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Pulmonary actinomycosis complicated by fistula of the chest wall

Abstract

Actinomycosis is a rare disease caused by *Actinomyces* spp. The clinical and radiological picture of the disease is uncharacteristic, which delays the diagnosis and can lead to complications. We present a case of pulmonary actinomycosis complicated by a chest wall fistula in a 43-year-old man with advanced tooth decay. The patient was admitted to our Department due to a chest wall fistula with bloody discharge. A few months earlier, he was treated with antibiotics for pneumonia. Since then, weakness, exertional dyspnoea, and weight loss had been observed. On admission, increased inflammatory markers were found in laboratory tests. Chest computed tomography (CT) revealed right-sided encapsulated pleural fluid collection containing gas bubbles, pleural thickening, anterior thoracic wall soft tissues thickening and subcutaneous fat stranding. CT suggested an empyema or a breast either pleural malignancy. The picture suggested a breast or pleural tumour to differentiate with an empyema. Videothoracoscopy was performed, the histological examination of the collected samples revealed granulation tissue and bacterial colony of a morphology corresponding to *Actinomyces* spp. Pulmonary actinomycosis was diagnosed. Antibiotic therapy according to the guidelines was initiated and dental treatment was recommended. Healing of the fistula and significant regression of lesions in the right lung were achieved. Although it is a rare disease, actinomycosis should be considered in the differential diagnosis of any chronic infiltrative lung lesions.

Key words: actinomycosis, tooth decay, fistula of the chest wall, antibiotics

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Introduction

Actinomycosis is a rare disease caused by *Actinomyces* spp., gram-positive anaerobic bacteria that normally live in the human oral cavity, digestive tract and urogenital system as commensals. *A. israeli* is considered to be the most common cause of the disease, followed by *A. naeslundii* and *A. mayeyari* [1]. These bacteria usually coexist with other microorganisms that reduce the oxygen concentration in the environment and weaken the body defences, allowing *Actinomyces* to grow [2]. The disease can affect many organ systems. Infections of the craniofacial area are the most common, followed by gastrointestinal and respiratory disease [3]. It may also involve the central nervous system, bones and joints and the genitourinary system [4]. Lung in-

fection occurs as a result of aspiration of infected contents from the oral cavity and the gastrointestinal tract [5]. Risk factors include lack of proper oral hygiene, alcoholism, chronic respiratory diseases such as chronic obstructive pulmonary disease, bronchiectasis, history of pulmonary tuberculosis, immunosuppression in the course of other diseases or treatment [4]. Males are more likely to be affected than females, which may be associated with less hygiene and more frequent facial injuries. Infection can occur at any age, but most often occurs in people aged 20–50 [5]. We present the case of a 43-year-old man suffering from actinomycosis complicated by a fistula of the chest wall. The aim of the study is to draw doctors' attention to the need for considering this disease at an early stage of differential diagnosis of ambiguous clinical cases.

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Case report

A 43-year-old smoking man with no history of chronic diseases was admitted to the National Tuberculosis and Lung Diseases Research Institute due to a chest wall fistula. His problem started five months earlier with dyspnoea and chest pain, for which he was evaluated in a different hospital. Tests performed at that time revealed significantly increased blood inflammation markers and right-sided pleural effusion up to the 8th rib with accompanying lung consolidations on chest x-ray. Community-acquired pneumonia was diagnosed. The patient refused hospital admission, so ambulatory antibiotic therapy was initiated (amoxicillin with clavulanic acid and clarithromycin). Despite treatment, mild chest pain persisted, deterioration of exercise tolerance and gradual weight loss developed. A fistula appeared with time in the right nipple area, oozing bloody discharge. Fever was not observed.

On admission to the Department, the patient's blood pressure was 140/95 mm Hg, heart rate regular 104/min, oxygen saturation 98% on room air. Chest auscultation revealed a decrease in breathing sounds at the base of the right lung, no adventitious sounds were heard. There were two striking findings from inspection: advanced tooth decay and cellulitis with fistula in the right mammary area. Blood tests revealed increased inflammatory markers and abnormal coagulation parameters (Table 1). Chest X-ray showed a large amount of fluid in the right pleural cavity (Figure 1). Contrast enhanced CT with pulmonary angiogram excluded pulmonary embolism. It revealed right-sided encapsulated pleural fluid collection containing gas bubbles, pleural thickening and contrast enhancement and features of anterior thoracic wall involvement: soft tissues thickening, discreet rib destruction and subcutaneous fat stranding (Figure 2). CT suggested a pleural empyema or a breast either pleural malignancy. Thoracentesis was performed and trace amount of bloody fluid was obtained — pH 8, brown colour, erythrocytes $3.85 \times 10^{12}/L$; haemoglobin 11,8 g/dL; the smear was dominated by leukocytes — 77%. The fistula swab cultures yielded the growth of *Acinetobacter baumani* complex. For diagnostic and therapeutic reasons, the patient was referred for video-assisted thoracoscopic surgery (VATS). A pleural empyema was evacuated, and the anterior chest wall was incised. Material for microbiological tests and histopathological evaluation was collected. *Parvimonas micra* was cultured on the pleural effusion in anaerobic conditions, and the culture

Table 1. Laboratory tests results

Parameter	Result	Norm
Leukocytes [$\times 10^3/mm^3$]	12	4.23–9.07
C-reactive protein (CRP) [mg/L]	122	< 10
D- dimers [ng/mL]	1242	< 500
Activated partial thromboplastin time (APTT, formerly kaolin- -cephalin time) [s]	38	24–35
INR	1.45	0.8–1.2

INR — international normalized ratio

was sterile under aerobic conditions. The smear of pleural fluid was negative for acid-fast bacteria (final cultures were also negative), and there was no fungal growth. The patient was managed with pleural drainage and antibiotic therapy in accordance with antibiogram. Clinical improvement was achieved. As results of the histopathological examination of the chest wall phlegmon became available, they revealed a nonspecific granulation tissue with massive inflammatory infiltrate rich in neutrophils and plasma cells and with multiple colonies of densely packed bacteria. The colonies were covered by eosinophilic proteinous deposits (Splendore-Hoeppli reaction). Grocott methenamine-silver stain (GMS) revealed the filamentous structure of the bacteria. Morphology of microorganisms corresponded with *Actinomyces* spp. (Figure 3). The culture targeted at *Actinomyces* spp were negative. Based on histopathological analysis and corresponding clinical picture, the diagnosis of actinomycosis complicated by fistula of the chest wall was established. The antibiotic therapy was started in accordance with the guidelines for treating actinomycosis (intravenous therapy with amoxicillin with clavulanic acid for 2 weeks during hospitalisation followed by oral treatment with amoxicillin 3g/day at home) and dental treatment was recommended. During the initial treatment, the fistula was healed and the lesions in the right lung regressed significantly. In good general condition, the patient was discharged home. A follow-up hospitalisation was planned, but for economic reasons, it was not performed, and antibiotic therapy was discontinued approximately 3 weeks after discharge. The further course of the disease remains unknown.

Discussion

The clinical presentation of the respiratory system actinomycosis is not characteristic,

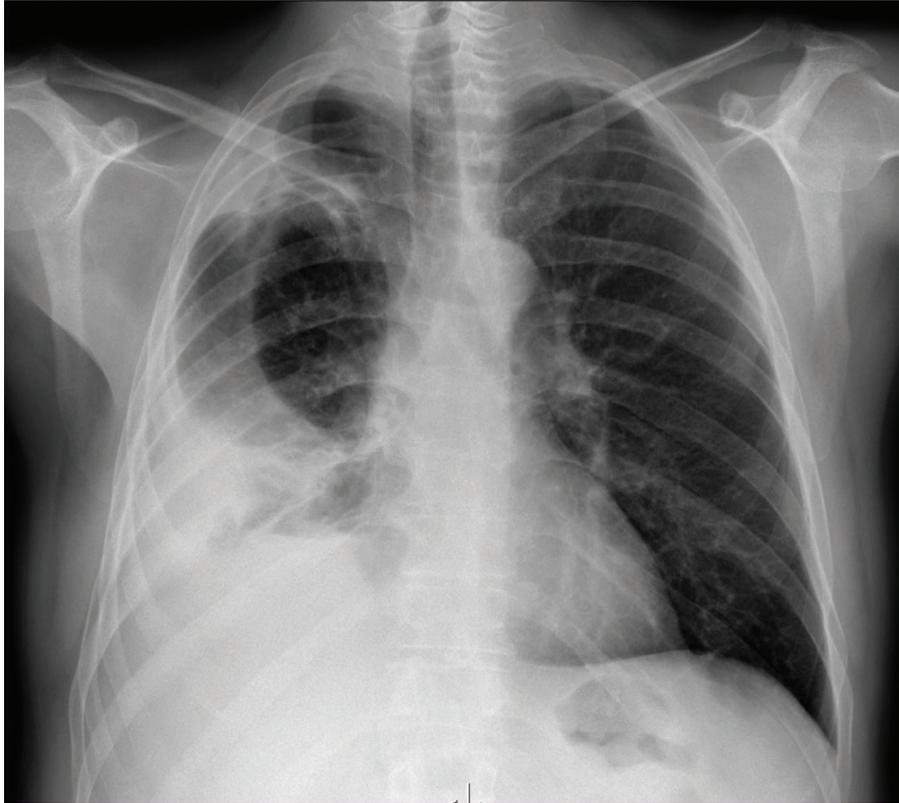


Figure 1. Posteroanterior chest radiograph shows a large amount of fluid in right pleural cavity



Figure 2. Axial contrast-enhanced CT image reveals right-sided encapsulated pleural fluid collection (arrow 1) containing gas bubbles (arrow 2), pleural thickening and contrast enhancement (arrow 3), anterior thoracic wall soft tissues thickening (arrow 4), subcutaneous fat stranding (arrow 5)

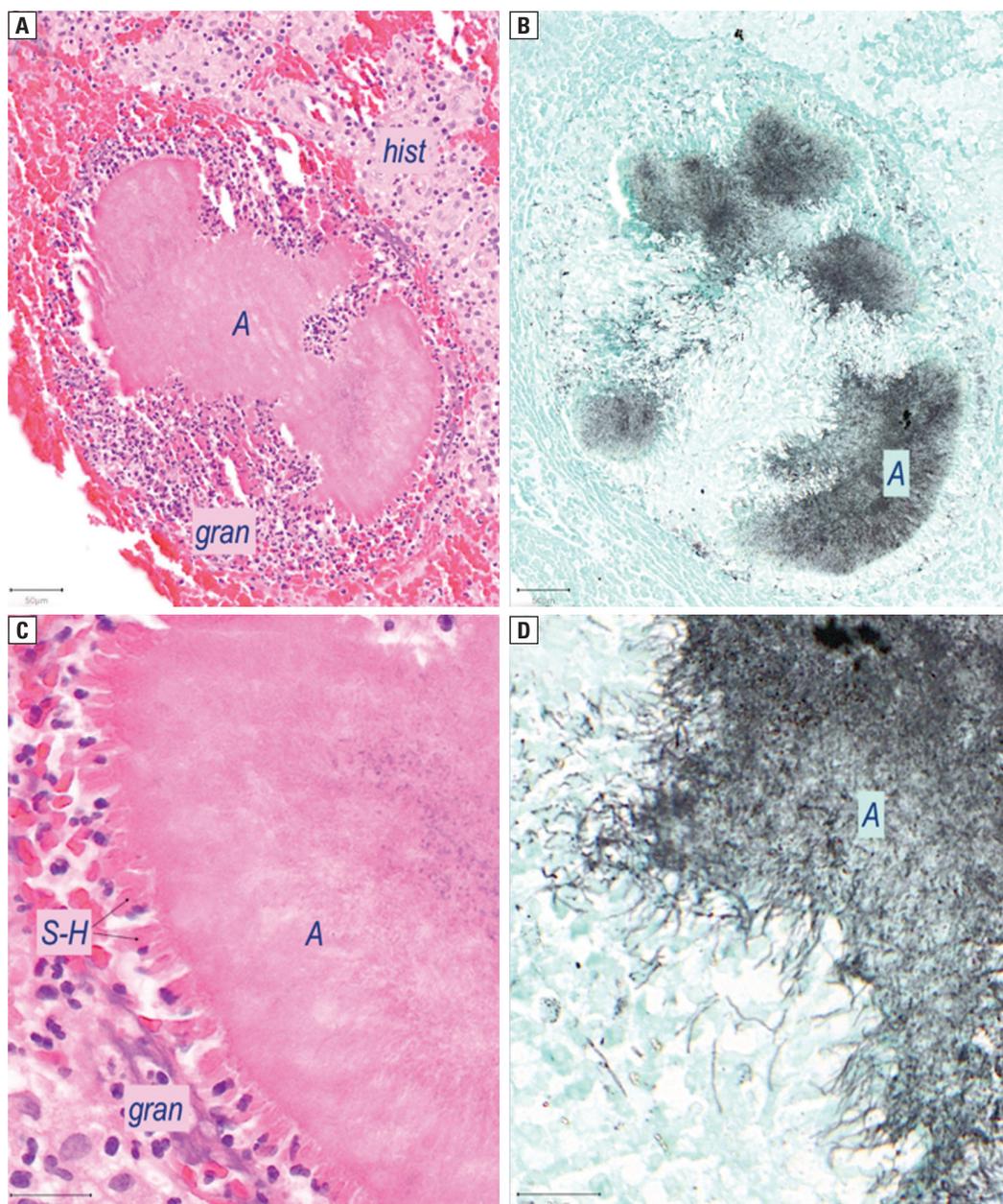


Figure 3. Microphotography of a colony of *Actinomyces*. **A, B.** Low-power of densely packed tangles of bacterial colony (A) surrounded by granulocytes (*gran*) and histiocytes (*hist*). **C.** High-power of bacterial colony (A) with eosinophilic deposits of proteinaceous exudate at the edge - so-called Splendore-Hoeppli phenomenon (S-P). **D.** GMS stain highlighted the filamentous structure of bacteria at the periphery of the colony (A and C — hematoxylin and eosin stain, magn. $\times 100$ and 400; C and D — grocott methenamine silver stain — GMS, magn. $\times 100$ and 400)

which is responsible for diagnostic difficulties and mistakes. It has been estimated that it takes approximately 3 months to make a proper diagnosis of pulmonary actinomycosis [6]. Initially, the disease may be asymptomatic. Later on, chronic cough, dyspnoea, chest pain, fever or low-grade fever, deterioration of exercise tolerance, weight loss, sweating, and recurrent respiratory infections appear. There are reports of massive or recurrent haemoptysis requiring pulmonary embolisation as the main clinical manifestation

[7, 8]. In our case, the first symptoms of the disease were dyspnoea and chest pain. On the basis of performed tests, pneumonia was diagnosed and antibiotic therapy was initiated. Despite the treatment, the patient observed a deterioration of exercise tolerance, weight loss and local chest skin changes, which prompted him to seek further medical assistance. First, chest CT was performed 5 months after the first symptoms. It indicated right-sided empyema and/or breast or pleural neoplasm. According to the literature, pulmonary

nodular infiltrates are the most frequent radiological findings at the initial stage of the disease. Other observations include cavitation within the nodular infiltrates, central necrosis, ground-glass opacities, subpleural consolidation, mediastinal lymph nodes enlargement, pleural thickening and effusion [1, 7]. At that stage, it is very difficult to differentiate actinomycosis from pulmonary tuberculosis, neoplasms, lung abscesses or fungal lesions. In further course of the disease, the lesions may progress locally and involve adjacent structures. The formation of fistulas (e.g., into the oesophagus or through the chest wall) and abscesses within the respiratory system is a rare form of the disease and it appears most commonly at the late stage when not properly treated [4]. For this reason, the presented case deserves special attention. Five months elapsed between first symptoms and the diagnostic work-up in our Department. This time was sufficient for the development of complications. This shows how important it is to consider actinomycosis at an early stage of the differential diagnosis, especially if no improvement is achieved with treatment targeted at the most common respiratory infection agents.

Diagnosis of the disease is based on the presence of *Actinomyces* spp in the microbiological examination and/or findings in the histopathological test. Bronchoscopy may be helpful, however, there is no bronchoscopic pattern characteristic of actinomycosis. Samples collected during the examination can be considered diagnostic only in the presence of pulmonary cavities [3, 4]. Otherwise, it is difficult to decide whether the bacteria are the causative factor or just a contamination. Suzuki *et al.* [7] reported a case where pulmonary actinomycosis was diagnosed by transbronchial lung biopsy, but it is to remember that the diagnosis was made based on the tissue histopathological examination, not the cultures. Ding *et al.* [5] and Tabarsi *et al.* [8] presented similar cases. In our patient, bronchoscopy was not performed because the disease process seemed to originate from the chest wall. Instead, urgent VATS was undertaken. The surgical intervention was the most appropriate, both for diagnostic and therapeutic reasons. Surgical or CT-guided lung biopsy is also recognised as an appropriate diagnostic tool for pulmonary actinomycosis [4]. Pleural fluid testing is reasonable, but it rarely yields positive results [3, 9]. Samples for *Actinomyces* spp cultures should be collected under anaerobic conditions and growth should last 15–20 days. However, positive results are obtained in less than 50% of cases. Reasons include recent antibiotic therapy,

abundant growth of other microorganisms, complicated procedure of specimen collection and the necessity to use non-standard conditions [3, 8]. In our case, cultures for *Actinomyces*, collected during thoracentesis and VATS, were negative. It is difficult to say which of the above-mentioned reasons played a role here. Perhaps it was influenced by other microorganisms' growth (*Acinetobacter baumani* complex, *Parvimonas micra*). In the presented case, histopathological findings were crucial for the final diagnosis. Characteristic lesions in the histological examinations include inflammatory granulation tissue with necrosis and colonies of gram-positive filamentous bacteria. Macroscopically, bacterial colonies form yellowish clumps, so-called sulfur granules of a diameter of 0.1–1 mm. It is important not to consider them pathognomonic as they can also occur in other diseases such as nocardiosis or mycoses [4]. The possibility of using molecular techniques in the diagnosis of actinomycosis has been reported [6].

The treatment scheme of pulmonary actinomycosis remains controversial. Antibiotics penetration to the infection site is poor due to low vascularisation of the lesions and a large number of fibrous lesions [6]. Therefore, high doses of antibiotics and prolonged time of treatment should be applied. Standard treatment regimen includes the use of intravenous penicillin (18–24 mln units/day) for 2 to 6 weeks followed by oral treatment for 6 to 12 months (amoxicillin 3 g/day) [1, 4, 10]. Alternative treatments are based on the use of clindamycin or macrolides. [2, 4, 11]. *Actinomyces* spp do not produce β -lactamase, so there is no need to use their inhibitors, however, some authors describe effective therapy with them [12]. The treatment should be continued for at least 3 months to prevent local complications like fistulas or phlegmon of the chest wall and disease recurrence [4]. However, some authors advocate shortening the therapy to less than 6 months, including reducing the intravenous treatment phase to less than 14 days [10]. The argument for such approach is earlier detection of the disease nowadays than it was in the past, when the disease was often diagnosed at the late stage, with complications [10]. Zhang *et al.* [3] analysed 145 cases of actinomycosis and reported an average treatment duration of 4.5 months. All patients were considered cured. Kinner *et al.* [13] described 19 patients who were considered cured after an average treatment duration of 6 weeks. It is suggested to consider discontinuation of antibiotic therapy 1–2 months after disappearance of

clinical and radiological symptoms of the disease. Surgical treatment may also allow for shortening the antibiotic therapy [10]. Indications for surgery are massive/recurrent haemoptysis, no improvement after antibiotic therapy or the need to supplement it in case of abscesses, fistulas or phlegmon. In addition, invasive procedures are performed to rule out neoplasms. In case of massive pleural effusion, drainage should be used [6]. Quickly applied, it can also shorten the time of antibiotic therapy. However, the small number of described cases does not allow to confirm this unequivocally.

Conclusions

Pulmonary actinomycosis is a rare disease, but it should be considered in all patients with progressing infiltrative lung/pleural pathology. Once the diagnosis is made, proper antibiotic therapy should be started immediately. Delay in diagnosis or incorrect treatment may lead to severe complications.

Conflict of interest

None declared.

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