



## Scientific letters

### *Actinomyces Meyer* Empyema<sup>\*</sup>



#### *Empiema por Actinomyces meyeri*

To the Editor,

Actinomycosis is a chronic infection caused by gram-positive anaerobic bacteria of the *Actinomyces* genus that are normally saprophytic colonizers of the oral cavity and gastrointestinal and urogenital tracts. Dissemination is generally hematogenous.<sup>1</sup> Unlike other *Actinomyces* species, *Actinomyces meyeri* (*A. meyeri*) can cause lung infections, although empyema caused by this strain is very rare. Actinomycosis is characterized by the development of fistulae in affected tissues and suppuration containing sulfur granules, and it is technically difficult to culture.

We report a case of empyema caused by *A. meyeri* recently treated in our hospital. Our patient was a 62-year-old man, smoker of 40 pack-years and alcohol consumption of 18 units/day, with severe neurosensory hypoacusia resulting from meningitis in his adolescence. He presented in the emergency department of our hospital with a 3-week history of left pleuritic pain, non-productive cough, a sensation of dysthermia, and unexplained weight loss. He was hemodynamically stable and afebrile, with normal breathing in room air. Physical examination revealed halitosis due to septic mouth with several missing teeth, reduced vocal fremitus throughout the left hemithorax and dullness on percussion, and hepatomegaly of 2 finger breadths.

Clinical laboratory tests showed: red blood cells  $3.77 \times 10^6/\mu\text{L}$ , hemoglobin 11.5 g/dl, hematocrit 33.9%, MCV 100, leucocytes  $8.87 \times 10^3/\mu\text{L}$  (85% neutrophils), sedimentation rate 120, total bilirubin 2.4 mg/dl (direct 1.9 mg/dl), GOT 114 IU/l, GPT 129 IU/l, GGT 280 U/l and alkaline phosphatase 245 U/l. Arterial blood gases (room air): pH 7.51, pCO<sub>2</sub> 33.1 mmHg, pO<sub>2</sub> 69.5 mmHg. Chest radiograph showed an apparently homogeneous increase in density occupying most of the left hemithorax, with a well-defined, convex upper border, that did not move when the patient was placed in lateral decubitus. Abundant left hyperechogenic pleural effusion with internal septa was observed on chest ultrasonography. Purulent fluid was obtained by thoracocentesis, showing pH 6.80, leucocytes  $173 \times 10^3/\mu\text{L}$  (75% neutrophils), glucose 15 mg/dl, LDH 20,000 U/l, proteins 4.7 g/dl, C-reactive protein 9.88 mg/dl, procalcitonin <0.020 ng/mL, interleukin-6 152,525 pg/ml and adenosine deaminase 227 U/l. A diagnosis of empyema was reached, and empirical antibiotic treatment began with i.v. amoxicillin/clavulanic acid 2 g every 8 h, chest tube (16F; 9 days), and intrapleural urokinase (100,000 IU/day, 3 days). Progress was favorable. Blood cultures were negative. Culture of pleural fluid for mycobacteria was negative, and anaerobic culture for *A. meyeri* was positive.

Two months later, the patient remains asymptomatic, and continues to receive oral amoxicillin (500 mg/8 h). Chest computed tomography shows pleural thickening throughout the lateral and posterior region of the left hemithorax with a minimum amount of associated pleural fluid.

Pleural infection with *A. meyeri* is very rare, and to date, only 12 cases have been published in the literature (Table 1).<sup>2–12</sup> Poor oral hygiene and alcoholism, as presented by our patient, are predisposing factors, since the bacteria reaches the pulmonary parenchyma via aspiration from the oral cavity. The pleura becomes involved either from contiguity or hematogenous dissemination.<sup>1,13</sup> Patients are usually men (11/13 cases; 84.6%), over 40 years of age (12/13; 92.3%), other organs in addition to the pleura may be involved (generally the lung), and fistulization may occur. Pleural fluid shows typical features of empyema: high LDH and leukocyte values (generally neutrophils), and low pH and glucose. Some cases may also involve high levels of adenosine deaminase and low proteins.<sup>14</sup>

The disease may coexist with lung cancer, since *A. meyeri* tends to colonize the necrotic tissue that often occurs with malignancy.<sup>15</sup> In the absence of characteristic sulfur granules in pus from the infected tissue, isolation in sputum can be a sign of simple colonization. In such cases, isolation of *A. meyeri* is of little diagnostic interest. In contrast, *A. meyeri* cultured in pleural fluid is the basis for the diagnosis of infection, and care should be taken to use appropriate anaerobic media. Treatment of choice is amoxicillin/clavulanic acid or penicillin G sodium (administered intravenously for 2–6 weeks, followed by oral amoxicillin for 6–12 months), depending on clinical and radiological progress. Other alternatives are clindamycin, doxycycline or erythromycin, if the patient has penicillin allergy or intolerance.<sup>7</sup> A chest tube and intrapleural fibrinolytics are generally required, and occasionally pleural decortication can be a last resort.<sup>14</sup> Progress is usually favorable, although one case of death has been reported.<sup>2</sup> Residual diffuse pleural fibrosis is a possible sequela. Our patient has only been receiving treatment for 2 months, but his clinical response appears to be favorable, pending evaluation of the possible sequela of his residual left pleural thickening with lung function testing.

The take-home message from this case is that when faced with slow-progressing pleural effusion that does not respond to standard antibiotics in a patient with known risk factors, cultures in the appropriate media should be performed to rule out empyema caused by *A. meyeri*.

#### Authors' contribution

Lucía Ferreiro: author and writer. Concept and design. Final approval of the manuscript.

María Luisa Pérez del Molino: co-author. Final approval of the manuscript.

Carlos Rábade: co-author. Final approval of the manuscript.

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**Table 1**  
Cases of Pleural Empyema Caused by *Actinomyces Meyeri* Described in the Literature.

Author (ref.)	Sex/Age (Years)	Risk Factor	Clinical Presentation	AB therapy	AB duration (Months)	CT	UK	Leuk. PF (cell)/seg (%)	pH	Glucose (mg/dl)	LDH (IU/l)	ADA (U/l)	Prot. (g/dl)	Progress
Rose et al. <sup>2</sup>	M/49	Alcoholism, poor oral hygiene	Empyema Pneumonia Bronchopleural fistula Osteomyelitis (sternum)	Penicillin G/clindamycin/ tetracycline	6 months (until death)	Yes								Death
	M/62	Alcoholism, poor oral hygiene	Empyema Pneumonia Subcutaneous abscess left hip	Penicillin G/amoxicillin	12 months	Yes								NS
Lentino et al. <sup>3</sup>	M/16	NS	Empyema Bone marrow	Clindamycin	6 months	Yes/thoracotomy (decortication)		141 × 10 <sup>3</sup> /83						Favorable
Alemanni et al. <sup>4</sup>	M/58	Alcoholism, poor oral hygiene	Empyema Muscle abscess	Penicillin G	NS	NS								Probably favorable
Del Castillo et al. <sup>5</sup>	M/61	Poor oral hygiene	Empyema	Penicillin G/amoxicillin	4 months	No		1 × 10 <sup>6</sup> /100	6.34	14	1367	74	5.1	Favorable Pleural thickening
Vallet et al. <sup>6</sup>	F/64	Alcoholism	Empyema Pleural-subcutaneous fistula	Penicillin	6 months	Yes/thoracotomy (decortication)								Favorable Pleural thickening
Fazili et al. <sup>7</sup>	M/45	Poor oral hygiene	Empyema Pneumonia	Penicillin G	12 months	Yes/thoracotomy (decortication)								Lost-to-follow-up
Porcel et al. <sup>8</sup>	M/49	Alcoholism	Empyema Pneumonia	Clindamycin/ doxycycline	6 months	Yes	Yes	160 × 10 <sup>9</sup> /neutroph	6.82	3	17,700	0.3	2.4	Favorable
Attaway et al. <sup>9</sup>	M/61	Alcoholism, poor oral hygiene	Empyema Pneumonia Lumpy jaw	Ampicillin/ penicillin G/doxycycline	6 months	Thoracotomy (decortication)								NS
Alonso et al., <sup>10 a</sup>	F/83	Dental abscess	Empyema	Imipenem/ doxycycline	6 months	Yes		649 × 10 <sup>3</sup> /neutroph	5	6	16,300		1.2	
Jung et al. <sup>11</sup>	M/49	Alcoholism	Empyema Pneumonia	Penicillin G/amoxicillin	4 months	Yes		56 × 10 <sup>3</sup> /89			20,530		3	Favorable
Sander et al. <sup>12</sup>	M/84		Empyema Pneumonia	Amoxicillin/ clavulanic acid	3 months	Yes	Yes	9.6 × 10 <sup>3</sup> /36	6.80	1	5560	117		Favorable
Our case	M/62	Alcoholism, poor oral hygiene	Empyema	Amoxicillin/ clavulanic acid	2 months <sup>b</sup>	Yes	Yes	173 × 10 <sup>3</sup> /75	6.80	15	20,000	227	4.7	Favorable <sup>b</sup> Pleural thickening

AB: antibiotic; ADA: adenosine deaminase; CT: chest tube; M: male; LDH: lactate dehydrogenase; Leuk.: leukocytes; PF: pleural fluid; F: female; NS: not specified; Prot.: proteins; ref: reference; UK: urokinase.

<sup>a</sup> *Actinomyces* spp.

<sup>b</sup> Treatment ongoing.

Luis Valdés: author and writer. Concept and design. Final approval of the manuscript.

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## Development and Co-existence of Sarcoidosis With Lymphoproliferative Processes<sup>☆</sup>



### Evolución y coexistencia de sarcoidosis con procesos linfoproliferativos

To the Editor,

Sarcoidosis is a multisystemic granulomatous disease during the course of which lymphoproliferative diseases, primarily Hodgkin lymphoma (HL), may be triggered.<sup>1,2</sup> In these cases, differential diagnosis between both diseases may be problematic.

We report the clinical case of 26-year-old woman, resident medical officer, with no significant history or toxic habits. She consulted in June 2013 with a clinical picture consistent with respiratory infection. Radiograph revealed right lower lobe pneumonia and she was treated with amoxicillin–clavulanic acid for 10 days. The follow-up radiograph showed regression of the pneumonia and increased bilateral hilar structures suggestive of lymphadenopathies, confirmed on computed tomography (CT), located in the mediastinum and bilateral hila, the largest being a conglomerate in the thymus. The patient was interviewed again, and reported a 2-year history of asthenia with no other symptoms. On examination, her breathing was normal with basal SatO<sub>2</sub> 99%, normal cardiopulmonary auscultation, no edemas or other findings. Lung function tests were normal: FVC 92% (3.320 ml), FEV<sub>1</sub> 100% (3.150 ml), FVC/FEV<sub>1</sub> 95%, DLCO 112%, TLC 96%, 6MWT 617 m (83% predicted), with no saturation or tachycardia. Clinical laboratory tests showed only mildly elevated angiotensin-converting enzyme 68 IU/l. Endobronchial ultrasound was performed and regions 7 and 10R were aspirated. The microbiological study was negative. Bronchoalveolar lavage immunophenotyping showed no changes. The

pathology study reported sarcoid-like non-necrotizing granulomatous structures with no signs of malignancy. Sarcoidosis stage I was diagnosed, with no other systemic involvement, and no indication for pharmacological treatment.<sup>3</sup>

Six months later, the patient reported clinical worsening, but no change was observed with respect to earlier clinical and functional findings. CT revealed a reduction in size of the mediastinal lymphadenopathies, and an anterior mediastinal mass, which corresponded to the lymph node conglomerate located in the thymus, with uptake of 11.5 SUVmax on PET/CT. Left anterior mediastinotomy was performed, which was diagnosed as nodular sclerosis HL.

The patient received 4 cycles of doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) over 5 months. The post-chemotherapy follow-up CT showed a 65% reduction in the size of the mass, and radiation therapy of the affected field began for 1 month. The patient improved clinically, and the follow-up PET/CT at 3 months revealed a reduction in size and metabolic activity of the mass (4.5 SUVmax), with pathologically increased metabolic activity in the mediastinal (5 SUVmax) and bilateral hilar (7 SUVmax) lymphadenopathies, in the hepatic hilum (3.3 SUVmax) and the splenic parenchyma, and no other evidence of malignant disease. The case was discussed in the multidisciplinary session, and with the patient's consent we decided to adopt a wait-and-see attitude and to repeat the PET/CT after 3 months. This procedure revealed disappearance of the mediastinal lymphadenopathies and absence of pathological metabolic activity and malignant disease. Since then the patient has remained asymptomatic, and no changes have been observed in the follow-up CTs, with both diseases being in complete remission. The patient may have had both diseases all along, and the anterior mediastinal image initially thought to be a sarcoid conglomerate in a lymph gland may actually have been HL.

Sarcoidosis is a systemic granulomatous disease of unknown etiology, unspecific clinical signs and symptoms, and variable radiological pattern and progress. Diagnosis is obtained from the visualization of non-necrotizing granulomas on histology.

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