

PULMONARY GANGRENE - SEVERE AND RARE COMPLICATION OF PNEUMONIA

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Received: November 02, 2014

Revision received: December 19, 2014

Accepted: December 19, 2014

Summary

Pneumonia is an inflammatory lung disorder characterized by consolidation due to presence of exudates in the alveolar spaces. Most pneumonias can be effectively treated with appropriate oral antibiotics, with intravenous antibiotics being reserved for those with severe infections. We present two cases of girls admitted in our clinic with pneumonia where our conventional therapy was not sufficient. Case 1: A 15-year-old girl with cystic fibrosis, with left lobular pneumonia, for which an aggressive conservative treatment was initiated. After significant improvement, sudden deterioration and pneumothorax of the left lung occurred. She was transferred to the surgical department for intervention. Due to failure to respond to initial drainage she underwent thoracotomy and resection of the left lower lobe of the lung. The histology result confirmed gangrene. Case 2: A four-year old girl was treated for pneumonia in the right lung with aggressive intravenous antibiotic. After temporary improvement sudden deterioration was observed. The patient was transferred to the surgery department, where pulmonary gangrene was confirmed. After the lower lobe of the right lung was resected, she was discharged in good health. The careful follow up, accurate diagnosis and correct medication choice are crucial for reducing the complications of "common" pneumonia.

Key words: pneumonia, gangrene, children

Introduction

Pneumonia is defined as an inflammatory disorder of the lung characterized by consolidation due to the presence of exudates in alveolar spaces. Most pneumonias can be treated effectively with appropriate oral antibiotics, with intravenous antibiotics being reserved for patients with severe infections or non-tolerance to oral therapy. Supportive care remains a vital aspect of care for those with severe infections [1]. The most common complication is development of pleural effusions and empyemata. In cases of compromised immunity or in the presence of very aggressive pathogens more rare complications may challenge the therapeutic process.

We present two cases of girls admitted to our clinic with pneumonia where our conventional therapy was not sufficient.

First case

A 15-year-old girl with a confirmed diagnosis of cystic fibrosis (CF) since the age of one year (prolonged diarrhea, failure to thrive, chronic cough and repeated pneumonias). When she was 2-year-old (in 1995) a chronic colonization with *Pseudomonas aerogenosa* was confirmed. She followed a strict regimen (physiotherapy, diet and medication) and received all newly introduced medications such as Pulmozyme® (in 1999) and inhaled Colistin® (in 2002). When she was seven, a CT-scan confirmed bronchiectases in both lungs, predominantly in the upper lobe of the right lung. Since 2004 all exacerbations of CF have been accompanied by hemoptysis. Treatment with Pulmozyme® and Colistin® was discontinued and Vitamine K® and *Dicynone*® were administered.

Three years later she was admitted with fatigue, augmented expectoration of greenish, smelly blood-stained sputum, fever and signs of respiratory failure, and x-ray findings (Fig.1a) for left lobular pneumonia. Aggressive conservative treatment (oxygen support,

bronchodilators and the highest allowed dose of Meronem®, combined with Amikacin®) was initiated. After significant improvement on the 14th day a sudden deterioration due to pneumothorax of the left lung occurred. The dynamics of X-ray changes is presented on figure 1 (Fig.1).

The patient was transferred to the surgical department for intervention. Due to failure to respond to initial drainage, she was given emergency video-assisted thoracoscopic surgery (VATS), which revealed a large abscess of the left lower lung. (Fig. 2a). VATS was followed by thoracotomy and the left lower lobe (segments VIII, IX and X) was resected. Histology confirmed gangrene: there was a sharp transition from normal lung to the affected area, which showed consolidated air spaces with preserved outlines (coagulative necrosis). Alveoli were filled with necrotic exudates. (Fig. 2b). The patient was discharged after 18 days of supportive and aggressive antibiotic treatment in good general health condition, with all laboratory data within normal limits, X-ray with acceptable changes (Fig.2c) and relatively conserved lung

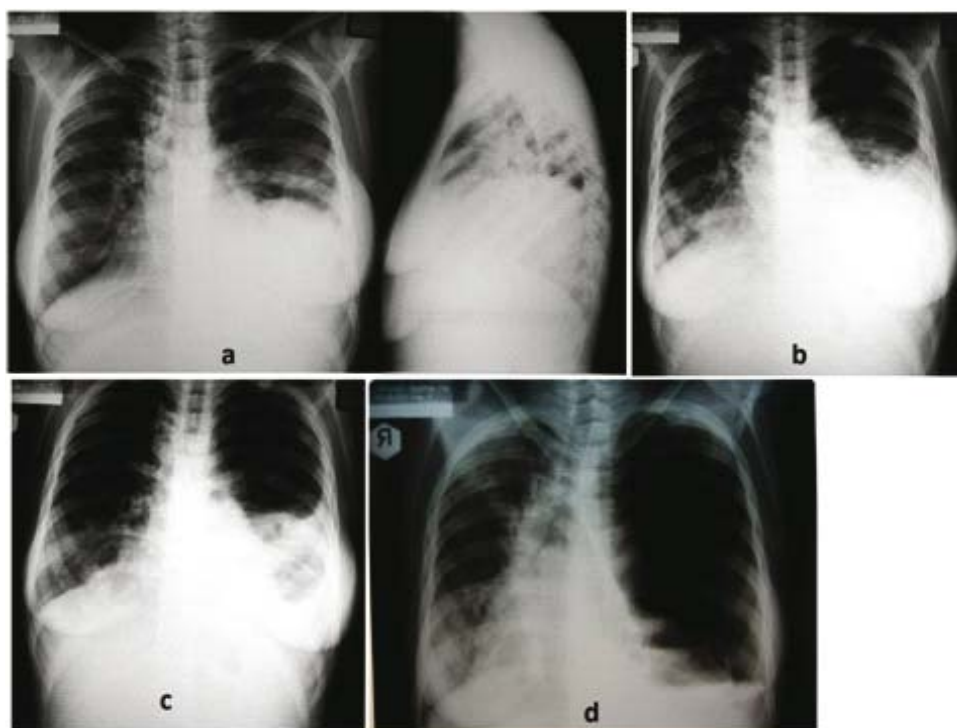


Figure1. Dynamic of lung X-ray changes. a) front and lateral view at admission - bilateral enhanced vascular markings, alveolar consolidation on day 9 and partly on day 10 - left lung segments, with relatively high position of the left diaphragm, no free liquid in the costophrenic recesses; b) on the 3rd day – persisting of the infiltration on the left with slightly marked pleura on the 3rd rib level, some irregular shadows in the right base of the lung; c) day 7 – the massive infiltration in the left has lower opacity, with some spaces inside, probably as a result of parenchyma destruction, small effusion with tendency to capsule; d) day 14 – full pneumothorax in the left. In the left base close to the heart there is a shadow of the collapsed lung, considerable mediastinal shift to the right.

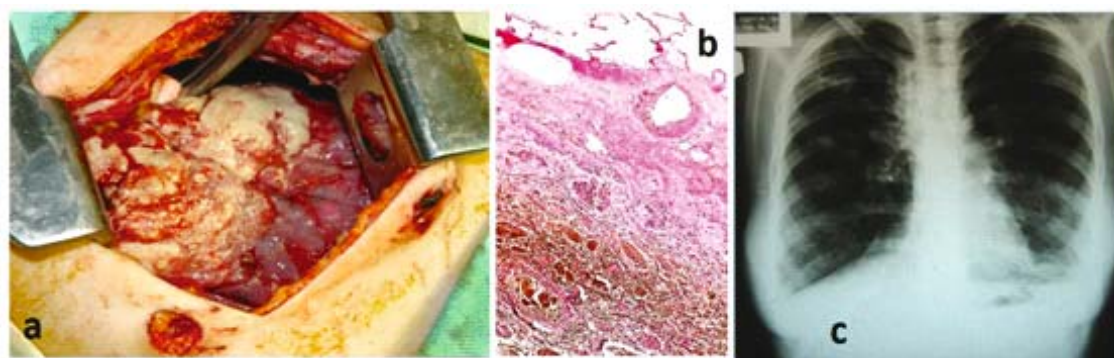


Figure 2. Intra- and postoperative findings. a) photo during the surgery – severely affected tissue of the lung; b) histology result - sloughing of a large amount of infected lung tissue with *in situ* thrombosis of large vessels; c) X-ray at discharge – no mediastinal shift, no pleural effusions; both lungs have equal opacity, reduced left lung volume after surgery) with higher position of the left diaphragm.

function for a CF patient and after partial lung resection (FVC 73.6%, FEV₁ – 57.7%, MMEF_{75/25} 24.6%).

Later on, the patient continued her strict regimen and for one year she was hospitalized once for exacerbated CF. Five years later, a fatal exacerbation of the chronic respiratory failure occurred and the patient died.

Second case

The second case is a 4-year-old girl, without any significant previous premorbidity and normal growth and development. Due to cough, fever, fatigue and pain in the right chest area, not resolving with oral therapy on an outpatient basis, she was admitted in the clinic.

At admission she was in poor general health, febrile, with broncho-vesicular murmur the right at auscultation and dullness at percussion, with laboratory data for severe infection: elevated WBC, toxic neutrophil granulation, elevated ERS, X-ray changes revealing pneumonia and a small effusion in the right lung (Fig. 3a). Treatment was started with Sulperazone® combined with Amikacin® but due to lack of response- worsening in X-ray changes (Fig. 3b) and laboratory data, Amikacin® was replaced with Vancomycin®. This combination led to temporary clinical improvement but then sudden deterioration occurred in both clinical status and laboratory data. (fig.3c). A CT-scan demonstrated a more advanced process in the lung and the patient was transferred to the surgery department for treatment (Fig. 3d). Image findings for this period are presented of figure 3 (Fig. 3).

Pig-tail drainage was applied for the effusion

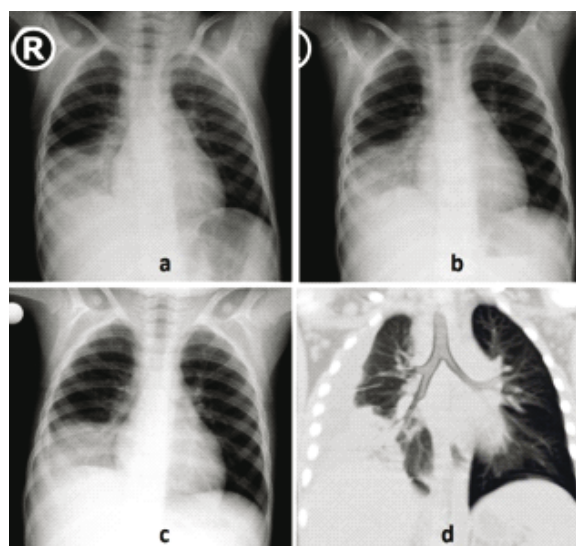


Figure 3. Image findings in pediatric clinic. a) X-ray on admission – massive infiltration in the right base with marked axillar pleura; b) X-ray on day 4 – enlarged infiltration with small pleural effusion on the right; c) X-ray on day 7 – worsening of changes with larger effusion; d) CT scan on day 7 – massive infiltration and effusion that compress the rest of the lung parenchyma

(Fig. 4a, b) with no response. A CT scan on the following day (Fig. 4c) showed that thoracotomy was necessary. An atypical resection of S₆ of the right lung was performed (Fig. 4d). Despite aggressive antibiotic treatment, the patient remained febrile and hypoventilation of the lower right lung persisted. A new CT-scan confirmed the expansion of the process (Fig. 4e) and re-thoracotomy with lower lobectomy was performed (Fig. 4f). Histology confirmed gangrene of the lung. A week later the girl was discharged in good general health and normal laboratory and X-ray findings (Fig. 5a).

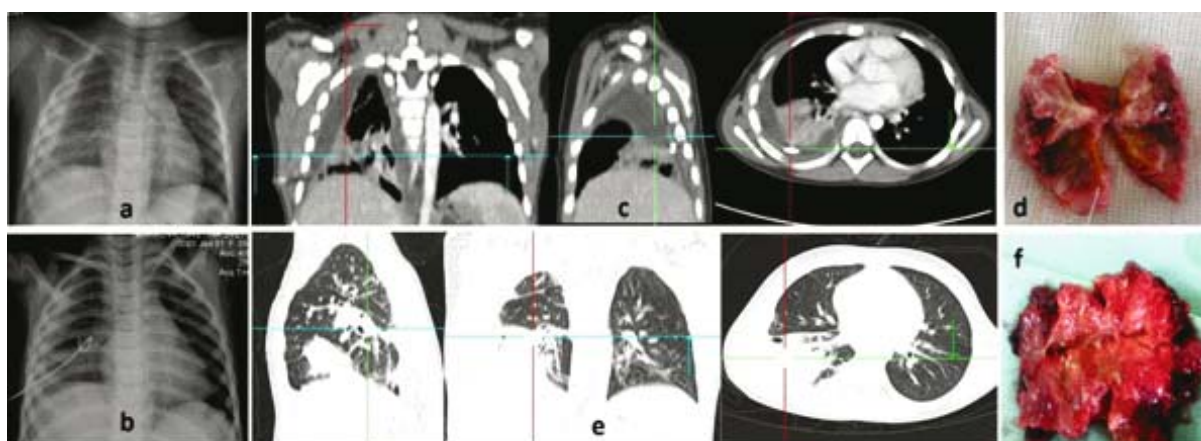


Figure 4. Images from the surgery unit before the second operation a) X-ray before the drainage (almost identical to X-ray on Fig.3d); b) X-ray after insertion of the pig-tail tube for drainage; c) CT scan after the drainage procedure failed - massive infiltration in the right and persisting huge effusion compressing the rest of the lung parenchyma; d) photo of the resected lung part during the first surgery; e) CT scan after surgery – persisting non-ventilated parts of the lung on the right; f) photo of the resected lung part during the second

Throughout the whole period in both clinics, no pathogens were isolated from the numerous sputum and swab tests.

A follow-up examination 6 months after discharge the patient was in good health, with normal laboratory and X-ray findings (Fig. 5b). Four years later she was a healthy girl without any complications or delays in growth and development. The girl has not had any significant illnesses after the aforementioned one.

Discussion

*“The service of the foote
Being once gangren'd, is not then respected
For what it was before.”*
Coriolanus, William Shakespeare [2]

Gangrene is a kind of necrosis, in which the affected tissues mummify (dry gangrene) or undergo a rotting decomposition (wet gangrene).

Usually gangrene is a result from infection or block of the arterial blood supply towards the affected area. The Latin term "*gangraena*" derives from Ancient Greek “γάγγραινα” which mean meaning “rotting ulcer”. The affected area turns black, green or yellowish-brown [3].

Gangrene is an extremely rare and severe complication of pneumonia. In the medical literature, the following terms are used as synonyms for *gangrene* are used: spontaneous amputation or lobectomy, and massive sequestration or necrosis. The main difference between gangrene and necrotizing pneumonia and lung abscess is that main vessels thrombosis is the leading factor for pathogenesis.

In 1808 the father of the stethoscope Rene Laennec described the anatomical changes in lung gangrene [4]. The first case reported was in 1836 – that of a 40-year-old construction worker back with fatal outcome [3]. Different microorganisms were suspected as etiological

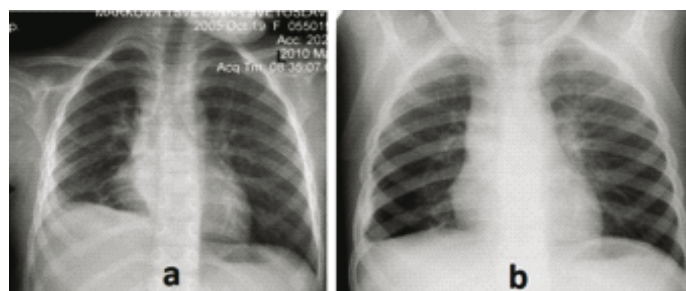


Figure 5. X-ray changes after the second surgery: a) on discharge - no infiltration, higher position of the right diaphragm, at the place of the resected lung parenchyma; b) 6 months after surgery – right lung is with normal opacity, traces of adhesions on the right, no other significant changes

agents. Leyden and Jaffe (1867) reported spiral-shaped organisms (probably spirochetes), while Rona (1905) showed some proofs that the gangrene was probably due to carious teeth. In the following years many experiments were performed on animals by Veszpremi, Bonnet and Peyre, Kline, Pilot and Davis and Smith. In 1923 Kline managed to induce lung gangrene in guinea pigs through injection of lung gangrene material [4].

Predisposing factors for developing gangrene are: diabetes, alcohol abuse, nutritional deficiency, chronic disease and compromised immunity. The upper left lobe is the most commonly affected part of the lung (roughly in 80% of the cases).

In microbiology cultures the prevalent isolates are those of gram-negative microorganisms. Olcott et al. report a fatal outcome: a 15-year-old girl who had been given a vaccine, died after a pertussis infection in the whole family [5]. In recent publications, *K. pneumoniae*, *P. aeruginosa*, *M. tuberculosis* and *S. pneumoniae* have been reported as first-line causative agents [6-9]. Additionally, cases with confirmed fungal infection (*Aspergillus*) or anaerobic super-infection have been reported [5].

Clinical signs of gangrene include intoxication, sometimes progressive respiratory and heart failure. The affected area could be painful, with excruciating cough and sometimes expectoration of smelly three-layer phlegm such as in patients with bronchiectasis) [3].

Initial image findings are as in lobar pneumonia (area with consolidation), followed by multiple small X-ray negative areas that gradually merge in one big cavity, the so called "mass within a mass", or form an air scythe [10, 11].

The differential diagnosis includes tuberculosis, bacterial, atypical or fungal pneumonia; hydatid cyst; lung cancer; lung thromboembolism and sarcoidosis. Treatment of lung gangrene should solve three main problems: correction of homeostatic disturbances; elimination of the infection, if possible; managing expected complications – with bronchoscopy to eradicate the pathogen, or pleural puncture [3]. If the expected results are not achieved, the next step is resection of the affected area.

To maintain the balance, various low-molecular plasma-expanders and electrolyte solutions, as well as glucose solutions and inhibitors of proteolysis are used. If necessary, in

cases with loss of proteins and liquids, enteral support, vitamins and heparin (if hypercoagulation is suspected) should be added. If signs of respiratory or heart failure occur, an oxygen support and cardiotonics, respectively, are needed. To control infection, it is obligatory to start intravenous application with two wide-spectrum antibiotics in maximal doses. A combination of a beta-lactam with aminoglycoside or quinolone has been reported as most effective. Antibiotic treatment should be reassessed once microbiology results have confirmed a specific germ. In the presence of pleural effusion, drainage should also be considered. This complex therapy helps to reduce the size of the affected area and formation of an abscess cavity. Radical therapies such as lobectomy or pneumonectomy are considered in cases with non- or very poor response [12].

Decision on the extent and time for surgical intervention is crucial for the outcome. Hoffer et al. (1996) reported data about 14 patients with lung abscess and 10 with necrotizing pneumonia without gangrene, put on conservative treatment. The patients with necrotizing pneumonia complications such as pneumatocele, broncho-pleural fistulae and persisting pneumothoraces were observed. There were no complications in the patients with abscess. Hoffer concluded that in cases with necrotizing pneumonia without gangrene, surgical intervention was even harmful [13]. Therefore, correct distinguishing necrotizing pneumonia from gangrene is extremely important.

In cases with gangrene, complete removal of all necrotized tissue is essential to prevent possible complications such as sepsis or multiple organ failure, and death. Once a gangrenous process has developed, surgery is necessary and even life-saving notwithstanding the application of an antibiotic to which the causative agent is sensitive. Danner published the results in 10 patients with lung gangrene – 6 with surgical intervention and 4 only on medication. All four patients, who did not receive surgery, died [11]. Since then, obligatory surgery in cases with gangrene has been accepted as the gold standard in management. The surgical procedures include one-stage resection; drainage and resection, or only drainage [14]. Large resection should be avoided at the beginning. Gangrene is often accompanied by empyema, and if an effusion occurs, mediastinitis or broncho-pleural fistula could develop [15, 16]. The best results in

surgical management have been reported for the so called two-stage therapy: immediate pleural fenestration, followed by delayed resection and fast closure of the pleural opening [17].

The prognosis is poor for very young children and immunocompromised patients. Complex and timely therapy considerably increases the chances for survival. Lobe- or pneumonectomy in gangrene cases reduces complications and improves life quality. The remaining lung tissue compensates for the resected one. Children have a normal development after surgery and do not present massive skeletal deformities [18].

Conclusion

Both cases illustrate the possible pulmonary complications requiring surgical management due to failure of conservative treatment and one very rare complication of pneumonia in childhood – pulmonary gangrene. Timely and complex therapy is crucial for normal development and life after recovery. Future hopes for this entity are connected with re-perfusion techniques of micro-invasive surgery, that could possibly allow for maximal conservation with least resection of the affected area but while those techniques evolve, the radical surgery remains a gold standard in treatment. Resection in the first case was followed by quick and satisfactory recovery and a good overall prognosis, ensuring at least 3 years with relatively good life quality. Unfortunately, the underlying condition led to untimely death. Our second case also illustrates that a good inter-disciplinary team approach produces excellent results with a good prognosis.

Acknowledgements

Assoc. Prof. Hristo Shivachev, for continuous follow up of the first patient after surgery.

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