Letter to the editor

Fernando Cobo
Jaime Borrego
Javier Rodríguez-Granger
Antonio Sampedro
José María Navarro-Marí

A rare case of pleural infection due to *Propionibacterium acnes* (*Cutibacterium acnes*)

Department of Microbiology, Hospital Virgen de las Nieves. Granada, Spain

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Sir,

Propionibacterium acnes is an anaerobic Gram-positive non-spore-forming rod which belongs to the newly described genus *Cutibacterium* [1]. This species is part of the normal microbiota of the skin, oral cavity, and genitourinary and gastrointestinal tracts, and has often been considered as a contaminant of blood cultures and other sterile fluids secondary to skin puncture. *P. acnes* is infrequently associated with invasive infections but sometimes it may cause a true bacteremia acting as opportunistic pathogen especially in neurosurgical and bone/joint infections [2]. However, as the cause of pleuropulmonary infections, *P. acnes* has been described in very few occasions [3-6]. We report a rare case of pleural infection caused by *P. acnes* in a patient with a concomitant pulmonary neoplasia.

A 66-year-old man came to the Emergency Department due to asthenia, dyspnea, productive cough, hemoptysis, and chest pain. The patient is a frequent smoker and his clinical history stands out for a rheumatoid arthritis and a chronic obstructive pulmonary disease (COPD) for over 10 years. The physical examination was unremarkable except for a small decrease of bilateral lung ventilation and the presence of sibilances. At this time the patient was not febrile and complete blood count, chemical profile, and urinalysis were all normal except the C-reactive protein (CRP) level of 15.85 mg/L and white cells blood count (WBC) level of 12,290/mm^3. The patient was admitted in the pneumology department for study and treatment with moxifloxacin (400 mg/day) was started. A chest x-ray was firstly performed showing a left hiliar mass. Also, a thoracic CT-scan was carried out showing a great left suprahiliar mass, multiple lymphadenopathies in the mediastinum, and a moderate left pleural effusion.

Both a tissue sample of the mass and the pleural fluid (PF) were obtained by bronchoscopy. Leukocytes of 7.475/µl (95% lymphocytes), glucose of 92 mg/dL, lactate dehydrogenase of 168 U/L, and pH 7.23 were obtained in the pleural fluid. The pathologist informed of a pulmonary adenocarcinoma, and the PF was sent for cytological and microbiologic study. The cytological study demonstrated no presence of malignant cells, and in the microbiology laboratory the PF was processed as follows: after centrifugation, the sample was inoculated in blood agar (either aerobic or anaerobic) (BD Columbia Agar 5% Sheepblood®, Becton Dickinson), chocolate agar (BD Choco Agar, Becton Dickinson) and thioglycolate broth (BD™ Fluid Thioglycollate Medium, Becton Dickinson). All media were incubated at 37ºC. Gram staining of the PF exhibited no microorganisms, and on the fifth day of incubation the growth of a large numbers of these microorganisms was reported only in the anaerobic blood agar. Abundant small and white colonies were observed in pure culture and a mass spectrometry method (Bruker Biotyper, Billerica, MA, USA) was employed to identify the strain as *P. acnes* (score 2.157). The MIC of the bacteria to different antibiotics was carried out by the E-test method. According the 2017 CLSI criteria [7], the strain was susceptible to penicillin, amoxicillin-clavulanate, piperacillin-tazobactam, meropenem, imipenem, linezolid, vancomycin, moxifloxacin, and resistant to metronidazole. No blood cultures were taken at this stage, and the patient is currently being treated for his cancer.

Anaerobic bacteria are relatively frequent pathogens in pleuropulmonary infections [8]. Several studies have shown that overall the most commonly encountered anaerobes were *Prevotella* spp, *Fusobacterium* spp, *Bacteroides* spp, and *Peptostreptococcus* spp. [9]. In the majority of cases a mixture of aerobes and anaerobes was found, but in a study only anaerobes were recovered in 14% of patients (16). Boyanova et al [9] found thirteen strains of *Propionibacterium* species in samples with thoracic empyema; no information of clinical

Correspondencia:
Fernando Cobo
Department of Microbiology, Hospital Virgen de las Nieves
Avda Fuerzas Armadas, 2 18014 Granada, Spain
Phone: +34958020364
Fax: +34958241245
E-mail: fernando.cobo.sspa@juntadeandalucia.es

significance of these bacteria was supplied and if the infection was produced within a polymicrobial context.

We undertook a search of the MEDLINE, Web of Science, CINAHL, and Cochrane systematic review databases to review previous reports of this rare condition, using the search terms "Pleural infection *Propionibacterium* acnes" and "Pleural infection *Cutibacterium acnes*". References cited in the retrieved papers were also searched to detect additional case reports published before 1966. Until now, only five strains of *P. acnes* have been isolated in pure culture from pleuropulmonary samples [3-6, present report] (table 1). Infection was located in the pleural tissue alone in two cases and in the lung tissue alone in one case, but in two patients the infection was found both in the lung and in the pleura. Mechanism of infection is unknown but it can hypothesize that pleuropulmonary infection may be due as a consequence of thoracocentesis, biofilm formation or pleuropulmonary seeding from the lymph nodes in patients with underlying diseases. Regarding to this, four of the patients here reported had underlying conditions that may help the microorganisms to spread to the pleuropulmonary tissue.

The diagnosis of *P. acnes* infection is mainly based on culture of an adequate sample obtained from the site of infection; in the cases here reported, the diagnosis was carried out from pleural fluid culture or lung biopsy culture. Identification of strains is based on phenotypic tests and/or molecular methods, while the recent introduction of mass spectrometry may strongly help in the final identification, as in our case. At this point, the main issue is to elucidate whether the presence of *P. acnes* in samples can be considered as a contaminant or not, because their presence as a skin commensal. In the patients presented here, it can be concluded that *P. acnes* was a true cause of infection because of the pathogen was present in large numbers, it was found from a normally sterile sample and associated to pleuropulmonary clinical symptomatology.

P. acnes is highly susceptible to many antibiotics such as β-lactams, vancomycin, quinolones, and clindamycin. However, resistance of antibiotics is progressively increasing. An European study showed resistance rates of 17.1% for erythromycin, 15.1% for clindamycin, and 2.6% for tetracycline, but no resistance to penicillin, vancomycin, or linezolid was found [10]. In the case reports here reviewed, only resistance to metronidazole was reported in two patients (case 2 and 5); the remaining antibiotics, if reported, were susceptible. Antibiotic resistance in *P. acnes* may be initially not considered a problem, although monitoring through susceptibility testing is advisable.

In summary, although *P. acnes* is a component of skin microbiota, it can present as an opportunistic pathogen to cause invasive infections such as pleuropulmonary-associated infections. The clinical implication of *P. acnes* at this location is not still clearly established since the scarcity of reports, but if clinical features are compatible with the disease and the microorganism is recovered from a sterile sample in a large number, the infection involving this anaerobe could be considered a true infection and should be immediately treated.

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CONFLICT OF INTEREST

The author declare that they have no conflicts of interest

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