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Pulmonary actinomycosis: cytomorphological features

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Abstract

Pulmonary actinomycosis is an uncommon infectious disease. Although the gold standard for diagnosis is histological examination with bacterial culture of lung tissue, cytology samples offer a fast and low-cost alternate diagnostic procedure. The cytology literature on this topic is limited to mostly case reports. Therefore, the aim of this study was to review cytological material in a series of patients with a diagnosis of pulmonary actinomycosis to characterize the main cytomorphological findings. Different cytological respiratory samples including sputum smears, bronchoalveolar lavages (BALs), transthoracic or endobronchial fine needle aspiration cytology (FNAC) and cell block preparations were used for retrospective examination. For all cases patient age, gender, symptoms, and radiological chest findings were recorded. A total of 26 cytological respiratory samples (14 sputum smears, 9 FNAC, two BALs) including direct smears and 6 cell blocks from 9 patients were examined. In sputum smears the most remarkable findings were the presence of dark cotton ball masses with projections like spider legs and/or mouse tails (75% of the samples). Sulfur granules were observed in 4 (40%) of the sputum smears and within FNAC cases. Various respiratory cytology samples including sputum smears, FNAC and BALs can reveal cytomorphological findings diagnostic of pulmonary actinomycosis. Characteristic cytological findings compatible with a diagnosis of this infection include cotton ball masses and less frequently sulfur granules.

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Introduction

Pulmonary actinomycosis is an uncommon infectious disease caused by *Actinomyces* spp., a genus of Gram-positive bacilli (1 µm in diameter) characterized by a growing filamentous pattern of these Actinobacteria with or without branching. Although currently 47 species of these bacteria have been identified, only six of them are incorporated in the genus *Actinomyces*, including *A. israelii, A naeslundii, A. odontolyticus, A. viscosus, A. meyeri* and *A. pyogenes*. *A. israelli* is g the most prevalent species to be isolated in human infections and has been found in most clinical cases of actinomycosis [1]. Some species are strict anaerobes and others are microaerophilic, all of which are slow growing.

This bacterial genus is part of the microbiota of the digestive tract, ranging from the oropharynx to the colon and is of low pathogenic potential [2]. The genitourinary tract is also a site of colonization. They may cause infections when they cross epithelial barriers under certain conditions that produce low oxygen tension, mainly in cases of tissue necrosis [3]. Thus, these infections usually occur endogenously such as after trauma, surgery and, quite often due to the presence of foreign bodies [4-8]. In older people with poor buccal hygiene and/or dental disease, whether or not accompanied by alcoholism, aspiration of oropharyngeal secretions containing these bacilli is one of the main forms of disease acquisition [9], although hematogenous spread from a distant infectious focus would be another infrequent source of infection [10,11].

Pulmonary actinomycosis constitutes approximately 15-20% of all cases of this infectious disease [12]. Pulmonary actinomycosis may manifest itself in various ways, mainly affecting the lung parenchyma with extension to the chest wall [13,14]. Many cases can be clinically mistaken for other diseases such as fungal infection (e.g., Aspergillosis), tuberculosis, and lung cancer [15-19]. Pulmonary actinomycosis may occur at any age, but it is more frequent in people aged between 30 and 65 years old. It is also more

frequent in men than in women. The clinical manifestations of pulmonary actinomycosis include fever, cough with phlegm (sputum), chest pain, dyspnea and hemoptysis [20]. Radiological findings may be non-specific, including the presence of masses, nodules, patchy infiltrates, segmental air-space consolidation, and cavitation [21,22].

The gold standard for diagnosing pulmonary actinomycosis is histological examination of tissue (e.g., lung biopsy) revealing the typical oval shaped "sulfur granules" along with bacterial culture [23]. However, pulmonary cytology samples provide an alternate faster and low-cost diagnostic procedure without the need for invasive lung procedures allowing afflicted patients to receive early treatment of this infectious disease [24]. However, the cytology literature on this topic is limited to mostly case reports. Therefore, the aim of this study was to review cytological material in a series of patients with a diagnosis of pulmonary actinomycosis to characterize the main cytomorphological findings.

Materials and Methods

In this retrospective study, different cytology respiratory samples from patients with a confirmed diagnosis of pulmonary actinomycosis were used for examination under a light microscope. Cytology samples included sputum smears, bronchoalveolar lavages (BALs), and transthoracic or endobronchial fine needle aspiration cytology (FNAC). Available cell blocks were also studied. Depending on the type of sample, different staining methods were employed such as Papanicolaou, Giemsa, Hematoxylin and Eosin (H&E), Periodic Acid Schiff (PAS), Grocott-Gomori and Gram stains.

In addition, the clinical records of included patients were searched to record age, gender, dental hygiene, alcoholism, symptoms, and radiological chest findings. The data presented in this article were collected as part of the routine work in a cytology laboratory. The study was undertaken in full compliance with the principles laid out in the Declaration of Helsinki.

Results

Clinical findings

The mean patient age was 68.6 years (range, 55 to 79 years) and all patients were males. In five patients (55.5%) poor dental hygiene was documented, two patients (22.2%) were diabetics and one (11.1%) was an alcoholic. Among their clinical symptoms, cough with phlegm and fever were the most frequent (100% of the cases), followed by hemoptysis (66.6%), dyspnea and weigh loss (55.5%), and finally chest pain (44.4%). Unilateral cavitary lesions were the most frequent type of radiological lesion observed in 5/9 (55.5%) of the cases (Figure 1 A,B) in both thorax x-ray and computerized tomography (CT) studies. Other radiological findings included a unilateral mass-like shadow in 2/9 (22.22%) of cases, unilateral consolidation in 1/9 (11.1%) cases, and bilateral patchy infiltrates in in 1/9 (11.1%) cases. All patients received antibiotic therapy for 2-6 weeks (7 of them with intravenous penicillin G and two with oral amoxicillin/clavulanic). Only two patients required surgical resection of the lesions. In all patients there was improvement of the symptoms and cure of the infection.

Cytology findings

A total of 31 cytology respiratory samples (14 sputum smears, 9 FNAC, two BALs), including 6 cases containing cell blocks, from 9 patients were examined. Of the sputum smears examined, 4 were considered unsatisfactory due to the existence of predominantly saliva with abundant pavimentous cells without the presence of alveolar macrophages. Hence, only 10 sputum smears were included in this study. In these sputum smears, the most remarkable findings were the presence of dark cotton ball-like masses with projections resembling spider legs and/or mouse tails

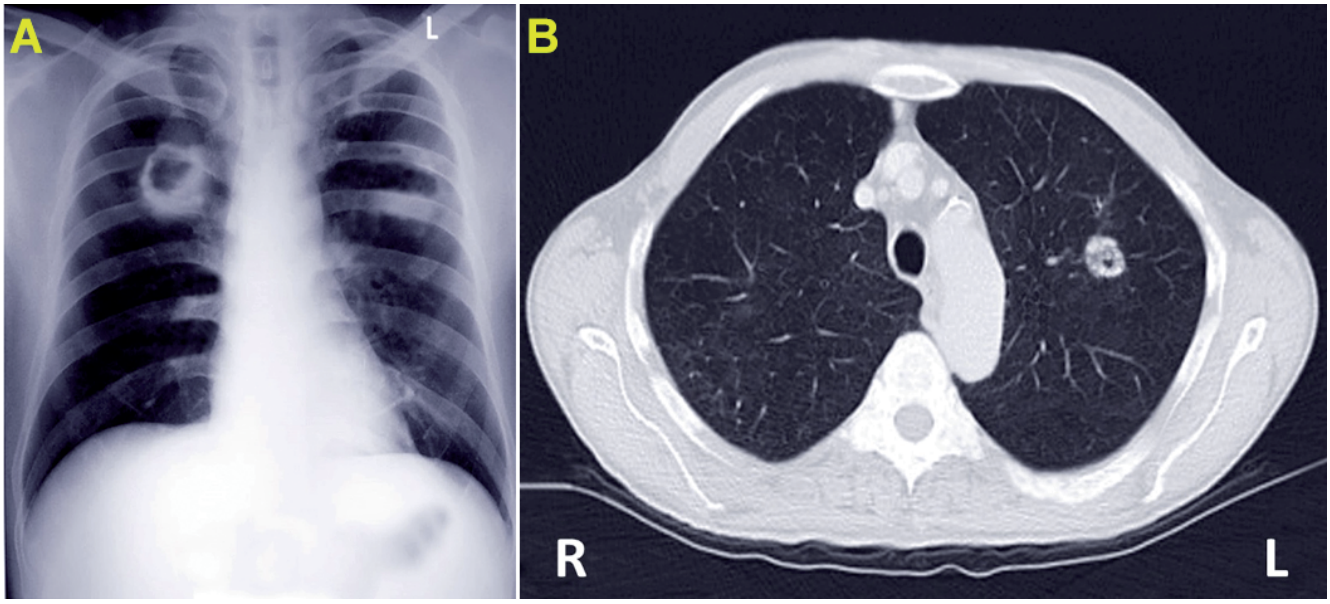

Figure 1. A) Chest x-ray showing a unilateral cavitary lesion in the right lung superior lobe. B) CT scan showing a unilaterally cavitary lesion in the left lung.

(Figure 2 A,B). This finding was observed in 7 of the 10 examined sputa (75%). Less frequently, the presence of sulfur granules was observed (Figure 2C). This finding was observed in only 4 of the 10 examined sputum smears (40%). In one of the two BALs elongated axis-like structures with numerous filiform projections was detected (Figure 2D). In FNAC samples the most characteristic finding was the presence of typical oval shaped sulfur granules, as masses of necrotic debris with radiating filaments and surrounded by inflammatory cells (Figure 3 A,B). Performing cell blocks, sulfur granules showed positivity with PAS, Giemsa and Grocott stains (Figure 4 B-D). This finding was observed in 100% of samples. The Splendore-Hoeppli phenomenon, characterized by intense eosinophilic material surrounding aggregated microorganisms, was seen in cell bock sections stained with H&E (Figure 4A). In all respiratory samples microbiological cultures were carried out, showing positivity in all cases. Unfortunately, the details of the species isolated was unavailable. Other bacteria or fungi were not reported in these cultures.

Conclusions

Pulmonary actinomycosis is an uncommon disease, especially in developed countries today where social and hygiene habits have considerably improved. A study by Kim *et al.* accordingly included only 94 cases during the first decade of the 21st century [25]. However, pulmonary actinomycosis remains a major cause of misinterpreted diagnoses related to lung infections [26]. For example, in a retrospective analysis of 145 cases by Zhang *et al.* only 5 patients had the correct initial diagnosis of primary pulmonary actinomycosis, and 60 patients were misdiagnosed with lung cancer [27]. In our study, 7 out of 11 (64%) were initially clinically diagnosed as having lung cancer. In another retrospective study involving 26 patients with pulmonary actinomycosis, an initial misdiagnosis of lung cancer was made in 50% of cases, and pulmonary tuberculosis in another 26.9% [28]. While pulmonary actinomycosis can clinically mimic other pulmonary infections (e.g., nocardiosis, aspergillosis, tuberculosis) or even malignancy [24,29-33], it is important to be aware that co-infections with other microorganisms creating lung masses have also been described [34-37]. Aspiration of oropharyngeal secretions or the presence of a foreign body in the bronchial tree seems to be the main cause of pulmonary actinomycosis. Other forms of thoracic involvement include endobronchial disease, mediastinal infection, and pleural effusion [38-41]. The clinical (e.g., productive cough with fever) and radiological findings (e.g., cavitary lesion) in our group of patients were in line with other reported cases of pulmonary actinomycosis.

Compared to tissue biopsy and culture, cytology sample procurement from the respiratory tract provides a faster, cheaper, and less invasive mechanism to definitively establish a diagnosis of pulmonary actinomycosis. If actinomycetes are found only in sputum, usually without sulfur granules, they may merely reflect colonization [42], specially from the tonsillar crypts [43]. In such sputum specimens non-pathogenic actinomycetes tend to be juxtaposed with pyknotic squamous cells and sometimes even admixed with oropharyngeal Candida microorganisms. In our series, 8 of the 10 examined sputa (80%) were positive for pulmonary actinomycosis and 4 of these samples (40%) also had sulfur granules. Apart from sputum, other cytology samples such as FNAC and BAL have also been shown to be useful in the diagnosis of pulmonary actinomycosis [44-47]. Actinomycosis should always be considered when a FNAC of a lung mass contains an inflammatory exudate rich in polymorphonuclear neutrophils [48]. In such cases, cell block preparation along with special stains for microorganisms will improve diagnostic efficacy [49]. In our study, actinomycetes were observed with the aid of histochemical stains in 100% of the samples obtained by FNAC. Our study is limited by preforming a retrospective review and the low number of samples analyzed.

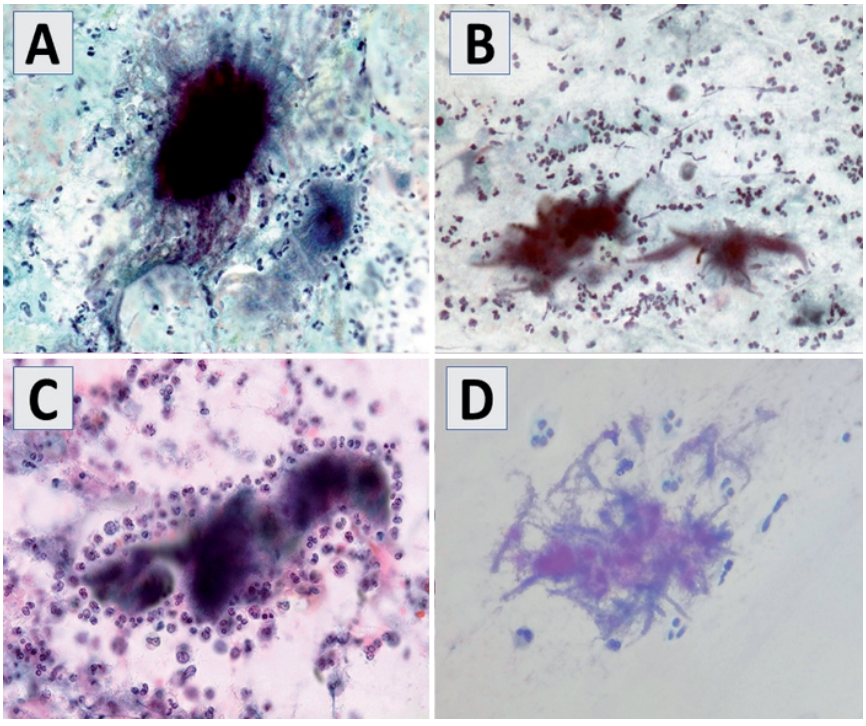

Figure 2. A) Sputum smear in pulmonary actinomycosis showing the presence of dark cotton ball-like masses with projections that resemble spider legs and/or mouse tails (Papanicolaou stain, x400). B) Sputum smear with dark cotton ball-like masses and mouse tail projections (Papanicolaou stain, x400). C) Sputum smear showing a typical sulfur granule (Papanicolaou stain, x400). D) BAL specimen with pulmonary actinomycosis showing elongated axis-like structures with numerous filiform projections (Papanicolaou stain, x400).

In conclusion, pulmonary actinomycosis is associated with characteristic cytological findings such as cotton ball-like masses and sulfur granules in respiratory specimens that can help make a timely and definitive diagnosis of this infection. The use of simple histochemical stains to identify actinomycetes embedded within these inflammatory structures can help confirm the diagnosis. This allows an early diagnosis and specific antibiotic therapy to be initiated, thereby avoiding unnecessary surgical intervention.

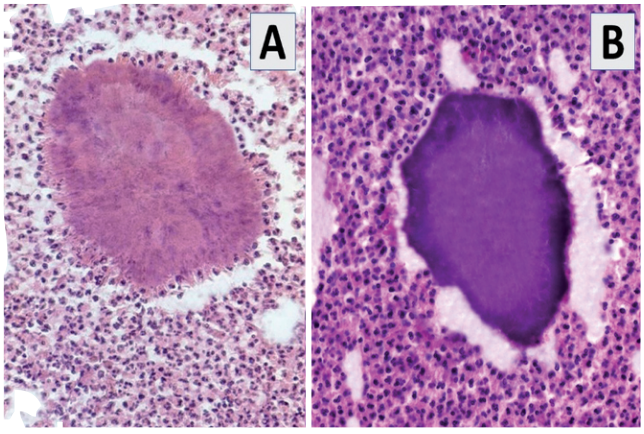

Figure 3. FNAC of pulmonary actinomycosis showing sulfur granules in cell block preparations surrounded by numerous acute inflammatory cells (H&E, x400).

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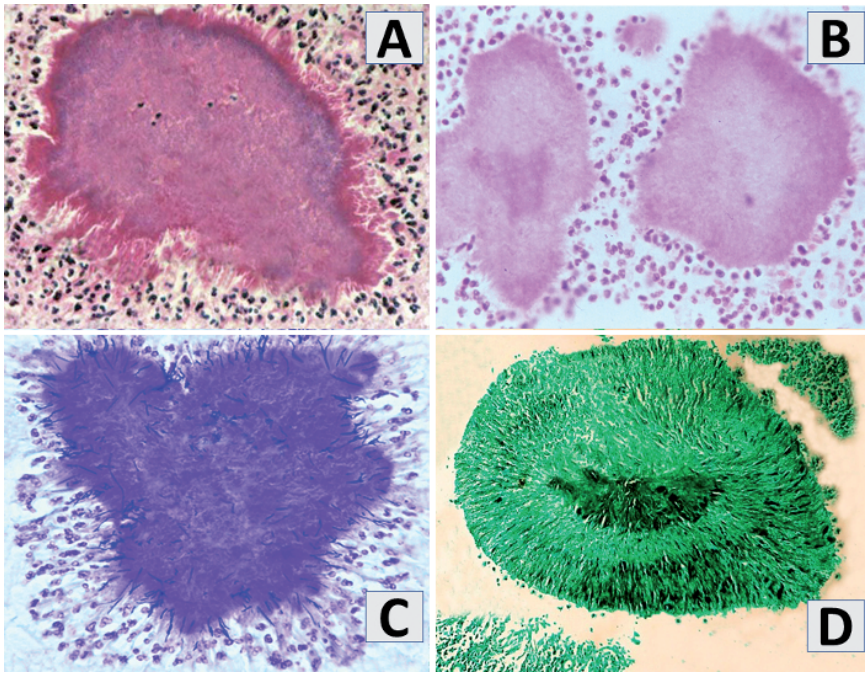

Figure 4. Cell blocks in pulmonary actinomycosis showing oval shaped sulfur granules with filiform bacilli mainly located at the periphery. A) H&E stain, x200; B) PAS stain, x200; C) Giemsa stain, x200; D) Grocott-Gomori stain, x200.

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