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Pulmonary actinomycosis mimicking lung malignancy: About two cases

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ABSTRACT

Pulmonary actinomycosis is a rare anaerobic infection with non specific clinical and radiographic presentations that delay diagnosis. Throughout literature, a significant number of misdiagnosed cases have been reported. The diagnosis is substantially based on histopathological pattern.

We describe the cases of two patients evaluated and treated in pulmonary department 1 of Abderrahmane Mami hospital of Tunisia with a diagnosis of pulmonary actinomycosis. There are two men. The first patient had hypertension and chronic obstructive pulmonary disease and the second one underwent surgery for bronchiectasis. Clinical presentation was consistent with productive cough, hemoptysis, and deterioration of general status. The medical examination was non-specific. The chest X-ray revealed an apical opacity, excavated in the first case and retractable in the second one. Biology showed an inflammatory syndrome. Bronchoscopy was performed in the two cases and showed lesions mimicking lung malignancy. Diagnosis is confirmed by histopathological examinations of surgical specimens in the two cases. Both patients were received antibiotic therapy. The results were excellent with a favorable clinical course and no deaths.

This study highlights the misleading patterns of actinomycosis to prompt accurate diagnosis and earlier treatment, thus improving the outcome. Given either its low culture yield or the limited use of new molecular diagnostic tools in routine clinical practice, histological examination of lung tissue specimens is crucial to get the correct diagnosis.

1. Introduction

Pulmonary Actinomycosis is a rare and suppurative infection caused by gram-positive, anaerobic filamentous bacteria belonging to the family *Actinomyceataceae*. It is mainly found in the human commensal flora of the oropharynx, gastrointestinal tract, and urogenital tract [1]. Clinical manifestations are so various. It may mimic other infectious lung diseases or malignancies. Pulmonary Actinomycosis can sometimes be misdiagnosed because of the slow-growing and fastidious nature of bacteria, making it difficult to culture and requires, then, surgical biopsy [2]. Timely identification is crucial as the prognosis is good with appropriate treatment but can be fatal if untreated. Herein, we describe two cases of pulmonary actinomycosis with nonspecific clinical and radiologic features representing, thus, a great diagnostic challenge.

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Case 1: a 70 - year - old, ex-smoker (45 pack-years) man with past medical history of systemic hypertension and untreated chronic obstructive pulmonary disease (COPD), was admitted to the department for a purulent productive cough and weight loss. Physical examination showed fever at 38 °C, tachycardia (95 beats per minute), rhonchi at auscultation, and poor dental hygiene with missing teeth. Chest X-ray film revealed excavated left apical opacity (Fig. 1).

Laboratory findings showed inflammatory syndrome (white blood cells: 10400/mm^3, C-reactive protein: 58mg/l), hemoglobin: 12.2 g/dl. Acid Fast Bacillus (AFB) search in sputum and cytobacteriological sputum analysis were negative. The diagnosis of necrotized pneumonia was made. The patient was treated with cefotaxime, metronidazole for two weeks, and gentamycin for five days. There was a clinical and biological improvement.

In the context of the etiological assessment of necrotizing pneumonia, a Computed tomography [3] was performed and revealed an excavated parenchymal opacity of the left upper lobe accompanied by thick wall enhancement after injection of contrast media and a suspicious adrenal mass (Fig. 2).

Bronchoscopy showed infiltration of the left upper lobe. Bronchoalveolar lavage [4] didn't show any bacteria. AFB search was negative in the bronchial fluid. The latter was examined by optic microscopy. It contained inflammatory but not neoplastic cells. Bronchial biopsy showed an inflammatory mucosa.

To better characterize adrenal mass, an adrenal MRI was requested but the patient was lost to follow-up. He presented to us five months later for hemoptysis, persistent productive cough, and deterioration of the general status. Another CT scan was obtained and revealed a left liquefied and excavated bilobar mass with convex margins associated with multiple nodes of the right upper lobe. The adrenal nodule was stable (Fig. 3).

A second bronchoscopy was performed. It showed an oedematous and erythematous mucosa of the left basal pyramid bronchi. Bronchial fluid was free of AFB and neoplastic cells. Another bronchial biopsy didn't reveal cancer.

As the opacity grew up on the CT scan, the diagnosis of lung cancer was suspected and a thoracotomy was performed.

Wedge resection was realized in the lingula. Histological examination of the surgical sample concluded with actinomycosis. The patient was therefore treated with amoxicillin-clavulanic acid for five weeks with a favorable clinical outcome.

Case 2: a 39-year-old man, ex-smoker (9 pack-years) underwent in 1994 a lower and middle lobectomy for bronchiectasis and was hospitalized in 2010 suffering from chest pain, hemoptysis, asthenia, and appetite loss. On examination, the patient was febrile at 38.2 °C. He had tooth decay. The chest X-ray revealed a heterogeneous retractile right apical opacity. Laboratory values showed an inflammatory syndrome (hyperleukocytosis at 10300, C-reactive protein at 221). AFB search in sputum was negative. Cytobacteriological sputum analysis was negative. A bronchoscopy was performed and showed a regular pedicled process of 1 cm, localized 2 cm from the lobectomy stump. Bronchial biopsies concluded to granulation tissue. The patient was treated empirically with amoxicillin-clavulanic acid for two weeks with biological improvement. However, clinically, the patient was getting worse. He presented with massive hemoptysis that was resistant to conservative treatment, requiring then, embolization. This hemoptysis was related to a right bronchial and peribronchial hypervascularization revealed with CT scan. Two months later, the patient underwent a right-completion pneumonectomy. A definitive pathological review of the surgical piece concluded with pulmonary actinomycosis (Fig. 4 (a,b)).

The patient received 18 million units of penicillin G per day for 3 weeks intravenously followed by oral therapy with amoxicillin 1 g 3 times daily for 9 months with clinical and biological improvement. Currently, he suffered from a gradual worsening dyspnea on exertion.

2. Discussion

In our study, we have described two cases of pulmonary actinomycosis, a rare life-threatening infectious disease with nonspecific features whose prognosis is excellent if treated early. This infection represents a great diagnostic challenge due to multiple alternative diagnoses including lung cancer.

Actinomycosis is a chronic suppurative infection caused by Actinomyces species most frequently *Actinomyces israelii*, a gram-positive, facultative anaerobic or microaerophilic branching, pleomorphic, non-spore-forming, nonacid-fast and slow-growing organisms belonging to the normal flora of the oropharynx, as well as the gastrointestinal and urogenital tracts [5,6]. Pulmonary

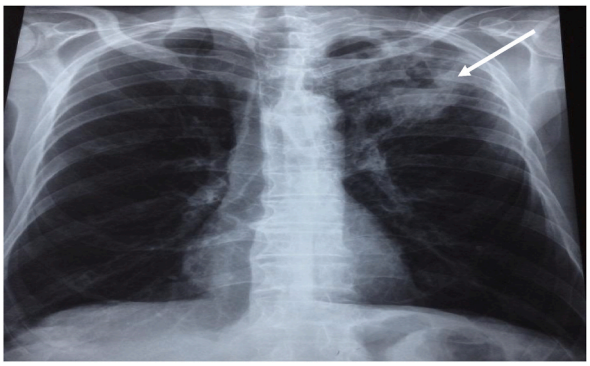

Fig. 1. Chest X-Ray film: left apical excavated opacity (arrows show the excavation).

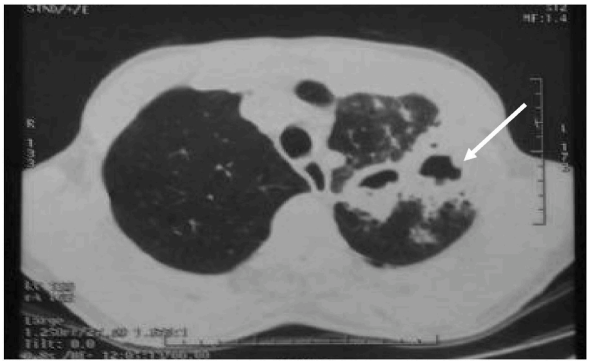

Fig. 2. Excavated left apical opacity noted by the white arrow.

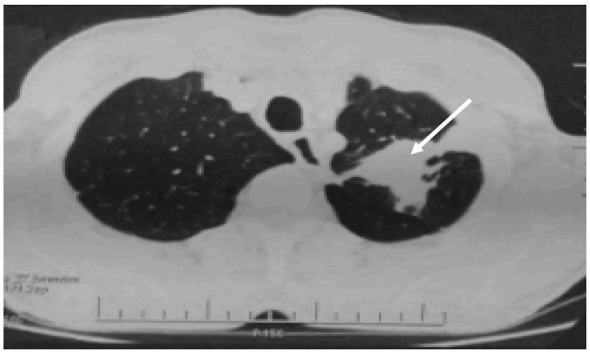

Fig. 3. CT view of excavated and liquefied tissue process (white arrow).

actinomycosis has a global prevalence, although there has been a significant decline in reported cases over the past forty years. The incidence of pulmonary actinomycosis is higher in developing nations as compared to developed countries [7].

Pulmonary actinomycosis is the third most common localization of actinomycosis, after cervicofacial and abdominopelvic actinomycosis [8]. Pulmonary actinomycosis can be found worldwide and accounts for 15–20% of the total burden of actinomycosis [9].

Pulmonary actinomycosis can occur at all ages. Men are more likely to be affected than women (3:1) [10]. In the context of pulmonary actinomycosis, several risk factors have been identified, including inadequate oropharyngeal hygiene, gingivitis, dental diseases, recent dental surgeries, trauma, aspiration, immunocompromised states, uncontrolled diabetes, and existing local or distant actinomycosis infections [11,12].

Limited case series have indicated an increased prevalence of pulmonary actinomycosis among individuals with pre-existing chronic respiratory conditions, such as chronic bronchitis, emphysema, and bronchiectasis [4,13].

The unique aspect of our two patients is that they presented not only with poor oral hygiene but also with underlying chronic respiratory diseases, namely COPD and bronchiectasis.

Up to now, 14 species have been characterized to date. Six among these are thought to be pathogenic in humans (*A. israelii, A. naeslundi, A. odontolyticus, A. viscosus, A. meyeri,* and *A. gerencseriae*). *A. israelli* is the organism most commonly incriminated in human disease and it affects the lungs following aspiration of oral bacteria in saliva. In contrast to other species, *Actinomyces meyeri* has been shown to have a predilection for causing pulmonary actinomycosis with dissemination to other organs [7].

Diagnosis of actinomycosis can be difficult and is frequently delayed owing to prolonged and nonspecific clinical signs [14]. In our study, the patients were complaining of hemoptysis, productive cough, and deterioration of general status with a consultation delay ranging from 1 to 3 months.

The diagnosis of pulmonary actinomycosis involves the histological and microbiological examination of tissue samples [7,8,15]. The best clinical specimens for microbiological diagnosis are deep-needle aspirates and tissue biopsies [11].

Actinomyces are difficult to culture because the organisms grow best at a temperature of 37 °C in an atmosphere of 6–10% ambient carbon dioxide and cultures require brain/heart-enriched agar [16].

Thus, in most cases, the diagnosis of actinomycosis is histological requiring invasive investigations to obtain samples for histopathological and microbiological identification [16,17]. Typical histological findings in pulmonary actinomycosis include a combination of suppurative and granulomatous inflammatory reactions, proliferation of connective tissue, presence of sulfur granules, and the identification of filamentous gram-positive ray-like bacilli [1].

In our cases, the diagnosis was established with positive samples of surgical biopsy of the lesion.

Molecular biological detection technology has emerged as a novel approach for diagnosing pulmonary actinomycosis.

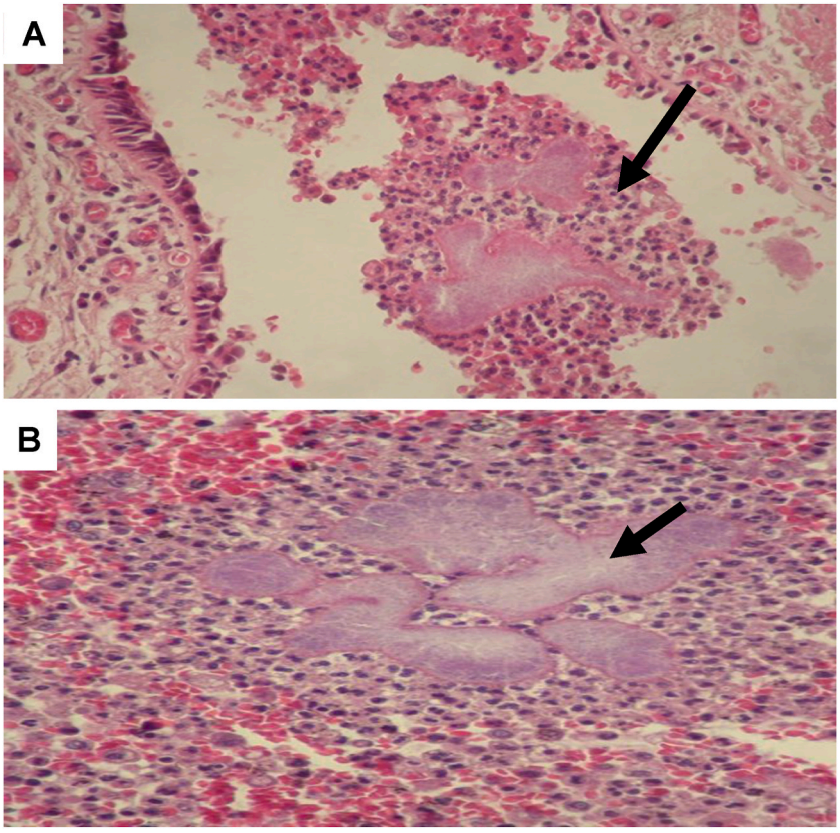

Fig. 4. A bronchial lumen with actinomycosis seeds **b** suppurated necrotic foci with characteristic sulfur granules (x 160, HE stain).

Metagenomic next-generation sequencing (mNGS) is a highly sensitive method that does not rely on bacterial culture and has shown great utility in diagnosing pulmonary actinomycosis. This technique offers increased sensitivity and overcomes the challenges associated with bacterial culture [18].

In the context of pulmonary actinomycosis, bronchoalveolar lavage fluid (BALF) is recommended as the preferred sample collection method. BALF offers improved detection of respiratory microbes specific to pulmonary actinomycosis [19]. Another diagnostic test includes using polymerase chain reaction with specific primers to Actinomyces clinical material [20,21] Matrix-assisted laser desorption ionisation time-of-flight (MALDI-TOF) has been previously used to identify Actinomyces [22].

Recently, molecular techniques such as fluorescence in situ hybridization (FISH) have emerged for the prompt detection of Actinomyces species [14]. In fact, FISH with actinomycetes specific fluro-probe against the Universal bacterial probe (EUB338) would be a valuable addition for Actinomycosis detection and compared the actinomycetes counts with available control lung tissues/biopsies.

The upfront diagnosis of pulmonary actinomycosis is uncommon [23,24]. The differential diagnosis of actinomycosis includes tuberculosis, semi-invasive pulmonary aspergillosis, and other sub-acute necrotizing bacterial pneumonia [5,17,25]. In Tunisia, diagnosing pulmonary actinomycosis can pose significant challenges due to the high incidence of tuberculosis in the country.

Though, the most concerning differential diagnosis for pulmonary actinomycosis remains lung cancer [26].

The main treatment, according to Mabeza et al., is high-dose intravenous penicillin for a long duration, and generally, 18–24 million units of penicillin per day are given for 2–6 weeks followed by oral therapy with penicillin V or amoxicillin for 6–12 months [7]. Alternatively, ampicillin and amoxicillin with or without clavulanic acid have been used successfully in case series as well as in our first case [27].

Actinomycosis is considered a rare disease with a very low mortality rate if the infection is recognized early and proper treatment is given [28]. An early accurate diagnosis will prevent the considerable morbidity associated with either delayed or missed diagnosis [7].

We present here two cases of pulmonary actinomycosis mimicking lung malignancies. This radio-clinical presentation is uncommon and the diagnosis is very difficult to acquire generally through surgery. Table 1 summarizes all series of pulmonary actinomycosis masquerading lung cancer across the literature.

2.1. Advances in knowledge

To our knowledge, this is the first reported case study with a review of pulmonary actinomycosis mimicking lung cancer. Differentiating between lung cancer and pulmonary actinomycosis is a challenging task, especially considering the limited availability

Table 1
Summary of all cases of pulmonary actinomycosis mimicking lung malignancies throughout literature.

Study (year)	country	Age, Sex	Signs and symptoms	Radiological features	Diagnosis confirmation	Treatment and course
Moore and Scannell (1968) [29]	USA	Case 1 34, man	hacking cough and increasing listlessness of 2 months	**Chest X ray:** in the right upper lobe, a rounded lesion in continuity with the chest wall	Histopathological examination (exploratory thoracotomy)	long-term penicillin therapy (dose?, duration ?) Good outcomes
		Case 2 50, man	asymptomatic	**Chest X ray:** mass in the left upper lobe	Histopathological examination (lobectomy with regional lymph node dissection than pneumonectomy)	
Rippon, J. W., & Kathuria, S. K. (1984) [30]	USA	55, Man	asymptomatic	**Chest X ray:** left upper lobe mass	Histopathological examination (lobectomy:lobular mass containing multiple micro-abscesses) Cultures of surgical piece (Actinomyces meyeri)	–
Aarnio et al. (1990) [31]	Finland	41, man	cough and fever for 3 weeks	**Chest X ray:** large opacity in the right upper lobe with pleural reaction. **CT scan:** solid infiltration in the periphery of the right upper lobe	Histopathological examination (Thoracotomy with resection of lung and ribs)	Intravenous (IV) benzylpenicillin, 4 million U x 4 for 15 days followed by phenoxymethylpenicillin 3 million U by mouth four times daily for 5 weeks and then 2 million U x 3 for 4 months Good short and long-term outcomes
Lau, K. Y. (1992) [32]	USA	60, man	fever, chills, hemoptysis, and left sided chest pain for 4 months	**Chest X ray:** infiltrate in the left lower lobe	Histopathological examination (bronchial biopsy specimen via bronchoscopy) Cultures of bronchial biopsy specimen: negative	Oral penicillin and probenecid for one year Clinical and radiological improvement
Nakamura, S (1993) [33]	Japan	45, man	hemoptysis	**Chest X ray:** mass in the S3 segment of the right lung	Histopathological examination (right upper lobectomy)	–
Izumi Y (2000) [34]	Japan	61, man	fever, productive cough, and occasional blood-streaked sputum	**Chest X ray:** mass in the right middle lung	Histopathological examination (right lower lobectomy)	–
M.-S. Lu et al. (2003) [35]	Taiwan	Case 2 53, woman	hemoptysis	Hilar mass in right lower lobe	Histopathological examination (right lower lobectomy)	12 million units per day of intravenous crystalline penicillin G during hospitalization. antibiotic treatment was completed in up to 3 months with oral procaine penicillin Good outcomes
		Case 4 55, man	Hemoptysis, cough	Right middle lobe mass	Histopathological examination (right middle lobectomy)	
		Case 5 53, man	Hemoptysis, chest pain	Right upper lobe mass	Histopathological examination (right upper lobectomy)	
		Case 8 74, man	hemoptysis	Right upper lobe mass	Histopathological examination (right upper lobectomy)	
		Case 12 56, man	hemoptysis	Right upper lobe mass	Histopathological examination (right upper middle bilobectomy)	
		Case 13 51, woman	hemoptysis	left upper lobe mass	Histopathological examination (left upper lobe wedge resection)	
		Case 14 57, man	hemoptysis	Right upper lobe mass	Histopathological examination (right upper lobectomy)	
Ganesan, K. (2005) [36]	United Kingdom	9, boy	right axilla pain and malaise for 1 week and	**Chest X ray**: opacity in the right upper zone with mild subperiosteal new	Histopathological examination(right thoracotomy and open	One week of IV penicillin (75 mg/kg/day) followed by oral penicillin (35 mg/kg/day) for

(*continued on next page*)

Table 1 (*continued*)

Study (year)	country	Age, Sex	Signs and symptoms	Radiological features	Diagnosis confirmation	Treatment and course
			productive cough with green sputum for 2 weeks	bone formation in the right first and second ribs **CT scan, thoracic MRI and bone scans:** pulmonary neuroblastoma or small cell tumor of the lung?	lung biopsy through the 4th intercostal space)	3 months Complete radiological resolution after 3 months of treatment
Madhusudhan K S (2007) [37]	India	Case1 63, man	cough and hemoptysis for six months with loss of appetite and weight	**Chest X ray:** peripherally located parenchymal opacity in the right upper and middle zone **CT scan:** mass in right upper lobe abutting the chest wall	Histopathological examination (CT-guided biopsy)	Not specified parenteral antibiotic therapy for a one month Significant resolution of radiological lesion after 3 weeks of treatment
Ferreira HPC (2010) [38]	Brazil	26, woman	chest pain for two months with fever, dyspnea, worsening of overall health status, and productive cough with mucoid expectoration	**MRI:** mass with irregular border occupying the entire left upper lobe invading the mediastinum and chest wall and involving the left common carotid artery, the left subclavian artery, and part of the aortic arch artery, and part of the aortic arch **CT scan:** invasion of the abovementioned structures and of the vertebral bodies and the left supraclavicular fossa	Histopathological examination (exploratory thoracotomy) CT-guided transthoracic needle biopsies: inconclusive	Crystalline penicillin (dose ?) for 30 days, then amoxicillin (dose?) for 6 months Complete remission but fibrosis of the left lower lobe
Wei-Sha Lin, Ching-Chi Lin et al. (2011) [39]	Taiwan	50, woman	progressive dyspnea on exertion and chest pain for 1 year, chronic cough with hemoptoic sputum and weight loss	**Chest X ray:** cavitary mass in the right upper lung patchy opacity in the left lower lung. **CT scan:** heterogenously enhanced mass in mediobasal portion of the right hemi lung and left lower lobe lung with enlarged nodes	Histopathological examination (bronchial biopsies via fiberoptic bronchoscopy: polypoid mass plug obstructing the orifice of the apical and posterior segment of the right upper lung)	IV penicillin G 5 million U started every 6 hours for 4 weeks and switched to oral penicillin V 1 g every 6 hours for 6 months Complete recovery
Kanda,H (2011) [40]	Japan	53, man	bloody sputum	**CT scan:** tumor in the anterior basal segment (S8) of the left lower lobe **PET CT:** accumulation at the same site	Histopathological examination (segmental resection)	–
PEREIRA, Nicolás et al. (2012) [41]	Chile	63, man	left hemi-thorax pain and weight loss	**Chest X ray:** opacity with ill-defined borders in the left perihilar region **CT scan:** tumor in the left upper pulmonary lobe with extensive involvement of the anterior chest wall	Histopathological examination (chest wall specimen via surgical biopsy)	Penicillin G IV for 2 weeks then amoxicillin for three months (dose?)
Fichte et al. (2013) [42]	Germany	55, man	gait disturbance ,weakness of the hands and weight loss	**MRI and CT of the cervical spine:** a destructing process in the vertebrae C7 (partial) and T1 causing relevant spinal stenosis and cord compression **MRI localizers:** apical lung mass on the right side **chest X-ray and CT scan:** pancoast tumor of the right lung with suspected	Histopathological examination (Corpectomy of T1) CT-guided biopsy for the lung Mass: fibrosis with inflammatory reaction Cultures of operative specimen negative	Ampicillin/sulbactam 3 × 3 g IV for 11 months complete clinical and radiological recovery

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Table 1 (*continued*)

Study (year)	country	Age, Sex	Signs and symptoms	Radiological features	Diagnosis confirmation	Treatment and course
				intrapulmonary metastases		
Taklit, R (2013) [43]	Turkey	50, man	asymptomatic	**Chest X ray:** irregular localized pneumonic consolidation in the middle zone of the right lung **CT scan:** mass lesion in the upper lobe of the right lung **PET CT:** linear F-18 fluorodeoxyglucose (FDG) uptake detected in the middle right lung	Histopathological examination (lobectomy of the middle zone of the right lung)	Oral amoxicillin (2 g/daily) for 30 days
Katsenos, S (2015) [5]	Greece	Case 1 67, man	Intermittent hemoptysis for one week	**Chest X ray:** infiltrate in the right upper lobe with associated mild pleural thickening **CT scan:** nodular opacity in the posterior segment of the right upper lobe accompanied by mild ipsilateral pleural thickening and bilateral mediastinal lymphadenopathy	Histopathological examination (EBUS-guided transbronchial biopsies from the peripheral lesion)	million units of penicillin per day for 3 weeks followed by amoxicillin 2 gr daily for a total of six months Complete clinical and radiological improvement
		Case 2 70, woman	persistent nonproductive cough with malaise	**Chest X ray:** right lung volume reduction with ill-defined consolidation in the right lower lung field **CT scan:** right hilar mass compressing the bronchus intermedius with accompanying dense airspace opacification of right lower lobe and atelectasis with enlarged nodes	Histopathological examination (Bronchial biopsy specimen via bronchoscopy)	24 million units of penicillin per day for 3 weeks, then amoxicillin 2 gr daily for a total of six months Complete recovery
Prakash et al. (2015) [44]	India	60, man	hemoptysis and chest pain for 7 months	**Chest X ray:** left upper zone lung mass **CT scan:** heterogeneously enhancing soft tissue attenuation lesion with irregular margin in left upper lobe infiltrating the overlying pleura and abutting with left subclavian and common carotid artery	Histopathological examination(CT guided fine-needle aspiration cytology and biopsy)	I.M Benzyl Penicillin 5 million IU/day for undefined duration Clinical improvement
S. Nakamura et al. (2017) [16]	Japan	73, man	left chest pain	**Chest X ray/CT scan:** left complicated effusion and a consolidation in the left upper lung	Histopathological examination (transbronchial lung biopsy specimen from the left B1/2) Culture of BALF negative	18 million units of IV penicillin per day given for 4 weeks followed by oral therapy with amoxicillin for twelve months Clinical improvement
Vidaur EA et al. (2017) [45]	Honduras	22, man	chronic cough, hemoptoic sputum, fever and pleuritic pain	**Chest X ray:** apical right rounded opacity **CT scan:** abscessed mass in the posterior segment of the right upper lobe	Histopathological examination (lung biopsy via right poster lateral thoracotomy)	crystalline penicillin 5 million IU IV modified every 6 hours with PPS Clinical improvement
Mutlu et al. (2018) [46]	Turkey	67, man	cough and hemoptysis for two months	**Chest X ray:** increased non-homogeneous density in the middle zone of the left hemithorax	Histopathological examination (Transthoracic fine needle aspiration biopsy)	Sulbactam + ampicillin for 15 days and amoxicillin clavulanic acid treatment for five months

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Table 1 (*continued*)

Study (year)	country	Age, Sex	Signs and symptoms	Radiological features	Diagnosis confirmation	Treatment and course
				CT scan: hypodense mass **PET scan:** malignant pleural hypermetabolic lesion		Significant regression clinically and radiologically
Grzywa-Celińska A (2018) [47]	Poland	77, man	massive hemoptysis of several days	**Chest X ray:** lung consolidation in the lower part of the right hilus **CT scan:** spicular consolidation at the base of segment 2 of the right lung, centrally located cavity in left lower lobe with enlarged nodes	Histopathological examination (peri bronchial lung biopsy in segment 2 of the right lung via bronchoscopy) Culture of Bronchoaspirate: negative	IV penicillin G started with a dose of 18 million units/day for 3 weeks, then with amoxicillin on an outpatient basis for a total duration of 6 months During IV treatment, hemoptysis subsided and after 6 months of treatment Radiological improvement
Papakonstantinou, N (2019) [48]	Greece	76, man	dyspnea	**Chest X ray**: right lower pulmonary lobe consolidation with large ipsilateral pleural effusion **PET-CT**: right lower lobe lesion measuring with high metabolic activity **Lung ventilation/ perfusion scan:** decreased activity of the right lung (29%)	Histopathological examination(right lower lobectomy)	Not specified antibiotic for six months Good outcomes
Chew, S. Y (2019) [49]	Singapore	78, man	hemoptysis	**Chest X ray:** vague right cardiophrenic lung opacity **CT scan**: right middle lobe nodule	Histopathological examination (transbronchial lung biopsy)	–
W. Wang, D. Ren, C. Xu et al. (2020) [50]	China	65, man	fever and dry cough for ten days	**Chest X ray:** fuzzy mass lesion in the upper lobe of the right lung **HRCT:** mass with an inhomogeneous density and irregular edges	Culture: radial endobronchial ultrasound coupled with metagenomic next-generation sequencing (PCR of BALF)	Azithromycin (0.5, intravenous/oral, QD) for six months Clinical improvement HRCT: remarkable absorption of the lung lesion
Florina Neacşu et al. (2021) [51]	Romania	Case 2 59, man	dyspnea and chest pain	**CT:** suspicion of mesothelioma	Histopathological examination of surgical piece (eighth segment a firm nodule showing aspects of pleural invasion)	–
Aydin, Y (2022) [52]	Turkey	54, woman	cough, fever, sputum, chest pain, and hemoptysis	**PET CT:** hypermetabolic lesion with irregular borders in the anterior segment of the left lung upper lobe	Histopathological examination (left upper lobectomy)	–
Miyazaki et al. (2022) [53]	Japan	64, man	painful solid lump in the chest wall with loss of appetite and weight	**Chest X ray:** consolidation in the left middle lung **CT scan:** mass-like consolidation in the left upper lobe **FDG-PET scan:** increased metabolic activity in the mass	Histopathological examination (Surgical extirpation of the mass with left upper lobe partial resection) Tissue cultures: negatives Culture of BALF: negative CT scan-guided transthoracic biopsy: inconclusive	Amoxicillin (1000 mg orally every 8 h) for 8 weeks Good outcomes
Khlaed D (2022) [54]	Algeria	71, man	hemoptysis for 2 weeks preceded cough with mucopurulent expectoration,pain in the left basithoracic side	**Chest X ray:** solitary pulmonary nodule left basal retrocardiac **CT scan:** inferior lobar para-aortic tissue mass	Histopathological examination (surgical specimen)	IV Cephalosporin (molecule? Dose?) for 02 weeks, then amoxicillin 3 g for 04 months

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Table 1 (*continued*)

Study (year)	country	Age, Sex	Signs and symptoms	Radiological features	Diagnosis confirmation	Treatment and course
			and asthenia and weight loss			
Our study	Tunisia	Case 1 70, man	purulent productive cough and weight and appetite loss	**Chest X ray:** excavated left apical opacity **CT scan:** left proximal bilobar tissue process	Histopathological examination (wedge resection in the lingual)	Amoxicillin-clavulanic acid for five weeks Good outcomes
		Case 2 39, man	chest pain, hemoptysis and weight and appetite loss	**Chest X ray:** heterogeneous retractile right apical opacity	Histopathological examination (right completion pneumonectomy)	18 million units of penicillin G per day for 3 weeks IV then oral therapy with amoxicillin one g 3 times daily for 9 months Clinical improvement

of advanced diagnostic techniques such as molecular biology in our country.

2.2. Application to patient care

This report can be a valuable tool for healthcare providers in Tunisia, assisting them in diagnosing and treating pulmonary actinomycosis. It presents multiple therapeutic protocols that can be applied in clinical practice.

3. Conclusion

The two cases provide useful information regarding the difficulties of diagnosis of pulmonary actinomycosis. Pulmonary actinomycosis and lung malignancy exhibit similar clinical and radiological findings, which can make it difficult to differentiate between the diseases. Pulmonary actinomycosis should be considered in case of the presence of predisposing risk factors. We emphasize that bacterial cultures and pathology are the cornerstones of diagnosis and require particular attention to prevent misdiagnosis.

Ethical approval

Ethical approval was waived by the local Ethics Committee of Abderrahmane Mami University Hospital in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Informed consent

informed consent was obtained from the patients for the publication of all images, clinical data and other data included in the main manuscript.

Learning points

- Pulmonary actinomycosis is uncommon but treatable condition.
- It is commonly misdiagnosed as lung malignancies and may require surgery to confirm diagnosis.
- With early diagnosis and proper treatment the prognosis is great.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] V.K. Wong, T. Turmezei, V. Weston, Actinomycosis. Bmj (2011) 343.

[2] A. Weissferdt, Infectious Lung Disease. Diagnostic Thoracic Pathology, Springer International Publishing, Cham, 2020, pp. 3–71.
[3] A.O. Vidaur Na, E.A. Vidaur, et al., Solitary pulmonary nodule, pulmonary actinomycosis of chronic, report. Eac. Solitary pulmonary nodule, pulmonary actinomycosis of chronic evolution: a case report, Electronic J Biol 13 (3) (2017), 265-8.
[4] T. Skuhala, D. Vukelić, B. Desnica, M. Balen-Topić, A. Stanimirović, K. Višković, Unusual presentations of actinomycosis: a case series and literature review, The Journal of Infection in Developing Countries 15 (6) (2021) 892–896.
[5] S. Katsenos, I. Galinos, P. Styliara, N. Galanopoulou, K. Psathakis, Primary bronchopulmonary actinomycosis masquerading as lung cancer: apropos of two cases and literature review, Case reports in infectious diseases 2015 (2015).
[6] S. Atay, F. Banki, C. Floyd, Empyema necessitans caused by actinomycosis: a case report, International journal of surgery case reports 23 (2016) 182–185.
[7] G. Mabeza, J. Macfarlane, Pulmonary actinomycosis, Eur. Respir. J. 21 (3) (2003) 545–551.
[8] F. Valour, A. Sénéchal, C. Dupieux, J. Karsenty, S. Lustig, P. Breton, et al., Actinomycosis: etiology, clinical features, diagnosis, treatment, and management, Infect. Drug Resist. 7 (2014) 183.
[9] N. Skehan, M. Naeem, R.V. Reddy, Endobronchial actinomycosis: successful treatment with oral antibiotics, BMJ Case Rep. 2015 (2015), bcr2015212754.
[10] J.Y. Park, T. Lee, H. Lee, H.-J. Lim, J. Lee, J.S. Park, et al., Multivariate analysis of prognostic factors in patients with pulmonary actinomycosis, BMC Infect. Dis. 14 (1) (2014) 10.
[11] S.R. Kim, L.Y. Jung, I.-J. Oh, Y.-C. Kim, K.-C. Shin, M.K. Lee, et al., Pulmonary actinomycosis during the first decade of 21st century: cases of 94 patients, BMC Infect. Dis. 13 (1) (2013) 216.
[12] M. Zhang, X. Zhang, Y. Chen, Primary pulmonary actinomycosis: a retrospective analysis of 145 cases in mainland China, Int. J. Tubercul. Lung Dis. 21 (7) (2017) 825–831.
[13] K.P. Schaal, H.-J. Lee, Actinomycete infections in humans—a review, Gene 115 (1–2) (1992) 201–211.
[14] L. Boyanova, R. Kolarov, L. Mateva, R. Markovska, I. Mitov, Actinomycosis: a frequently forgotten disease, Future Microbiol. 10 (4) (2015) 613–628.
[15] A. Moniruddin, H. Begum, K. Nahar, Actinomycosis: an update, Med. Today 22 (1) (2010) 43–47.
[16] S. Nakamura, M. Kusunose, A. Satou, K. Senda, Y. Hasegawa, K. Nishimura, A case of pulmonary actinomycosis diagnosed by transbronchial lung biopsy, Respiratory medicine case reports 21 (2017) 118–120.
[17] Y. Higashi, S. Nakamura, N. Ashizawa, K. Oshima, A. Tanaka, T. Miyazaki, et al., Pulmonary actinomycosis mimicking pulmonary aspergilloma and a brief review of the literature, Intern. Med. 56 (4) (2017) 449–453.
[18] W. Wang, D. Ren, C. Xu, Q. Yuan, Q. Zhang, H. Hu, et al., Pulmonary actinomycosis diagnosed by radial endobronchial ultrasound coupled with metagenomic next-generation sequencing: a case report and brief literature review, Int. J. Infect. Dis. 100 (2020) 379–381.
[19] W. Huang, C. Yin, G. Wang, J. Rosenblum, S. Krishnan, N. Dimitrova, et al., Optimizing a metatranscriptomic next-generation sequencing protocol for bronchoalveolar lavage diagnostics, J. Mol. Diagn. 21 (2) (2019) 251–261.
[20] V. Hall, Actinomyces—gathering evidence of human colonization and infection, Anaerobe 14 (1) (2008) 1–7.
[21] D. Himeji, S. Hara, T. Kawaguchi, G-i Tanaka, Pulmonary Actinomyces graevenitzii infection diagnosed by bronchoscopy using endobronchial ultrasonography with a guide sheath, Intern. Med. 57 (17) (2018) 2547–2551.
[22] L. Ng, J. Sim, L. Eng, S. Menon, T. Tan, Comparison of phenotypic methods and matrix-assisted laser desorption ionisation time-of-flight mass spectrometry for the identification of aero-tolerant Actinomyces spp. isolated from soft-tissue infections, Eur. J. Clin. Microbiol. Infect. Dis. 31 (2012) 1749–1752.
[23] M. Suzuki, K. Araki, S. Matsubayashi, K. Kobayashi, E. Morino, J. Takasaki, et al., A case of recurrent hemoptysis caused by pulmonary actinomycosis diagnosed using transbronchial lung biopsy after bronchial artery embolism and a brief review of the literature, Ann. Transl. Med. 7 (5) (2019).
[24] D.C. Sullivan, S.W. Chapman, Bacteria that masquerade as fungi: actinomycosis/nocardia, Proc. Am. Thorac. Soc. 7 (3) (2010) 216–221.
[25] M. Thomas, T. Raza, M. Al Langawi, A 37-year-old man with nonresolving pneumonia and endobronchial lesion, Chest 148 (2) (2015) e52–e55.
[26] M. Boot, J. Archer, I. Ali, The diagnosis and management of pulmonary actinomycosis, Journal of Infection and Public Health 16 (4) (2023) 490–500.
[27] M. Kalditz, A. End, Actinomycosis of the lung and pleura. Complex pleuropulmonary infections, Eur. Respir. Monogr. 61 (2013).
[28] T.F. Pézier, N. Kastrinidis, G.M. Widmer, G.F. Huber, R. Probst, Fatally invasive actinomycosis masquerading as a tonsillar carcinoma, Head Neck 36 (12) (2014) E129–E130.
[29] W.R. Moore, J.G. Scannell, Pulmonary actinomycosis simulating cancer of the lung, J. Thorac. Cardiovasc. Surg. 55 (2) (1968) 193–195.
[30] J.W. Rippon, S. Kathuria, Actinomyces meyeri presenting as an asymptomatic lung mass, Mycopathologia 84 (2) (1984) 187–192.
[31] P. Aarnio, E. Keskitalo, E. Nieminen, Actinomycosis simulating pulmonary neoplasm in a previously healthy man, Scand. J. Thorac. Cardiovasc. Surg. 24 (1) (1990) 93–94.
[32] K.-Y. Lau, Endobronchial actinomycosis mimicking pulmonary neoplasm, Thorax 47 (8) (1992) 664–665.
[33] S. Nakamura, I. Hashizume, N. Kasamatsu, H. Kawana, S. Hanzawa, K. Sasaki, et al., A case of pulmonary actinomycosis that was difficult to distinguish from pulmonary carcinoma, Jpn. J. Thorac. Dis. 31 (1) (1993) 103–108.
[34] Y. Izumi, Y. Moroe, A. Onaka, R. Kato, S. Hirose, Pulmonary Actinomycosis presenting as a mass lesion on chest X-Ray film, Nihon Kokyuki Gakkai Zasshi= the Journal of the Japanese Respiratory Society 38 (3) (2000) 186–189.
[35] M.-S. Lu, H.-P. Liu, C.-H. Yeh, Y.-C. Wu, Y.-H. Liu, M.-J. Hsieh, et al., The role of surgery in hemoptysis caused by thoracic actinomycosis; a forgotten disease, Eur. J. Cardio. Thorac. Surg. 24 (5) (2003) 694–698.
[36] K. Ganesan, R. Khan, M. Eisenhut, Pulmonary actinomycosis masquerading as a malignant lung tumor in a 9-year-old boy, Clin. Pediatr. 44 (2) (2005) 181–183.
[37] K. Madhusudhan, S. Gamanagatti, A. Seith, S. Hari, Pulmonary infections mimicking cancer: report of four cases, Singap. Med. J. 48 (12) (2007) 1149.
[38] HPdC. Ferreira, CAAd Araújo, J.F. Cavalcanti, RLAd Miranda, RdAO. Ramalho, Pulmonary actinomycosis as a pseudotumor: a rare presentation, J. Bras. Pneumol. 37 (2011) 689–693.
[39] W.-S. Lin, C.-C. Lin, M.-J. Peng, Pulmonary actinomycosis mimicking cancer: a case report, 胸腔醫學. 26 (6) (2011) 346–351.
[40] H. Kanda, Y. Nakamura, T. Nagata, K. Fukumori, Y. Imoto, K. Tabata, et al., Surgery for pulmonary actinomycosis that was difficult to differentiate from lung cancer; report of a case, Kyobu geka The Japanese Journal of Thoracic Surgery 64 (9) (2011) 864–867.
[41] N. Pereira, P. Cuevas, C. Valencia, J. Vega, I. Gallegos, J.G. Fernández, et al., Thoracic actinomycosis in the differential diagnosis of neoplasm: a propos of a case, Rev. Chil. infectol.: Organo Oficial de la Sociedad Chilena de Infectologia 29 (4) (2012) 455–458.
[42] S. Fichte, M. Brodhun, S. Göttinger, S. Rosahl, J. Klisch, R. Gerlach, Vertebral and pulmonary actinomycosis mimicking metastatic lung cancer, J. Neurol. Surg. Cent. Eur. Neurosurg. 74 (S 01) (2013) e188–e192.
[43] R.O.S.A.K. Taklit, E. Bir, Incidentally detected pulmonary actinomycosis mimicking lung cancer: a case report, FLORA 18 (2) (2013) 90–93.
[44] K.S. Prakash Ved, Ashwini Kumar Mishra, Ajay Kumar Verma, Saumya Shukla, S.N.S. Yadav, Pulmonary actinomycosis masquerading as a malignant lung tumor, CHRISMED J. Health Res. 2 (3) (2015) 298–301.
[45] N. Vidaur, O. Alvareng, E. Vidaur, K. Vásquez, J. Cordón, A. Flores, et al., Solitary pulmonary nodule, pulmonary actinomycosis of chronic evolution: a case report, Electronic Journal of Biology 13 (3) (2017) 265–268.
[46] P. Mutlu, N.A. Mïrïcï, M.İ. Güven, Primary pulmonary actinomycosis mimicking malignancy, Haseki Tıp Bülteni 56 (1) (2018) 74–77.
[47] A. Grzywa-Celińska, J. Emeryk-Maksymiuk, K. Szmygin-Milanowska, E. Czekajska-Chehab, E. Czekajska-Chehab, J. Milanowski, Pulmonary actinomycosis - the great imitator, Ann. Agric. Environ. Med. 25 (2) (2017) 211–212.
[48] N.A. Papakonstantinou, G. Vlachou, C. Vourlakou, C. Zisis, Pulmonary actinomycosis masquerading as lung cancer: keep it in mind, ANZ J. Surg. 89 (7–8) (2019) 966–968.
[49] S.Y. Chew, C.S. Tan, Y. Puan, J.M.K. Koh, A 78-year-old man with recurrent hemoptysis and persistent pulmonary nodule, Chest 157 (3) (2020) e79–e84.
[50] W. Wang, D. Ren, C. Xu, Q. Yuan, Q. Zhang, H. Hu, et al., Pulmonary actinomycosis diagnosed by radial endobronchial ultrasound coupled with metagenomic next-generation sequencing: a case report and brief literature review, Int. J. Infect. Dis. : IJID : official publication of the International Society for Infectious Diseases 100 (2020) 379–381.

[51] F. Neacşu, A. Vârban, G. Simion, R. Şurghie, O.M. Pătraşcu, M. Sajin, et al., Lung cancer mimickers - a case series of seven patients and review of the literature, Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie 62 (3) (2021) 697–704.
[52] Y. Aydin, R. Arslan, M. Filik, Pulmonary actinomycosis mimicks lung cancer, Rev. Soc. Bras. Med. Trop. 55 (2022), e0195.
[53] S. Miyazaki, T. Fujito, Y. Kondo, Y. Kuno, S. Mori, R. Yamashita, et al., Pulmonary actinomycosis mimicking lung cancer on 18F-fluorodeoxyglucose positron emission tomography: a case report, J. Med. Case Rep. 16 (1) (2022) 255.
[54] D. Khaled, T. Besma, A. Kamel, B. Rachid, Pulmonary actinomycosis revealed by a solitary pulmonary nodule, Case Reports in Pulmonology 2022 (2022), 7877729.