Case Report

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Untreated pulmonary sequestration with recurrent superinfection supporting COPD development in a 42 year old male patient

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ABSTRACT

Background: Pulmonary sequestration is a congenital malformation in which nonfunctional lung tissue develops without connection to the bronchial system. The main complication is the occurrence of recurrent pneumonia.

Case presentation: We describe the case of a patient who was incidentally diagnosed with PS as part of the diagnostic algorithm for community-acquired pneumonia. Due to the relatively late diagnosis, the recurrent bronchopulmonary was conducive to the development of COPD and pulmonary emphysema. For prognostic reasons, surgical resection was performed by posterolateral thoracotomy.

Conclusions: Although cigarette smoking is the main risk factor for developing COPD, recurring lung infections may have a synergistic effect. Sometimes recurrent infections are caused by a congenital malformation. Especially in adults who have had recurrent pneumonia since childhood.

Key words: Pulmonary sequestration, congenital pulmonary malformation, COPD, pneumonia, surgical sequestrectomy

Background

Pulmonary sequestration (*lat.* sequestare = to separate) is a congenital pulmonary malformation in which lung tissue exists without communication with the bronchial tree. Since the segment is not ventilated, it remains non-functional [1]. It receives its blood supply not from the pulmonal artery, but from anomalous systemic arteries. Most commonly from the descending thoracic aorta (73%), less frequently from the abdominal aorta, celiac trunk, splenic artery or intercostal arteries [2].

They can appear as extralobar pulmonary sequestrations (ELS), which are covered with their own visceral pleura. With a proportion of 75-85%, the more common type is the intralobar sequestration (ILS), where the lesion lies within the pleural layer surrounded by a functioning lobe [3].

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The etiology remains unclear, but the most plausible hypothesis is the formation of an additional lung bud below the normal lung bud in organogenesis. Along with the normal bud, it moves caudally. If it ripens before the development of the pleura, an intralobar sequestestration results. Conversely, a later development of the bud leads to an extralobar sequestration [3].

In most cases, ILS get symptomatic with recurrent pneumonias of the surrounding pulmonary lobe. Since it is a congenital condition, issues start usually in childhood. In ELS, the sequester is separated from the functional lung tissue by pleura so that it is less likely to become infected [4].

The standard treatment for pulmonary sequestration is surgical removal. It is recommended to avoid progressive inflammation of the lung parenchyma due to recurrent infections. Endovascular embolization is a therapeutic alternative. It aims to reduce blood flow of the sequestered tissue, leading to progressive involution [3].

Case presentation

A 42-year-old male patient presented to the emergency department with fever and productive cough with a yellowish sputum and abdominal pain. The symptoms gradually developed over the past few days. For several months now, he has had an increasing amount of stress dyspnea and loss of weight.

The patient was born in Syria and came to Germany as a refugee in 2015. He reported recurrent bronchopulmonary infections since childhood occurring about twice a year, including multiple hospitalizations and antibiotic treatments. At the age of 25 he was treated against tuberculosis over six months. No preexisting diagnoses or regular medication intake could be determined. There was a continued cigarette abuse with 5-10 cigarettes daily and cumulatively 10 pack/years. Currently, he was working as a gardener in the public sector.

On initial examination he had a blood pressure of 94/73 mmHg with a heart rate of 89/min. The respiratory rate was 25/min with an oxygen saturation of 97% on room air. The tympanic body temperature was 37.7°C. The patient was awake and oriented to all qualities. Heart-sounds were normal. The lung examination revealed expiratory crackles on the basal lung-sections. The abdominal wall was slightly painful to pressure on the left upper quadrant.

After fluid substitution of 2L crystalloid, blood pressure returned to normal. Laboratory investigations revealed elevated inflammatory markers (CRP 111.2 mg/L, leukocytes 12.200/microliter). The chest x-ray showed bilateral atypical infiltrates and a cavernous process on the right basal lung-section.

For further specification, a CT-scan of chest and abdomen was performed. A pronounced paraseptal pulmonary emphysema could be shown. Small-spotted infiltrates on the left lower lobe were present. A consolidation, interspersed with partially secretion-filled caverns, was observed in the right lower lobe (Figure 1). No connection to the genuine bronchial system could be detected. The lesion was supplied from two large-caliber arterial branches, arising from the abdominal aorta. The accessory blood

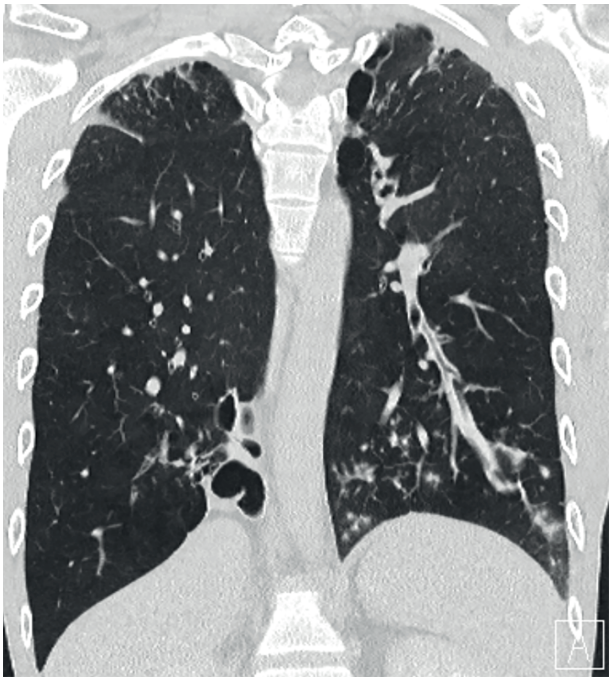

Figure 1. CT scan indicates signs of lung damage known as pulmonary emphysema. Small-spotted pneumonic infiltrates found in the lower left lobe. Fluid-filled cavities observed within the lower right lobe.

vessel showed an aneurysmal dilation of 11 mm from which two separate branches arise, supplying the consolidation (Figure 2). These findings suggest a superinfected intralobar pulmonary sequestration (ILS).

Blood cultures were drawn and a calculated antibiotic therapy with Piperacillin/Tazobactam 4.5g three times a day was initiated. The patient was admitted to a normal care ward. Regarding the differential diagnosis of reactivated tuberculosis, the patient was isolated. An interferon-gamma-release-assay (IGRA) was performed, and sputum was sampled.

On the next day the examinations were supplemented by a flexible bronchoscopy. A significant quantity of purulent secretion was observed, primarily originating from the right bronchial system. Bronchoalveolar lavage fluid (BALF) was sampled from the right lower lobe.

After starting antibiotic treatment, the patient's condition improved, and the inflammation markers decreased (CRP: 55.1 mg/l on day 3; 29.6 mg/l on day 4). The IGRA test was positive, which can be attributed to a past tuberculous infection that occurred 19 years ago. But sputum, BALF and bronchial secretion all were negative by Auramine-fluorescence staining, PCR and cultural. However, BALF exhibited mixed colonization with *Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae* and *Haemophilus influenzae*. Blood cultures stayed negative after seven days of incubation. After discharge, oral sequence therapy with Cotrimoxazol 960mg twice a day was given for additional 14 days.

Three months after discharge the patient was seen in the outpatient clinic. The cough had almost completely disappeared. Though, dyspnea persisted during physical effort. Body plethysmography revealed an obstructive ventilation disorder with a Tiffeneau index of 59,45% (LLN = 69,7%) without reversibility after salbutamol inhalation. FEV_1 was 3.0L accordingly 64,9% target value. The CT scan graphically confirmed structural emphysema and in a bodyplethysmography, the residual volume was increased (134% of target value).

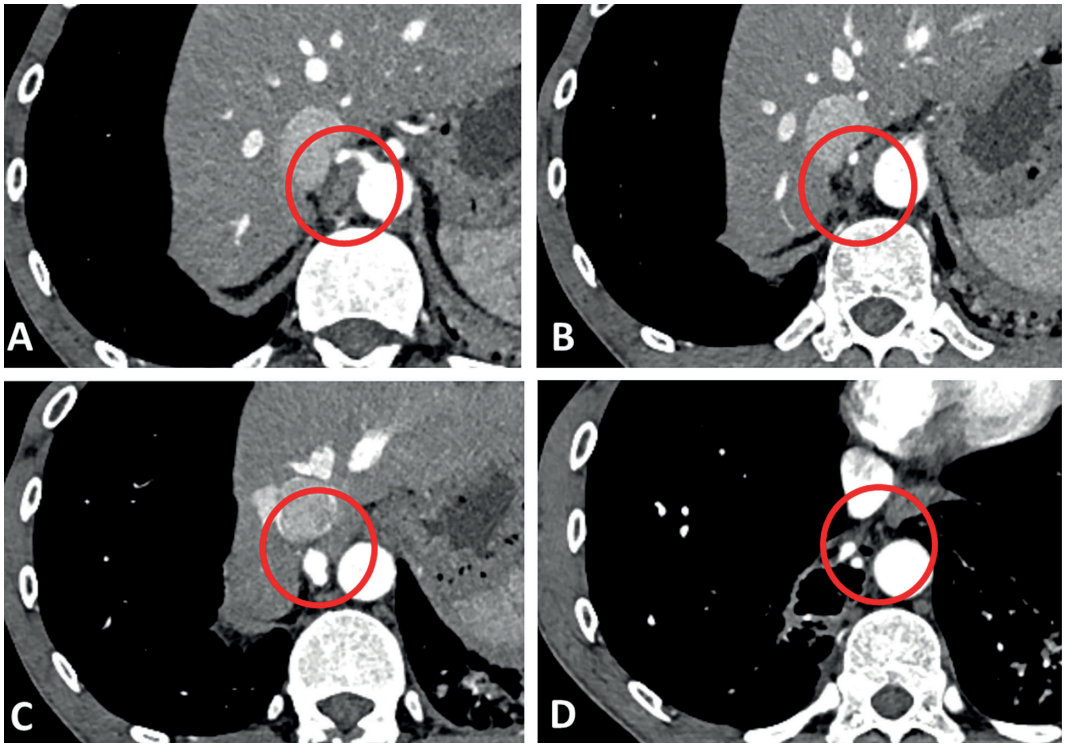

Figure 2. Vascular supply to the PS is through an accessory vessel that originates from the abdominal aorta (A), passes through the diaphragm (B), and ends in an aneurysmal dilation (C) before dividing into two supplying branches (D).

There was no evidence of bronchial asthma in the patient's medical history. The diagnosis COPD GOLD II stadium E was made, and a therapy with a dual bronchodilatator (Indacaterol and Glycopyrroniumbromid) was initiated. An evaluation was conducted for alpha-$_1$-antitrypsin deficiency due to the patient's young age and relatively low cigarette consumption (10 pack/years). The serum concentration of alpha-$_1$-antitrypsin was 179 mg/dL (normal range 90-200 mg/dL). An incorrectly high determination in acute inflammation could not be assumed because leukocyte count, CRP and fibrinogen were also within the normal range at the time.

CT-scan in elective interval exhibited a significant regress of the left sided infiltration. The basomedial sequestration within the right lower lobe had been detected again, but the fluid-levels within the cavities were reduced (Figure 3).

It could be concluded that the recurrent superinfections of the sequestration contributed to the development of COPD and lung emphysema at a relatively young age. For prognostic reasons, the case was discussed with the Department for thoracic surgery for an elective sequestrectomy.

Surgery was scheduled a few weeks after the outpatient presentation. The right hemithorax was opened via posterolateral thoracotomy. Pleural adhesions were carefully detached, the two supplying arterial branches were disconnected, and the sequestration was resected using a stapler. After insertion of two chest drains, the patient was extubated and transferred to an intermediate care unit.

On the second postoperative day, the patient could be transferred to a normal ward. Later on, he developed an acute exacerbation with increased amount of sputum, leading to an antibiotic therapy with Ampicillin/Sulbactam orally for seven days. Chest drains were removed at fourth and fifth postoperative day. On the sixth day after surgery, the patient was discharged home in a good condition.

Gross Pathology exhibited a triangular shaped, 8 x 6 x 5 cm measuring resected lung tissue, including two clipped blood vessels. An afferent bronchus could not be defined. On the cut surface, the tissue was of brownish colour and interspersed with numerous cavities. A viscous white liquid flowed out of the cavities after slicing (Figure 4). Histopathologically, the tissue presented with fibrosis and advanced

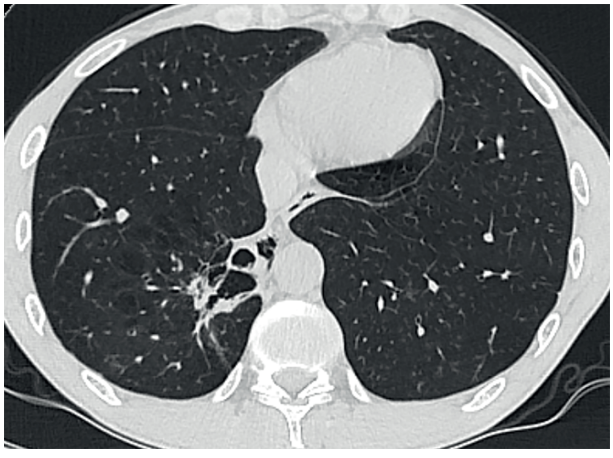

Figure 3. CT-scan in elective interval.

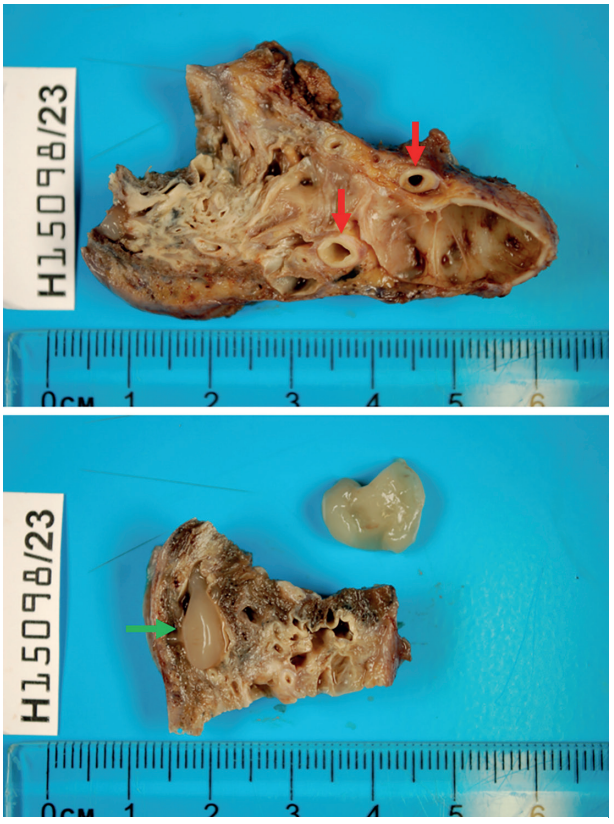

Figure 4. Resected, formalin fixed, pulmonary sequestration, revealing two supplying arterial branches (red arrows) and mucoid filled caverns (green arrow).

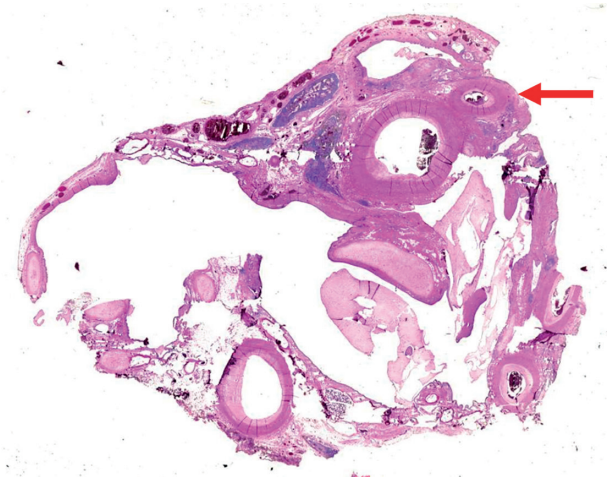

Figure 5. Examination of pulmonary sequestration stained with Hematoxylin and Eosin. The feeding vessel shows the characteristic wall structure of a systemic elastic artery (red arrow).

organized alteration. The feeding vessel exhibited the characteristic wall structure of an elastic systemic artery (Figure 5).

The patient was followed up two months after discharge and reported no new respiratory infections since then. Dyspnea and cough were no longer present. There was an allodynia in the area of the thoracotomy scar, which was treated with analgesics.

With a Tiffeneau index of 67.15% (LLN = 69.7%), body plethysmography continued to show a slightly improved bronchial obstruction. In contrast, residual volume increased to 154% of target value. In this stable phase of the disease, the total IgE level was 104 IU/ml and the eosinophil granulocyte count was 130,9/microliter, ruling out an asthma/COPD overlap. For this reason, the dual bronchodilator therapy was continued without any changes.

Discussion

The patient presented here was first diagnosed with PS in adult age, although he had reported numerous pneumonias since childhood. The late diagnosis is probably due to the fact that the patient grew up in a structurally less developed country, where CT scans are probably not as common as in Western countries.

In a case collection from Mayo Clinic databases, between 1997 and 2016, 32 patients were identified with PS first diagnosed as adults. 15 out of 32 adults with PS were asymptomatic, most common complaint was cough (34%), followed by dyspnea, chest pain, fever and, like in our case, recurrent respiratory infections (16% each) [3].

Historically, COPD has been described as a condition caused by years of cigarette smoke [5]. Thus COPD prevalence correlates with age and smoking duration [6,7]. Even in younger patients, smoking is the main risk factor for development of COPD [8].

Key aspect of COPD-pathogenesis is an imbalance between inflammation and anti-inflammation in lung parenchyma [5]. Therefore, recurrent infections, especially in early development, may also lead to chronic damage to the respiratory tract. A synergistic effect of smoking and frequent pulmonary infections can be assumed. Within smoker-stratified models, FEV_1 deficits among smokers associated with infant lower respiratory infections, compared to smokers without infections, were recently described [9].

The patient was a current smoker, which is indeed a factor for development of his pulmonary emphysema. However, the numerous cases of pneumonia in his history will have contributed significantly to his lung disease.

It is also worth mentioning tuberculosis at the age of 25. Tuberculosis infection is also a risk factor for developing COPD [6]. Unfortunately, tuberculosis treatment was based only on anamnestic reports, without written prescriptions. Except for the cavernous changes, which can be adequately explained by the sequestration, there were no other image morphological residues.

Following the initiation of inhalation therapy, the question arose of a specific therapy of the PS. The therapeutic indication consisted mainly of prognostic aspects. On the one hand, recurrent lower respiratory infections can promote the development of emphysema, on the other hand, chronic infections are also associated with more decline of lung function [10].

As mentioned earlier, treatment options for PS are surgical excision or interventional embolization of the

supplying artery. Embolization seems to be the gentler procedure, as no thoracotomy is necessary. But studies have shown that only some of the endovascular treated PS achieved complete remission. Another drawback is that there is no tissue obtained for pathologic examination [11]. In the case of our patient, there was also a risk that the caverns would melt down abscessing during ischemia conditions.

Surgical methods include thoracotomy and video-assisted thoracoscopy (VATS). VATS is considered a good choice in selected cases of simple PS without adhesions [12]. Due to numerous superinfections, our patient has developed major pleural adhesions in the area of the diaphragm and mediastinum (Figure 1), which is why we opted for an open thoracotomy.

A significant surgical pitfall is the systemic vascular supply of the sequester. Because the lesion is supplied by accessory arteries, accurate preoperative imaging is helpful. This allowed us to target the arteries and clip them before resection. In this way, a large perioperative blood loss could be avoided.

Conclusion

When pulmonary emphysema is diagnosed at a young age, cigarette smoke may not be the only cause. Recurrent respiratory infections can contribute synergistically to the development of COPD. In this case of recurrent lower respiratory tract infections, a predisposing factor may be present. In addition to an immune deficiency, a congenital malformation, like in our case pulmonary sequestration, might be a rare cause of COPD development.

In our patient, an intralobar pulmonary sequestration was diagnosed relatively late; recurring infections led to morphological lung damage. We decided to remove the lesion for prognostic reasons. Different treatment options were available. Due to the cavernous changes and the pleural adhesions, an open operation through posterolateral access, seemed appropriate.

List of abbreviations

BALF = Bronchoalveolar lavage fluid
COPD = Chronic obstructive pulmonary disease
CRP = C-reactive protein
CT = Computer tomography
ELS = Extralobar lung sequestration
FEV1 = Forced expiratory volume in one second
GOLD = Global initiative for chronic obstructive lung disease
IGRA = Interferon gamma release assay
ILS = Intralobar lung sequestration
LLN = Lower limit of normal
MSSA = Methicillin sensitive *Staphylococcus aureus*
PCR = Polymerase chain reaction
PS = Pulmonary sequestration
VATS = Video-assisted thoracoscopy

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