small amounts. Glucose and pH are normal, lactate dehydrogenase (LDH) is <1000 IU/L, and it contains a small amount of polymorphonuclear leukocytes. Antibiotic alone is an adequate treatment at this stage (Figure 1).[5] Inadequate or no treatment leads to a rapid transition to the fibropurulent stage. Pleural fluid has a dense consistency and is abundant. Fibrin membranes forming loculations in the pleural space due to numerous polymorphonuclear leukocytes, bacteria, and cell debris are observed. Antibiotics cannot penetrate well into the empyema cavity. Although tube thoracostomy is the appropriate treatment, the success of thoracentesis and tube thoracostomy decreases due to loculations. Lung expansion becomes difficult due to inadequately drained fluid. Glucose and pH decrease and LDH rises >1000 IU/L. It is the most common stage at the time of diagnosis. In organization stage, the loculations are separated by thick layers due to dense fibroblast formation. Expansion of the lung becomes difficult due to the dense layer formed on the visceral and parietal pleura. Pleural fluid is very dense, pH is <7.0, glucose is <40 mg/dL, LDH is >1000 IU/L,

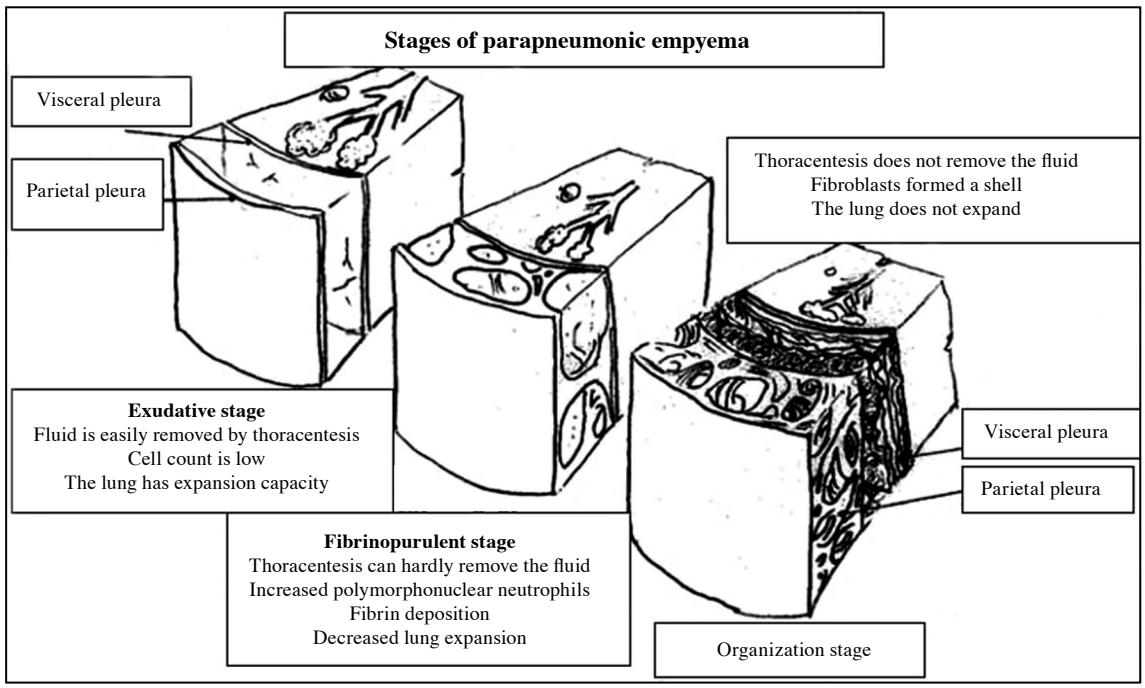

Figure 1. Stages of parapneumonic empyema.

and leukocytes are >15,000/mm^3. The septic focus formed in organized empyema causes the patient to have a chronic patient appearance, developmental retardation, and inadequate respiratory reserve.[6] It occurs as a result of untreated pleural effusion in other stages. Untreated cases result in bronchopleural fistula, empyema necessitates, and permanent loss of lung function.[7] At this stage, the success of treatment with thoracentesis and tube thoracostomy is very low.

ETIOLOGY

Empyema in children often develops after pneumonia that has not been treated properly. Trauma, thoracic and cardiac surgeries, collagenoses, rheumatological diseases, metastases, and cardiac diseases are other causes.

Bacteriological evaluation of infected pleural fluids in children is slightly different from adults. Although the causative agents vary according to age in children, *Haemophilus influenzae* type B, *Streptococcus pneumoniae*, and *Staphylococcus aureus* are the most frequently isolated microorganisms. *Staphylococcus aureus* is the dominant pathogen in developing countries, and it increases in hot and humid months. Anaerobic microorganisms are rarely detected. It is more common in boys than girls. Although most children are healthy in the period before the formation of empyema, underlying predisposing diseases are also reported.[5]

DIAGNOSIS

Patients with aerobic empyema often have fever, malaise, nonproductive cough, pleuritic chest pain, dyspnea, and weight loss.[8] Severe respiratory distress may be observed in infants. An increase in symptoms in children followed for pneumonia should suggest empyema. Anaerobic empyema is rare in children. In children who develop chronic empyema as a result of delay in diagnosis and inappropriate treatment, signs of chronic lung disease such as anemia, clubbing, and weakness may be detected.

Physical examination reveals fever, tachypnea, decreased chest movements, decreased respiratory sounds, and dullness on percussion in the affected hemithorax. In chronic cases, discharge from the chest wall and dense sputum suggestive of bronchopleural fistula may be observed. Chest deformities and scoliosis may be detected.

In addition to bidirectional chest radiographs, decubitus radiographs may be taken to detect pleural fluid loculations. X-ray findings are similar to those in serofibrinous pleurisy. Atelectatic lung and pleural fluid cause similar opacity on chest radiographs. If pleurisy increases to cover the whole hemithorax, the heart and mediastinum are pushed to the healthy side.

Computed tomography (CT) is the gold standard radiological imaging in the diagnosis of empyema. However, in a patient with pleural effusion, a CT scan may be recommended as the first radiological examination if the fluid cannot be aspirated in thoracentesis or if tube thoracostomy is not beneficial. Computed tomography performed after drainage is valuable for parenchymal evaluation. Computed tomography is used to evaluate the location and viscosity of loculated fluid and parenchymal damage. Ultrasonography (USG) is useful for the diagnosis of pleural effusion and the location of planned thoracentesis, particularly in young children.[9]

Thoracentesis is the most sensitive and specific diagnostic method in the diagnosis of pleural effusion and empyema. Pleural fluid obtained with 18- to 20-G (Gauge) needles is examined macroscopically, microscopically, biochemically, and microbiologically. If the pleural fluid is light in color, transudate-exudate differentiation should be made. However, there are also publications stating that the criteria in adults are not valid in children.[10] Gram staining, aerobic, anaerobic, and, if suspected, tuberculosis culture should be performed in pleural fluid. The fluid's pH can be evaluated. Purulent fluid is diagnostic for empyema.

TREATMENT

The main aim in the treatment of empyema is to drain the pleural cavity to provide the reexpansion of the compressed lung, to treat the parenchymal infection with appropriate antibiotic therapy, and to prevent complications that may develop in the acute and chronic period. Meanwhile, nutritional support is beneficial for patients who are in a weakened state. If there is another underlying disease, it should be diagnosed and treated. There are treatment options such as repeated thoracentesis, catheter applications, closed underwater drainage with tube thoracostomy, open drainage, fibrinolytic therapy, thoracoscopy, and decortication with thoracotomy.[7] Success in treatment often depends on the stage and treatment of empyema (Table 1).[2]

In addition, the isolated bacteria, response to initial treatment, and the degree of lung entrapment also affect the success of treatment. In general, antibiotics, repeated thoracentesis, and tube thoracostomy are recommended in the early exudative and early fibropurulent phase. In cases that cannot be treated

Table 1. Classification and treatment of parapneumonic effusion and empyema

	Name	Explanations	Treatment
1	Indeterminate pleural effusion	Less than 10 mm thickness on decubitus radiographs	Thoracentesis is not required.
2	Typical parapnomonic pleural effusion	Thicker than 10 mm. Glucose >40 mg/dL, pH>7.20, Gram stain and culture negative	Only antibiotics
3	Borderline complicated pleural effusion	7.00<pH<7.20 and/or LDH>1000 IU/L, Glucose>40 mg/dL, Gram stain and culture negative	Antibiotics and serial thoracentesis.
4	Simple complicated pleural effusion	pH<7.00 and/or glucose<40 mg/dL, and/or Gram staining or culture positive, No loculation and no obvious pus	Tube thoracostomy and antibiotics
5	Complex complicated pleural effusion	pH<7.0 and/or glucose <40 mg/dL, and/or Gram stain or culture positive, multiloculation	Tube thoracostomy and thrombolytics
6	Simple empyema	There is obvious pus. Single pouch or easy-flow.	Tube thoracostomy + decortication
7	Complex empyema	Obvious pus. Multiloculated	Tube thoracostomy and thrombolytics. May require thoracoscopy or decortication

LDH: Lactate dehydrogenase.

with tube thoracostomy, intrapleural fibrinolytics should be added to the treatment. If no results are obtained despite this, good results can be obtained by deloculation with VATS (video-assisted thoracoscopic surgery). It is useful to avoid decortication in children.

TREATMENT IN THE ACUTE PERIOD

The fluid obtained by thoracentesis in this period may have different densities. The aim of treatment in this period is to drain the pleural fluid urgently, control the infection, and eliminate the pleural dead space. If serous fluid is aspirated during thoracentesis, repeated thoracentesis and antibiotics may be sufficient. If there is purulent fluid, glucose <40 mg/dL, pH <7, or positive findings on gram staining, tube thoracostomy should be performed. If the lung is unlikely to be extensible, tube thoracostomy may contaminate the pleural space. In a study, VATS was used as the first choice in patients hospitalized for empyema.[11] It is useful to investigate the presence of an endobronchial tumor by bronchoscopy. Antibiotic treatment should be continued for six weeks. In more advanced stages, tube drainage becomes difficult with the increase of dense fluid and fibrin walls. Drainage should be provided by reaching localized areas with CT or USG guidance, and surgical drainage should be considered if no benefit is obtained.

TREATMENT OF CHRONIC EMPYEMA

Empyema may become chronic in untreated or inappropriately treated patients, in the presence of endobronchial obstructive lesions, in residual cavities after surgery, and after conditions such as tuberculosis and interstitial lung disease. In this stage, it should be aimed to evacuate infected material and fibrin deposits, reexpand the trapped lung, reestablish the movement of the chest wall and diaphragm, restore respiratory functions, reduce the length of hospital stay, and reduce morbidity and mortality. Tube thoracostomy should be tried first. If the empyema cavity has thick walls and there is no reduction in the dead space, decortication can be performed after the inflammatory reactional phase has passed. After decortication, the lung may expand and fill the dead space. It is known that the best results are obtained in the early chronic phase of empyema secondary to traumatic hemothorax and pneumonia.

In Türkiye, most of the empyema cases are in the chronic stage, and usually, repeated thoracentesis is not a good option. A large diameter chest tube will both help to drain the fluid and provide preparation for possible decortication.

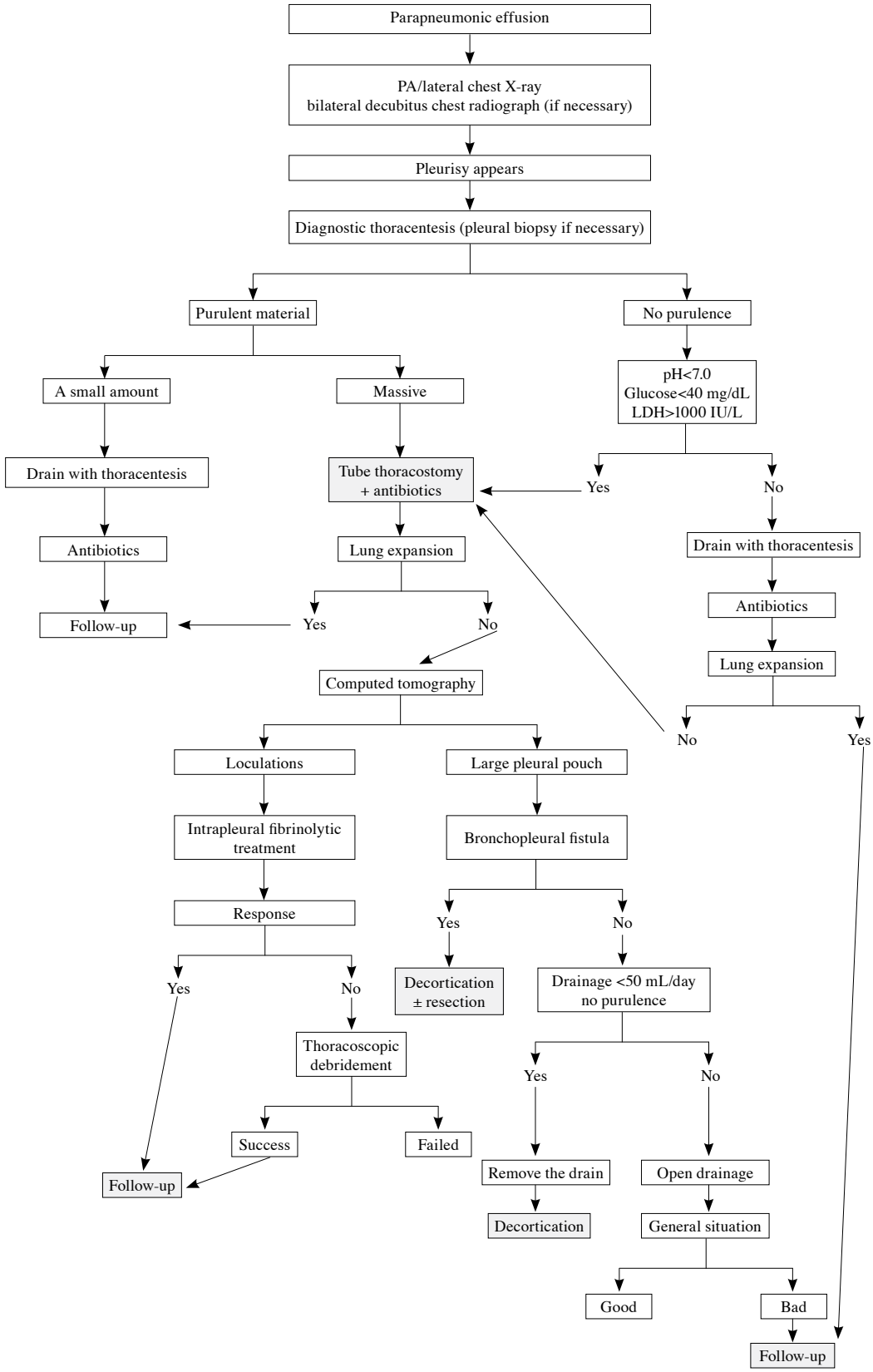

Figure 2. Diagnosis and treatment algorithm for childhood parapneumonic effusion and empyema.

TREATMENT METHODS

If pleural effusion is suspected on imaging, thoracentesis should be performed. For thoracentesis, 18- to 19-G needles are used. Treatment should be decided quickly as a result of pleural fluid investigations obtained during thoracentesis. Leukocyte count, gram staining, culture, and glucose and LDH values should be checked. Repeat thoracentesis may be beneficial, but this method is appropriate in older children who can tolerate local anesthesia and sedation. Gram staining and culture results are negative in most patients.[12] Effusions may vary from clear and odorless to green, dark, and malodorous. The repulsive, fecaloid odor of pleural fluid suggests anaerobic infection. Patients benefit from broad spectrum antibiotics. Third generation cephalosporin or clindamycin may be the initial treatment, but it would be better to decide on the choice of antibiotic according to the antibiogram (Figure 2).

Dark and purulent thoracentesis fluid suggests empyema and tube thoracostomy should be performed immediately. The treatment success rate of tube thoracostomy alone is 80-90%.[13] However, fluid examination is still recommended for nonempyema diseases, in which pleural fluid may be dark. Failure of tube thoracostomy is usually due to inappropriate localization and small diameter chest tubes. Localization should be determined by USG or CT if necessary, and the largest diameter chest tube possible should be used. Applying negative pressure to the chest tube will help lung expansion. The therapeutic properties of negative pressure and endobronchial valves have been demonstrated in adults, but their application in children is not possible due to anatomical features.[14,15] If necessary, a second chest tube should not be hesitated. The chest tube can be removed when the daily drainage decreases to 50 mL and the lung expands on chest radiography. Antibiotic treatment should be continued for six weeks after the chest tube is removed (Figure 3).

In localized pleural effusions, intrapleural fibrinolytic agents can be used for enzymatic lysis of pleural adhesions and debridement. For this purpose, agents such as streptokinase, urokinase, alteplase, and tissue plasminogen activator are used.[16,17] Dose calculation is made according to height and weight

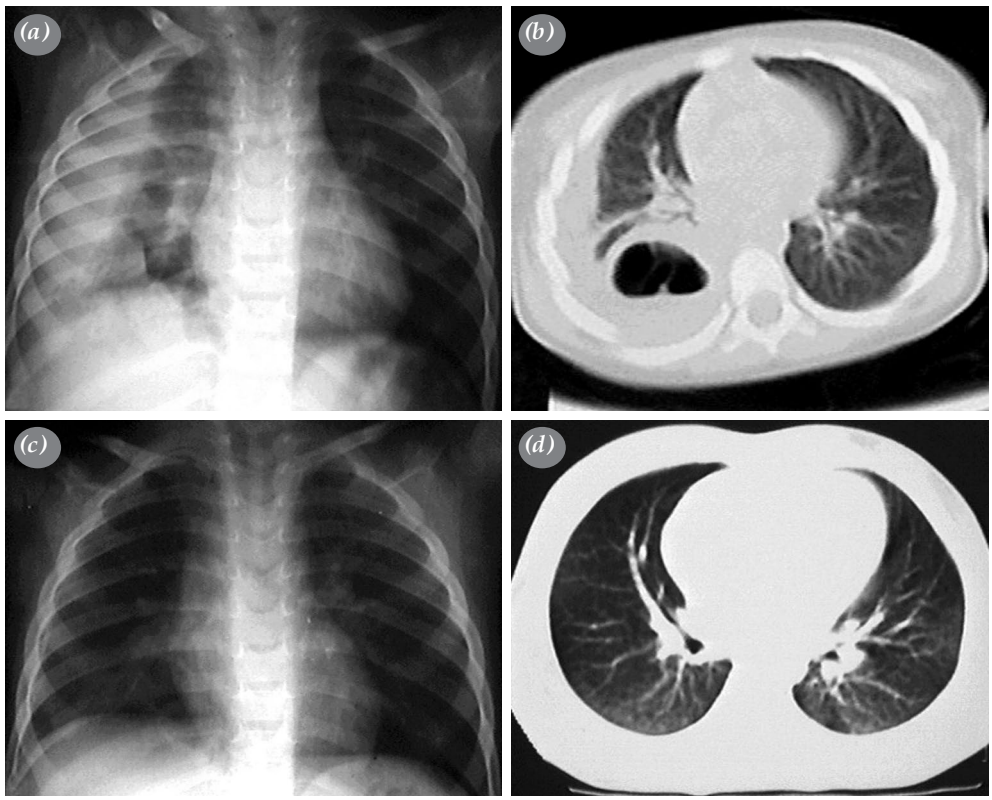

Figure 3. (a) Chest X-ray of a patient with empyema. **(b)** Thorax CT of a patient with empyema. **(c)** Chest X-ray after treatment. **(d)** Thorax CT after treatment.
CT: Computed tomography.

in children, and the agent to be used is diluted with saline and given into the intrapleural space. It is appropriate to keep the fibrinolytic agent in the pleural space for 6-8 h. This procedure can be repeated daily to increase its success. It has been shown that 1 mg of tissue plasminogen activator applied to the intrapleural space is 97% successful.[18] Fibrinolysis with tube thoracostomy has been shown to be superior to chest tube drainage alone.[19] It should be kept in mind that side effects such as major hemorrhage, fever, pleural pain, and anaphylaxis may occur in intrapleural fibrinolytic treatments.

In cases where tube thoracostomy and fibrinolytic therapy are not successful, thoracoscopy can be used for separation of loculations and debridement. In pediatric empyema, VATS is considered to have some advantages over open surgery due to safety, efficacy, shorter hospital stays, and earlier recovery.[20] One study showed that one third of patients previously treated noninvasively needed invasive treatment modalities.[21] However, the most important disadvantage is that it cannot be performed without general anesthesia.

Although open drainage is a treatment method in adults, it is not suitable for use in children. It is known to cause skeletal deformities in children in late periods (Figure 4).

Although the treatment of children with parapneumonic empyema is similar to that of adults, there is still controversy. There are publications advocating the benefit of early decortication.[22] On the other hand, there are publications stating that surgical interventions are rarely necessary.[23] Decortication/ pleurectomy may be preferred in patients who cannot be treated with other treatment methods. With this method, all fibrous tissues on the visceral pleura that cause lung entrapment are peeled off, and the purulent fluid is removed from the pleural space.

The aim is to fully expand the lung so that no fluid accumulates in the pleural space again. At the same time, if the parietal pleura is very thick and restricts the movement of the thorax, peeling it will increase the success of treatment. The operation is performed by entering the thorax through the fifth intercostal space as standard. Empyemectomy, which is the process of completely removing the empyema sac, can be performed. Regional vascularization is increased due to chronic infection. It should be kept in mind that massive hemorrhages may occur during the operation and blood supply should be ensured. Although aggressive surgical interventions such as thoracoplasty can be performed in adults, it is not recommended in children.

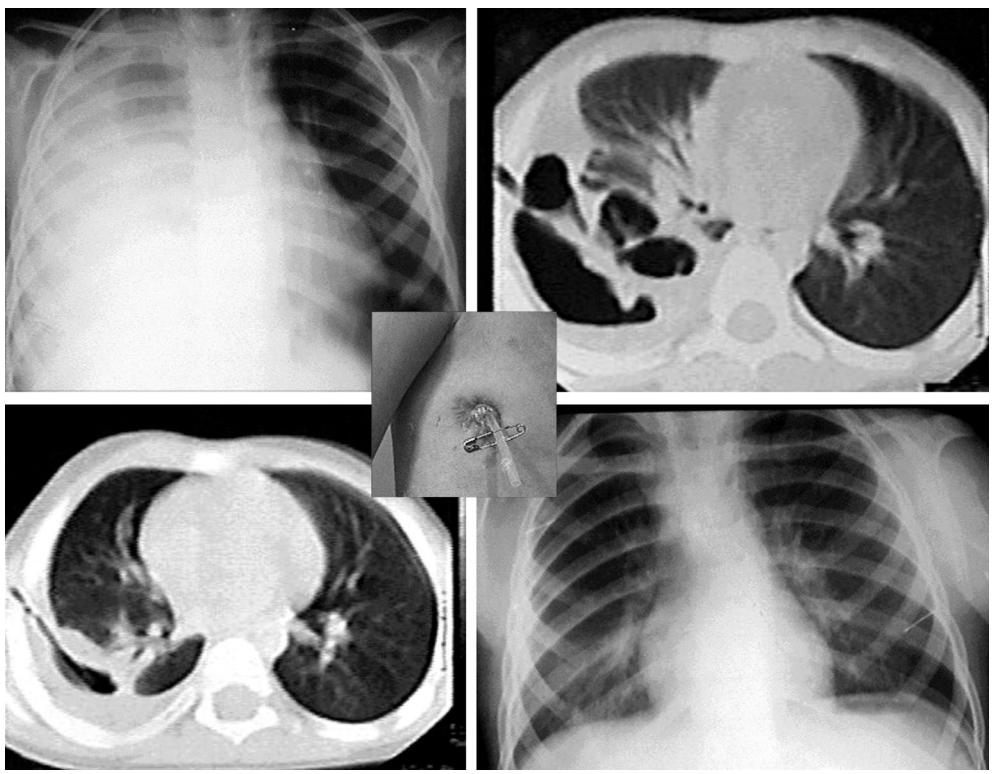

Figure 4. Pre- and posttreatment images of a patient with open drainage.

In conclusion, the most common cause of empyema in childhood is pneumonia. The results are favorable with prompt drainage and appropriate antibiotic use. Unlike adults, it is beneficial to avoid more aggressive surgeries, such as thoracotomy, since pleural thickening is likely to spontaneously resorb with appropriate treatment in children.

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