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Case report

Loculated empyema in a neonate successfully treated with chest tube thoracostomy and antibiotics

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ABSTRACT

Empyema thoracis, defined as the accumulation of pus in the pleural space, is a rare entity in the neonatal period. There are very few cases described in the medical literature and there are still no treatment protocols in the management of empyema in neonates. In older infants and children, intrapleural fibrinolytics and surgery are often utilized since treatment of complicated parapneumonic effusions with chest tube and antibiotics alone often fail due to the viscous fluid and presence of loculations. Presented here is a case of a term neonate who exhibited symptoms of respiratory distress on the sixth day of life. Imaging modalities revealed massive left sided pleural effusion with loculations and mass effects. Pleural fluid was grossly pus and exudative in nature. Gram stain revealed gram-positive cocci but culture was negative. Empiric broad-spectrum antibiotics and chest tube drainage were utilized and patient was discharged after forty-seven days of hospital admission. In spite of prolonged hospital stay, patient survived with no complications. Therefore, nonoperative therapy could still be an option for neonates with loculated empyema. The key to success in treatment is immediate identification of effusion, prompt initiation of antibiotics, and early effective chest tube drainage.

1. Introduction

Pleural effusion is the accumulation of excess fluid in the pleural cavity. It is a rare entity in the neonatal period with an estimated incidence of 20–440 cases in 20 000 neonatal admissions [1–3]. When it is associated with an underlying infection of the lung, it is termed as *parapneumonic effusion*. If left untreated, this effusion can result in fibrin deposition, loculations, and pus formation [4]. In the 18-year study by Barbosa et al., 82 (1.1%) cases of pleural effusion were diagnosed out of 7,200 NICU admissions. Among those, only 3 (4.7%) were classified as empyema [1]. Due to the paucity of cases in the medical literature, the predisposing factors, etiology, and pathogenesis in the neonate are still unclear.

Treatment of empyema was first described in the ancient texts of Hippocrates – "First, cut the skin between the ribs with a bellied scalpel; then wrap a lancet with a piece of cloth, leaving the point of the blade exposed a length equal to the nail of your thumb, and insert it. When you have removed as much pus as you think appropriate, plug the wound with a tent of raw linen, and tie it with a cord" [5]. Since then, developments in radiology, antimicrobials, and surgery resulted in further improvements in care of patients with empyema [4]. Even so, protocol in the management of empyema in the neonates still does not exist. Presented here is a rare case of complex empyema in a neonate successfully treated with nonoperative therapy.

2. Case report

A 6-day old female presented with tachypnea, circumoral cyanosis, and undocumented fever. She was born term at 38 weeks age of gestation from a 23-year old primigravid mother via spontaneous vaginal delivery at a tertiary hospital. Mother had adequate prenatal checkup and the whole pregnancy was uneventful. Mother did not have difficult delivery and the membranes were ruptured artificially 30 min prior to giving birth. At birth, the newborn had an APGAR score of 7 and 9 at 1 and 5 minutes respectively. Weight was 2,500 g, which was appropriate for gestational age. Facial features and physical examination findings compatible with a congenital anomaly were not identified. BCG and Hepatitis B vaccine were given. Patient had good suck, cry, and activity and was sent home after 48 hours. Upon follow-up at the outpatient clinic on her 4th day of life, patient was asymptomatic. Breath sounds were symmetric and no adventitious breath sounds were heard. Umbilical cord showed no signs of infection. At home, patient was exposed

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to cigarette and incense smoke. There were no household contacts with illnesses or skin lesions. Patient was exclusively breastfed until the fifth day of life when she was given formula milk. She was reported to have fast breathing and circumoral cyanosis, which spontaneously resolved after an hour. On the sixth day of life, fast breathing and circumoral cyanosis recurred after breastfeeding, now associated with undocumented fever and alar flaring. Patient was then rushed to the hospital.

At the Emergency department, patient was tachycardic, tachypneic at 70 cycles per minute, afebrile, with an oxygen saturation of 70%. Weight was 2,500 g. Alar flaring, grunting, deep intercostal and subcostal retractions were appreciated. Breath sounds were markedly decreased on the left hemithorax. Point of maximal impulse was heard at the fourth intercostal space, right parasternal area. There were no murmurs. Umbilical stump is dry with no discharge. Patient was intubated and was hooked to a mechanical ventilator. Complete blood count revealed leukocytosis (62.8 $\times$ 10^9/L) with segmenter predominance (66%). Complete opacification of the left lung with the trachea deviated to the right was noted on chest x-ray (Fig. 1). There were also hazy opacities in the right lower lung.

Patient was diagnosed with Massive Pleural effusion secondary to Neonatal Pneumonia. Vancomycin and Ceftriaxone were started. Chest Ultrasound showed approximately 205ml fluid in the left hemithorax with septations and atelectasis of the underlying lung (Fig. 2).

Chest CT scan with IV contrast was done revealing massive left sided pleural effusion with mass effects and area of atelectasis/consolidation on the posterior basal segment of the right lower lobe (Fig. 3). Chest tube was then inserted on the fourth intercostal space left mid-axillary line and pleural fluid was sent for analysis.

Pleural fluid was exudative (Table 1) and the initial drain was 40 ml. Patient then had stable vital signs and had more audible breath sounds on the left upper lung fields. Feeding via orogastric tube was started on the fifth hospital day. Both the white blood cell count and the C-reactive protein were decreasing in trend. She was then extubated on the sixth hospital day. However, chest xray still revealed no change in the amount of pleural effusion. Video assisted thoracic surgery was contemplated but was also not done since the equipment is not available at the hospital and the patient is responding to medical therapy. Chest CT scan on the fifteenth hospital day (Fig. 4) showed significant but partial regression of pleural effusion and atelectasis. Repeat gram stain of pleural fluid revealed gram-positive cocci in pairs and in clusters but culture was still negative. Ceftriaxone was given for 14 days and was then shifted to

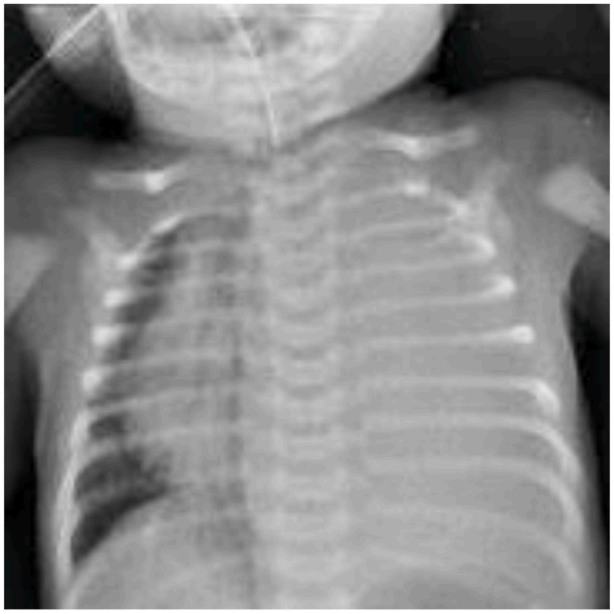

Fig. 1. Chest xray on admission.

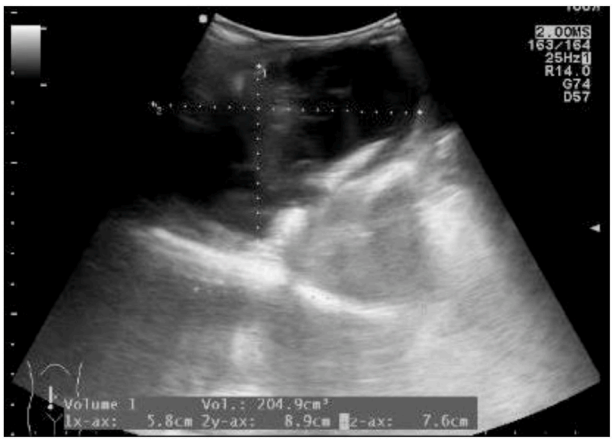

Fig. 2. Chest ultrasound, 2nd hospital day.

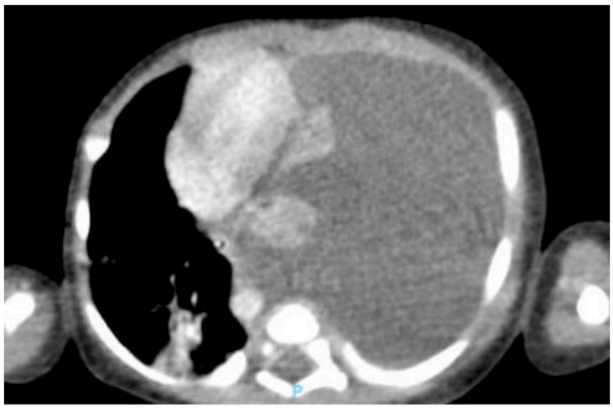

Fig. 3. Chest CT scan, 2nd hospital day.

Table 1
Pleural fluid analysis.

Pleural Fluid	
Gross	Turbid, yellow
Cell count	16,,966 cells/mcL
RBC	1,434 cells/mcL
WBC	15,.562 cells/mcL
Segmenters	73%
Lymphocytes	26%
Monocytes	1%
LDH	8255 U/L (Pleural fluid:Serum 22.7)
Protein	380 g/dL (Pleural fluid:Serum 8.8)
Glucose	11.2 mg/dL
AFB	Negative
Gram Stain	Moderate Gram positive cocci with moderate leukocytes
Culture	No growth
Cytology	Negative for malignant cells, suggestive of acute inflammatory process

Meropenem at 80mg/kg/day in 3 divided doses. On the other hand, Vancomycin was discontinued after twenty-eighth day of therapy. Intravenous Amikacin at 15mg/kg/day was added to Meropenem. Chest tube was removed at the thirty-fifth hospital day, draining a total of 467ml of pleural exudate. Meropenem was completed for 28 days and the patient was discharged after forty-seven days of hospital admission.

Patient was seen at the outpatient clinic at monthly intervals, was asymptomatic, and was steadily gaining weight. Repeat chest x-ray six weeks after discharge revealed no significant chest findings.

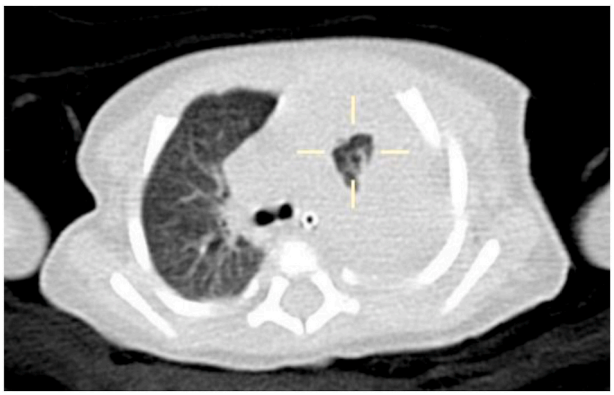

Fig. 4. Chest CT scan, 15th hospital day.

3. Discussion

Effusions can appear at any time during the neonatal period. They may be asymptomatic or present with respiratory distress. As large effusion develops, it results in tachypnea, retractions, and cyanosis [6]. As in the case presented, the patient was initially asymptomatic with normal physical examination on follow-up, and then suddenly developed signs of respiratory distress on the sixth day of life. Physical examination on admission was compatible with a massive left-sided pleural effusion. The onset of symptom was early in the patient presented but comparable to the literature reviewed. Mean age of occurrence of parapneumonic effusions or empyema in the study of *Shih* et al. was 13.5 days with a range of 6–38 days [7]. Also, in the reviewed case reports of neonatal empyema, age of occurrence was 1–24 days with a median of 7 days [8–16]. This rapid accumulation of pleural fluid without an associated prodrome is unique from the other cases reviewed. From the few case reports of empyema, neonates were noted to have poor suck [9,10], jaundice [9], pallor, and lethargy [11] for a few days before presenting with respiratory distress and physical findings of effusion. In addition, three cases were diagnosed with sepsis treated with antibiotics before symptoms of pleural effusion manifested [13–15]. All of these cases had predisposing factors that could lead to infection such as premature rupture of membranes [8,9], maternal fever in the immediate postpartum period [10,11], and prematurity with extremely low birthweight [15]. Primary immunodeficiency was ruled out through physical examination specifically the timely separation of umbilical cord, absence of congenital deformities, and characteristic facial features. Also upon follow-up, failure to thrive and recurrent infections were not noted. Hence, it could be postulated that the absence of prodrome and rapid accumulation of effusion could reflect neonate's impaired immunity and also the virulence of the infecting organism.

Chest radiograph is frequently used as the first investigation method to suggest the presence of a parapneumonic collection. Chest ultrasonography confirms the presence of a pleural fluid and it is useful to detect amount of fluid, fibrinous septations, debris or loculations in the pleural space [17]. Chest x-ray, ultrasound, and Chest CT scan were utilized in the case revealing massive left-sided pleural effusion with septations and area of atelectasis/consolidation in the right lower lung. However, in a study comparing chest ultrasound and chest CT scan in children with parapneumonic effusion, Chest CT did not provide any additional clinically useful information that was not also seen on chest ultrasound [18]. While unnecessary for most cases of pediatric empyema, it has a role in complicated cases and particularly in immunocompromised children where a CT scan could reveal other serious clinical problems [19]. In the case presented, CT scan provided an assessment of the pulmonary parenchyma (ruling out possible malformations) beneath the effusion. It also provided an accurate representation of the thoracic anatomy if future surgical interventions would be necessary.

In patients with exudative pleural effusions, the differential cell counts provide clues for the etiology of pleural effusions. High total white blood cell count (WBC) with predominance of polymorphonuclear cells, as in the case, indicates bacterial infection [20]. Bacterial infection causes a fall in pleural fluid pH and glucose with an increase in the pleural fluid LDH, brought about by increased glycolysis due to bacterial metabolism and cell lysis [21]. The result is a patient having a pleural fluid with a high LDH, low pH, and low glucose which may or may not have a positive gram stain or culture. This could be distinguished from chylothorax, which demonstrates a lymphocytic predominant exudate with an elevated protein but not LDH [22]. Pleural fluid cholesterol and triglyceride were not done since the pleural fluid of the index patient is grossly pus with an LDH $>$ 1,000, glucose $<$ 40 mg/dL, and a positive gram stain which fits the criteria of a complex empyema based on Light's classification [23].

Adequate antimicrobial treatment is the primary therapeutic target at the onset of parapneumonic effusion. While initial broad-spectrum antibiotics should cover the typical bacterial flora of the underlying disease, it is adapted to the results of the bacterial culture of the pleural samples later on [19]. However, cultures are slow and can have false-negative results because of small sample volume, previous antibiotic therapy, or unsatisfactory conditions of transport and storage which can impair the viability of pathogens [24]. This was evident in multiple studies with low yield of pleural fluid culture. In one study, only 40% of 50 pediatric patients had positive pleural fluid culture [25]. In another study of 58 children with empyema, only 39% had positive pleural fluid culture and 5% had positive blood culture [26]. This was not different from the case, since the patient had gram-positive cocci in pleural fluid gram stain but had negative blood and pleural fluid culture two days after the initiation of antibiotic.

Intravenous Cefotaxime or Ceftriaxone could be used as empiric treatment until culture results are known. Clindamycin or Vancomycin could be added if community-acquired MRSA is suspected [27]. Vancomycin and ceftriaxone were used as initial antibiotic therapy in the case and was continued for 4 weeks and 2 weeks respectively. Although there were studies demonstrating the risks of hyperbilirubinemia in neonates receiving ceftriaxone, the index patient did not have any adverse effect from this drug. Meropenem with amikacin was started due to nonresolution of effusion in the imaging studies. The effectiveness of Meropenem for neonatal infections has been assessed in small, non-comparative studies that demonstrated a favorable clinical response in neonates in whom previous conventional therapy had failed. An aminoglycoside was added for synergistic bactericidal activity [28].

Although no evidence exists for the recommended duration of treatment for empyema, a total of three to four weeks duration is reasonable if there is adequate drainage and no evidence of additional complications [29]. Normally, *H. influenzae* and *S. pneumoniae* need 7–14 days course of antibiotics while *S. aureus* needs 3–4 weeks [21]. In a case series by Sharma et al. on neonatal empyema with growths of *S. aureus*, all three cases were treated with antibiotics for three weeks in addition to intercostal tube drainage [8]. In contrast, antibiotics were used for six weeks in the case presented. Chest tube drainage was also prolonged at thirty-three days compared to the range of one to thirty days in the literature.

Chest tube drainage is indicated for complicated parapneumonic effusions. However, larger pleural fluid collections are frequently loculated. Thus, simple drainage by chest tube alone commonly fails if empyema is greater than forty percent of the hemithorax [30]. Complex complicated parapneumonic effusions should be given thrombolytic agent intrapleurally in addition to tube thoracostomy. Thrombolytic agents will dissolve the fibrin membranes that are responsible for the loculation and facilitate drainage of the effusion [23]. However, there is conflicting evidence of the benefit of pleural antifibrinolytic therapy in the pediatric population [30]. With the increased use of the minimally invasive surgery, video assisted thoracoscopic surgery (VATS) has been proposed as a first-line therapy in patients with empyema, especially

those with more advanced disease. A number of retrospective reviews have demonstrated that VATS decreases the length of chest tube drainage and hospitalization [31]. In a meta-analysis by Avansino et al. pediatric patients with empyema who underwent primary operative therapy (antibiotics and either VATS or thoracotomy) had a lower aggregate in-hospital length of stay, duration of tube thoracostomy, and duration of antibiotic therapy compared with patient who underwent nonoperative therapy (antibiotics and thoracentesis and/or tube thoracostomy) [32]. Due to the institution's limited resources, only nonoperative therapy was received by the index patient resulting to a prolonged hospital stay. But in spite of this, patient still improved with no complications observed.

A loculated empyema is a potentially lethal condition. Failure to control the pleural process may lead to persistent sepsis, disseminated abscess, bronchopleural or bronchocutaneous fistula or progress to restrictive lung disease [13]. Nevertheless, children with pleural effusion usually do well and their lung functions return to normal in the majority of children regardless of the management mode of pleural effusion [27]. In the thirteen cases of neonatal empyema reviewed, only one patient succumb to death secondary to acute renal failure probably due to severe sepsis [9]. Other patients survived with no associated complications. Likewise, the patient in the case presented survived despite receiving only nonoperative therapy for complex empyema.

Children with pleural effusion should have a follow-up within 4–6 weeks of hospital discharge depending on the child's clinical status. Also, a chest radiograph should be requested at 4–6 weeks. The index patient's chest x-ray revealed normal results 6 weeks after discharge although complete radiological resolution is usually expected by 3–6 months [27].

4. Conclusion

Empyema thoracis is rare in the newborn period. Several modalities of treatment have been suggested to treat empyema in among the pediatric population. In this report, a successful management of a rare case of complex empyema in a neonate was described. The key to success is immediate identification of effusion, prompt initiation of empiric broad-spectrum antibiotics, and early effective chest tube drainage. In spite of patient's prolonged hospital stay, nonoperative therapy could still be an option in treating patients with loculated empyema, especially in resource-limited institutions.

References

[1] M. Barbosa, G. Rocha, F. Flôr-de-Lima, H. Guimarães, Neonatal pleural effusions in a level III neonatal intensive care unit, J Pediatr Neonat Individual Med 4 (1) (2015) 1, https://doi.org/10.7363/040123.

[2] W.A. Long, E.E. Lawson, H.S. Harned Jr., E.N. Kraybill, Pleural effusion in the first days of life: a prospective study, Am. J. Perinatol. 1 (2) (1984) 190–194, https://doi.org/10.1055/s-2007-1000001.

[3] G. Rocha, P. Fernandes, P. Rocha, C. Quintas, T. Martins, E. Proenca, Pleural effusions in the neonate, Acta Paediatr. 95 (7) (2006) 791–798, https://doi.org/10.1080/08035250500477545.

[4] J.G. Wheeler, R.F. Jacobs, Complications of pneumonia, in: J.D. Cherry, G. J. Harrison, W.J. Steinbach, S.L. Kaplan, J.H. Peter (Eds.), Pediatric Infectious Diseases, seventh ed., Elsevier Saunders, Philadelphia, 2014, p. 308.

[5] H. Christopoulo-Aletra, N. Papavramidou, "Empyemas" of the thoracic cavity in the Hippocratic corpus, Ann. Thorac. Surg. 85 (2008) 1133–1134, https://doi.org/10.1016/j.athoracsur.2007.11.031.

[6] G. Rocha, Pleural effusions in the neonate, Curr. Opin. Pulm. Med. 13 (4) (2007) 305–311, https://doi.org/10.1097/MCP.0b013e3281214459.

[7] Y.T. Shih, P.H. Su, J.Y. Chen, I.C. Lee, J.M. Hu, H.P. Chang, Common etiologies of neonatal pleural effusion, Pediatr Neonatol 52 (5) (2011) 251–255, https://doi.org/10.1016/j.pedneo.2011.06.002.

[8] S. Sharma, A. Sharma, M. Sharma, S. Ghosh, Neonatal empyema thoracis, Pediatr. Oncall J. 15 (1) (2018), https://doi.org/10.7199/ped.oncall.2018.2.

[9] J. Mazumdar, S. Sen, Neonatal empyema thoracis, J. Nepal Paediatr. Soc. 34 (1) (2014) 65–67, https://doi.org/10.3126/jnps.v34i1.8233.

[10] K.A. Nathavitharana, M.A. Watkinson, Neonatal pleural empyema caused by group A Streptococcus, Pediatr. Infect. Dis. J. 13 (1994) 671–672, https://doi.org/10.1097/00006454-199407000-00023.

[11] L. Lequier, W.L. Vaudry, Puerperal fever and neonatal pleural empyema and bacteremia caused by group A streptococcus, Can. J. Infect Dis. 9 (3) (1998) 185–189, https://doi.org/10.1155/1998/470984.

[12] I. Aliyu, I.M. Inuwa, Neonatal empyema thoracis in an African child: a case report, Int Med J Sifa Univ 2 (2015) 18, https://doi.org/10.4103/2148-7731.145815.

[13] A.N. Prasad, Intrapleural fibrinolytic therapy in a neonate, Indian J. Pediatr. 78 (2011) 1154–1156, https://doi.org/10.1007/s12098-011-0383-3.

[14] L. Cha, S. Choi, T. Kim, S. Yoon, Intrapleural urokinase therapy in a neonate with pleural empyema, Pediatr. Int. 58 (2016) 616–619, https://doi.org/10.1111/ped.12906.

[15] K. Lohmeier, E. Mayatepek, T. Hoehn, Neonatal pleural empyema in an extremely low birth weight infant, J. Matern. Fetal Neonatal Med. 22 (2009) 940–942, https://doi.org/10.1080/14767050902994630.

[16] J. Thaarup, S. Ellermann-Eriksen, J. Stjernholm, Neonatal pleural empyema with group A Streptococcus, Acta Paediatr. 86 (1997) 769–771, https://doi.org/10.1111/j.1651-2227.1997.tb08585.x.

[17] Evaluation of complicated and uncomplicated parapneumonic effusion in children, Turk. J. Pediatr. 58 (2016) 623–631, https://doi.org/10.24953/turkjped.2016.06.008.

[18] J. Kurian, T.L. Levin, B.K. Han, et al., Comparison of ultrasound and CT in the evaluation of pneumonia complicated by parapneumonic effusion in children, AJR Am. J. Roentgenol. 193 (2009) 1648–1654, https://doi.org/10.2214/AJR.09.2791.

[19] I.M. Balfour-Lynn, E. Abrahamson, G. Cohen, J. Hartley, S. King, D. Parikh, D. Spencer, A.H. Thomson, D. Urquhart, BTS guidelines for the management of pleural infection in children, Thorax 60 (2005) i1–21, https://doi.org/10.1136/thx.2004.030676.

[20] M.J. Na, Diagnostic tools of pleural effusion, Tuberc. Respir. Dis. 76 (5) (2014) 199–210, https://doi.org/10.4046/trd.2014.76.5.199.

[21] M. Singh, S.K. Singh, S.K. Chowdhary, Management of empyema thoracic in children, Indian Pediatr. 39 (2002) 145–157.

[22] J.E. Heffner, Non-malignant pleural effusion, in: F.A. Fishman (Ed.), Fishman's Pulmonary Diseases and Disorders, fifth ed., McGraw Hill, New York, 2015, pp. 2337–2340.

[23] R.W. Light, A new classification of parapneumonic effusions and empyema, Chest 108 (2) (1995) 299–301, https://doi.org/10.1378/chest.108.2.299.

[24] S. Togo, M. Ouattara, I. Sangaré, J. Saye, C. Touré, I. Maiga, D. Dakouo, L. Guo, S. Koumaré, A. Koita, Z. Sanogo, S. Yéna, Management for pediatric pleural empyema in resource-poor country is chest tube drainage with antiseptic lavage-irrigation better than tube thoracostomy alone, Surg. Sci. 6 (2015) 541–548, https://doi.org/10.4236/ss.2015.612077.

[25] D. Narayanappa, N. Rashmi, N.A. Prasad, A. Kumar, Clinico-bacteriological profile and outcome of empyema, Indian Pediatr. 50 (2013) 783–785, https://doi.org/10.1007/s13312-013-0215-9.

[26] K. Ramireddy, Y. Siva Rama Krishna, A study of pediatric empyema thoracis in a tertiary care hospital, International Journal of Contemporary Medical Research 3 (10) (2016) 2838–2840.

[27] A.M. Hendaus, I.A. Janahi, Parapneumonic effusion in children: an up-to-date review, Clin. Pediatr. 55 (2015) 10–18, https://doi.org/10.1177/0009922815589917.

[28] C. Garcia, G.H. McCracken Jr., Antibacterial therapeutic agents, in: J.D. Cherry, G. J. Harrison, W.J. Steinbach, S.L. Kaplan, J.H. Peter (Eds.), Pediatric Infectious Diseases, seventh ed., Elsevier Saunders, Philadelphia, 2014, pp. 3201–3202.

[29] T. Chibuk, E. Cohen, J. Robinson, S. Mahant, D. Hartfield, Paediatric complicated pneumonia: diagnosis and management of empyema, Paediatr. Child Health 16 (7) (2011) 425–427, https://doi.org/10.1093/pch/16.7.425.

[30] M. Reichert, M. Hecker, B. Witte, J. Bodner, W. Padberg, M.A. Weigand, A. Hecker, Stage-directed therapy of pleural empyema, Langenbeck's Arch. Surg. 402 (2017) 15–26, https://doi.org/10.1007/s00423-016-1498-9.

[31] K.D. Schultz, L.L. Fan, J. Pinsky, L. Ochoa, O. Smith, S. Kaplan, M. Brandt, The changing face of pleural empyemas in children: epidemiology and management, Pediatrics 113 (2004) 1735–1740, https://doi.org/10.1542/peds.113.6.1735.

[32] J.R. Avansino, B. Goldman, R.S. Sawin, D.R. Flum, Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis, Pediatrics 115 (2005) 1652–1659, https://doi.org/10.1542/peds.2004-1405, 2005.