

Case Report

Alveolopericardial Fistula Secondary to Pulmonary Nocardiosis: a Case Report

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Abstract

The alveolopericardial fistula is a rare pathology, finding only reports and case series in the world literature. It has multiple causes. We present a rare case of a patient with alveolopericardial fistula caused by an infection. The female 29 years old patient with fever, cough, 0 and moderate exertional dyspnea. Chest X-ray with consolidation and pneumomediastinum and the computed tomography shows a compatible image with fistula between lung and pericardium. Patient had a clinical deterioration and required a surgical intervention with a thoracotomy because of cardiac tamponade symptoms. Pulmonary Nocardiosis was confirmed in cultures and specific treatment was given. The patient had a better condition after surgery. We describe the first case of pulmonary Nocardiosis, which can cause an alveolopericardial fistula. The surgical treatment can be an urgent procedure.

Keywords: Hydropneumopericardium, Nocardiosis, Pleuropericardial Fistula, Pericardial Window.

1. Introduction

A 29-year-old woman presented four months of fever, cough, and dyspnea, which was initially treated as pneumonia with antibiotics for 28 days. Her evolution was torpid. A chest CT scan was performed with evidence of right apical consolidation and pneumomediastinum. The woman underwent a pericardial window finding of purulent fluid with a report of negative adenosine deaminase (ADA), and cultures. One month later, the initial symptoms persisted, an initial chest X-ray was performed with findings of consolidation in the right upper lobe, additionally, sputum smear microscopy, reverse transcription polymerase chain reaction (RT-PCR), and sputum culture were performed, with negative results for mycobacteria. A new chest CT scan showed a cavitated lesion in the upper lobe of the right lung and due to persistent chest pain and dyspnea (fig. 1a).

The alveolopericardial fistula was suspected, so fibero bronchoscopy was performed; however, no evidence of a fistulous trajectory to the pericardium. Then, management with levofloxacin, linezolid, meropenem, and tetraconjugate anti-tuberculosis regimen was given, with no symptoms released. She started with clinical deterioration, a new chest X-ray was

performed with evidence of a large hydropneumopericardium (fig. 1b), associated with heart failure and septic shock, so it was decided to perform a left anterolateral thoracotomy with the next findings: Tension hydropneumopericardium with thickening of the pericardium and mediastinal pleura, associated with multiple small collections, purulent versus caseous material. A saline solution with iodopovidone was administered in the pericardium trying to find a fistula but no bubbling was seen, but iodopovidone is observed at the level of the orotracheal tube suggesting the diagnosis of alveolopericardial fistula. The pericardial cavity was washed, and a chest tube is left intrapericardially and another in the pleural space. A sample was obtained for pericardial biopsy, with findings of acute and chronic pericarditis with abscess formation and granulomatous reaction with focal necrosis with positive culture for *Nocardia* spp. (fig. 2), and *Candida* spp. Therefore, management with trimethoprim-sulfamethoxazole and fluconazole was initiated. During the postoperative period, she presented air leakage in the intrapericardial tube, which ceased after 4 days, and the hydropneumopericardium resolved (Fig. 3). The postoperative evolution was favorable, and the patient was discharged on day 15.

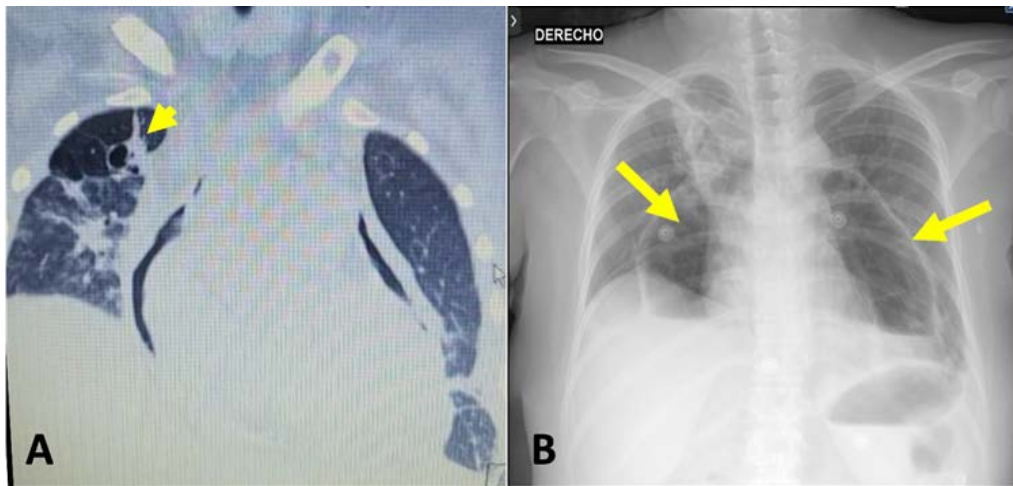


Figure 1: A: Chest CT scan in a : Pulmonary cavity in tight upper lobe (arrow); B: Chest X-ray: Hydrneumopericardium (arrows).

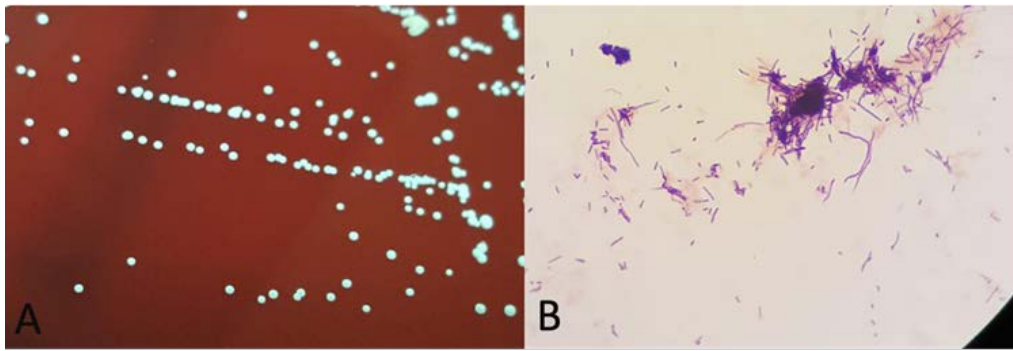


Figure 2: Nocardia spp culture. A) Agar blood. Sandy white dot colonies. B) Gram positive filamentous bacilli. Observed in 100X objective.

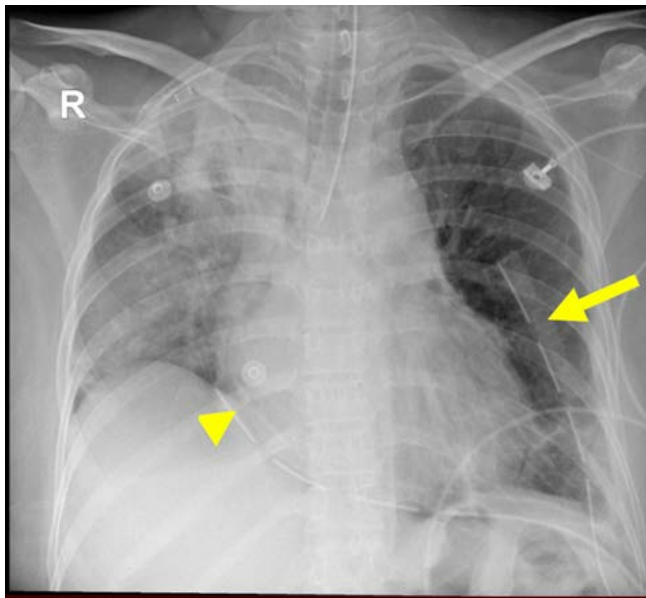


Figure 3: Chest X-ray on POP Day 4 with resolved hydropneumopericardium, showing the two drains, in the pleural space (arrow) and intrapericardial space (arrowhead).

2. Discussion

The alveolopericardial fistula is a rare pathology, there are only case series in the world literature. We report the first

case of an immunocompetent patient with an alveolopericardial fistula secondary to pulmonary nocardiosis. It has multiple causes, among them, myocardial ablation for arrhythmia, malignancy, trauma, post-surgical, pneumonia by *Staphylococcus aureus* or *M. tuberculosis* can cause severe inflammation and pulmonary destruction leading to the formation of a fistula between the lung and the pericardium. Infectious etiology is one of the least common. Nocardial pneumonia is a very rare infection, mainly affecting immunocompromised patients [1]. The clinical presentation of these patients can range from non-specific respiratory symptoms like to tuberculosis, presenting with chronic cough, fever, dyspnea, and chest pain, simple pneumopericardium to hemodynamic compromise due to cardiac tamponade [2]. *Nocardia* spp. must be considered and the recommendation is to rule out *Nocardia* infection in patients with chronic respiratory symptoms and negative tests for tuberculosis [3]. In our case, we have decided to define it as an alveolopericardial fistula because of its communication between the periphery of the lung and pericardium. The alveolopericardial fistula can be seen hydropneumopericardium seen in the chest X-ray or chest CT scan and fibrobronchoscopy or intraoperatively as in our case [4].

Definitive treatment of the fistula will depend on the etiology and hemodynamic status of the patient. The initial approach

consists of decompression of the pericardium through a pericardial window and drainage. If there is an evident fistula in the fiber bronchoscopy, we would be in front of a bronchopericardial type, where the possibility of endoscopic management should be evaluated [5]. Antibiotics therapy must be guided by cultures. Our patient was treated with trimethoprim-Sulfamethoxazole for Nocardia, which is the first choice. Other alternatives described are ceftriaxone, minocycline, and amikacin [6].

The Nocardia can be a cause of severe lung infection and cause an alveolopericardial fistula, we have to remember that Nocardia's symptoms are similar to M. tuberculosis. This fistula can cause cardiac tamponade and we must get the patient to the operating room as soon as possible.

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1. Introduction

Cancer frequency is expanding around the world, in part due to the populace ageing [1]. This may be connected to progressed and open restorative care. This drift speaks to a challenge for healthcare frameworks in numerous nations. Improvement of unused demonstrative methods and restorative approaches appears to be fundamental for sensible care for restoratively delicate elderly patients. The cancer microenvironment, particularly cancer-associated fibroblasts, speaks to a promising target for restorative control, which has not however been completely misused.

The position of cancer-associated fibroblasts within the tumor cellular biological system has been built up, and their impact on cancer cell multiplication, separation, relocation and helpful resistance is broadly perceived. Fibroblasts are a heterogeneous populace of resident cells in numerous typical tissues [2]. They create the most components of the extracellular framework and are fundamental for the auxiliary judgment of the connective tissue. Additionally, they play an critical part in numerous forms, such as wound recuperating, maturing, and carcinogenesis. Amid the improvement of cancer, cancer cells are able to actuate inhabitant fibroblasts into cancer-associated fibroblasts (CAFs), which express α -smooth muscle actin (α -SMA) in differentiate to inert fibroblasts inhabitant in typical pancreas.

Amid this enactment, cancer cells express Hedgehog ligands, which lead to the paracrine enactment of fibroblasts by means of the Sonic Hedgehog (SHH) signaling pathway. Moreover, prove for the exosomal microRNA (miRNA) interceded enactment of fibroblasts by cancer cells in different cancers such as the pancreatic cancer or melanoma exists. Besides, CAFs can too infer from the separation of bone marrow determined stem cells, from the change of epithelial cells through an epithelial-mesenchymal change (EMT)-like handle, and from calm stellate cells. Classically, two subsets of CAFs have been portrayed: myofibroblastic CAFs (myCAF) and inflammatory CAFs (iCAF). Whereas myCAF have a better expression of α -SMA and are localized specifically adjoining to neoplastic cell locales, iCAF are localized more remotely from the neoplastic cells and express tumor-supporting cytokines such as IL-6. Additionally, single-cell examination of pancreatic adenocarcinoma (PDAC) has uncovered a modern subtype, to be specific, the antigen-presenting CAFs (apCAF), which enact CD4+ T cells within the TME (The Tumor Microenvironment). This revelation is in back of the speculation that there are unmistakable parts for distinctive subsets of CAFs. Whereas a few CAFs create incendiary ligands and development variables, in this manner advancing tumor development, or upgrade the forcefulness and sedate resistance of cancer cells in an exosome intervened way, a few CAFs appear to have tumor-restraining properties, such as the T cell actuation and the limitation of the tumor angiogenesis. In addition to the coordinate impact CAFs might have on cancer cells, there appears to be a near relationship between CAFs and nerves within the tumor environment, which is however to be explained.

1.1 Issue

Cancer speaks to an vital therapeutic, sociological and financial issue [1]. The aggregate number of patients enduring from harmful illness of any sort is expanding around the world. In this setting, causative investigation of this non-favourable slant highlighted maturing as an viewpoint of essential significance. Be that as it may, there are a few key variables to be talked about in closer detail. These incorporate (a) harm to the macromolecules, counting DNA, by receptive radicals, (aa) decreased movement of the quality repair apparatus and (aaa) decreased number of grown-up tissue stem cells.

The human life span is of restricted length, which appears to be formatively modified. Verifiably, it was altogether shorter than we see these days in created nations. Ready to conjecture that the reason for such prolonged lifetime anticipation can lie within the surprising advance within the quality of therapeutic care. Vitally, this made strides care too got to be broadly open to the common populace. The coincidence of these two variables appears to be mindful for such critical prolongation. With a prevalent express, this includes a few “years to your life”, but not essentially “life to your years”. Due to our population’s delayed survival, we anticipate that the number of patients enduring from cancer will indeed increment. Straightening of the rate bend and stagnation of the numbers is however an neglected objective in numerous cancer sorts. Additionally, the tall cancer rate within the elderly population represents a genuine helpful challenge. These matured patients are remedially delicate. Due to different comorbidities and age-related pathologies, they regularly don’t endure forceful oncological treatment well. Current major treatment alternatives for cancer incorporate surgery, cytotoxic chemotherapy, radiation treatment, endocrine treatment, atomic focused on treatment and most as of late immunotherapy. Without a doubt, numerous classical, e.g. chemotherapeutic operators, are profoundly toxic. Nevertheless, the more dynamic strategies, e.g. immunotherapy, are too related with a plenty of antagonistic impacts.

Maintaining a strategic distance from the side impacts of treatment could be a particularly critical assignment within the care of elderly cancer patients. Be that as it may, finding the ideal adjust between decreased harmfulness and maximal adequacy is challenging. Basic dosage decrease can instantly lead to a problematic helpful reaction; indeed more worryingly, it can moreover offer assistance set up procured resistance. Subsequently, a combination of, e.g., a low-dosed “soft” chemotherapy with antiHER2 inhibitors, was demonstrated to be especially advantageous to this slight populace.

1.2 Cells

Cancer-associated fibroblasts can possibly result from move from a wide board of cell types [1]. The foremost pertinent component appears to be enrollment of typical tissue fibroblasts and mesenchymal stem cells. This is often accomplished by implies of paracrine emission from cancer cells or through discharged exosomes. CAFs (cancer-associated fibroblasts) are heterogeneous and represent a powerful source of development variables, pro-inflammatory cytokines, chemokines conjointly exosomes that essentially en-

act expansion and movement of cancer cells.

Cancer-associated fibroblasts speak to a naturally powerful and non-malignant population of cells in threatening tumors. CAF discovery and phenotypic and useful characterisation within the unmistakable sorts of tumors can refine diagnostics. In addition, CAFs are an accessible target for restorative mediations, which can possibly progress oncological treatment.

Harmful cells have numerous exceptional highlights expanding their chance of surviving the cataclysmic affect of oncological treatment. These organic highlights of therapy-resistant cells essentially cover with those watched in stem cells. These highlights, alone or in combinations, incorporate heterogeneity, versatility, selfrenewal capacity and tumour-initiating capacity. Be that as it may, each stem cell fundamentally requires a particular tissue microenvironment known as the specialty to preserve its stemness. Out of this consolation zone, cancer cell gets to be helpless. This could have certain helpful suggestions.

All organs and tissues contain a variable number of fibroblasts. Concurring to the classical morphological clarification, the fibroblast part was absolutely auxiliary. Fibroblasts and their item – extracellular matrix (ECM) – were seen as nothing more than a 3D framework for cells of other sorts, basically epithelial. The current view on the part of the fibroblast in organ work is contrastingly profoundly complex. Other than ECM, fibroblasts moreover create a wide range of bioactive variables that effectively take part within the control of organ morphogenesis conjointly its work.

1.3 SASP

In expansion to cell cycle capture, the foundation of a develop senescent phenotype includes broad metabolic reprogramming, as well as the usage of complex characteristics such as the SASP (The Senescence-Associated Secretory Phenotype) [3]. The SASP alludes to the nearly widespread capacity of senescent cells to deliver and emit a assortment of dissolvable and insoluble variables, counting extracellular proteases, cytokines, chemokines, and development variables. This capacity of senescent cells to possibly alter the tissue microenvironment (neighboring cells and the ECM) by means of SASP includes a advance layer of complexity to the suggestions of cellular senescence to tissue homeostasis and infection.

A common include of maturing and age-related infections is persistent irritation. The term “inflamm-aging” has been coined to depict a low-grade, incessant, and systemic aggravation related with maturing and maturing phenotypes within the nonattendance of prove of disease. In line with this concept, numerous of the components emitted by senescent cells are too well-known pro-inflammatory particles with the potential to actuate incessant irritation in certain natural settings. In fact, early microarray investigations uncovered that senescent fibroblasts show an expression profile that takes after the one shown by fibroblasts in early stages of wound repair. More as of late, a interesting sort of

aggravation activated by senescent cells, the senescence-inflammatory reaction, has been distinguished. Interests, comparative to constant irritation created by other components, the incendiary “secretoma” created by senescent cells too appears to depend on enactment of the NF- κ B and C/EBP- β transcriptional controllers. Illustrations of conserved components of the SASP with known master provocative activities incorporate IL-6, IL-1- α macrophage provocative protein, different metalloproteinases (MMP-2, -4, -1), GM-CSF, and cathepsin B.

As anticipated, the SASP can have complex impacts on tissue microenvironments. Hence, a few components of the SASP can proliferate or strengthen the senescent phenotype through autocrine or paracrine components, driving to assist discharge and intensification of the SASP. In addition, SASP components may draw in resistant cells, which in turn can organize the disposal of senescent cells and the end of a senescence-associated incendiary reaction. Imperatively, clearance of senescent cells appears to manage the net impact of cellular senescence at the organismal level. Whereas temporal and constrained cellular senescence can be advantageous within the setting of the ordinary tissue remodeling that happens amid embryonic advancement and wound mending, unremitting aggregation of senescent cells—owing to age-dependent weakening of the natural or adaptive immunity—can have vital hindering results. For illustration, pro-inflammatory cytokines discharged by senescent cells may advance persistent aggravation and, depending on the natural setting, lead to neurotic conditions characterized by an overabundance of fibrosis (e.g., liver cirrhosis). In addition, the SASP, especially its incendiary component, can quicken tumor start and movement by cultivating a pro-tumorigenic microenvironment. In like manner, clearance of tumor cells (or cells of the tumor stroma) experiencing hereditarily or drug-induced senescence leads to long-term relapse and decreased repeat of tumors in mouse models of liver and breast.

The complex heterotypic intelligent in which senescent cells can participate were expected by early in vitro tests appearing that senescent fibroblasts can upgrade expansion and tumorigenesis of epithelial cells of different types. For case, variables emitted by senescent fibroblasts, such as amphiregulin and GRO α , fortify the expansion of premalignant prostate epithelial cells. Additionally, tall levels of IL-6 and IL-8, moreover created by senescent fibroblasts, can advance attack of pitifully dangerous keratinocytes. Critically, coinjection of senescent fibroblasts with either premalignant or dangerous mammary epithelial cells can lead to, or quicken, tumor arrangement in mice. Moreover, typical human prostate epithelial cells experiencing senescence can too improve in vivo tumorigenicity of moo- or non-tumorigenic prostate cancer cells, proposing that components discharged by senescent epithelial cells can moreover be protumorigenic. It is worth specifying that the SASP-dependent capacity of senescent cells to advance tumorigenesis has been primarily detailed in cellular frameworks including co-cultures of epithelial cells and fibroblasts. Therefore, it remains obscure in case comparative intuitive can be watched in other cellular

settings. Finally, it is imperative that not all components of a SASP are pro-tumorigenic. A few SASP components have anti-angiogenic impacts or are indeed able to initiate apoptosis or senescence in non-senescent neighboring cells.

Carcinoma-associated fibroblasts (CAFs) are regularly show within the stroma and have been appeared to advance tumor progression [4]. In separation into CAFs, inhabitant fibroblasts set up two autocrine signaling circles, intervened by TGF- β and stromal cell-derived factor-1 (SDF-1). The CAFs secure a tumor-promoting action, conceivably by means of advancement of EMT (Epithelial-to-Mesenchymal Transition) by TGF- β delivered within the tumor microenvironment.

Endothelial cells are too strong inducers of EMT, actuating a move from E-cadherin to N-cadherin expression and causing expanded transient properties in carcinoma cells and the securing of stem cell-like properties. In clinical tests, tumor

cells close the vasculature have had small or no E-cadherin expression, proposing that cells in these ranges experience EMT. Cancer spheroids have too demonstrated valuable for evaluating attack and relocation [5]. Deciding the intrusive and transient capacity of tumor and stromal cells, and supporting their basic instruments, is profoundly significant in cancer investigate, from determination to sedate advancement to treatment. Picking up motility and transitory potential is an amazingly vital trademark of dangerous tumors. Hypoxia and the interaction of dissolvable go between with stromal cells, cell/ECM attachment, actin skeleton remodeling, and protein corruption of ECM, among. Hence, it is wrong and highly reductionist environment for examining the multistep handle that's metastasis, as this prepare depends intensely on a threedimensional environment where tumor cells can entry and coordinated unreservedly. Since of these reasons, 3D tumor spheroids are respected nowadays as exceedingly significant in vitro models for examining the forms of movement and attack. In a perfect world, relocation