Evaluation of CT Pulmonary Angiography in Patients with Suspected Pulmonary Embolism: Use or Overuse

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Introduction: In the evaluation of patients with suspected pulmonary embolism (PE), the frequency of ordering computed tomography pulmonary angiography (CTPA) has considerably increased, prompting concerns of overuse. This retrospective study evaluates the utilization and diagnostic outcome of CTPA, using the Well’s Criteria and serum D-dimer level, in patients with suspected PE, at the West Palm Beach Veterans Affairs Medical Center. We propose a clinical predictive model in the diagnosis of PE to reduce the overuse of CTPA ordering.

Methods: The medical records of one hundred fifty-two veterans who underwent CTPA for suspicion of PE were studied retrospectively. Modified Well’s Criteria of each patient were calculated and risk probability was based on a three-tier model. Patients were determined to have high-risk clinical probability (score 6+), moderate-risk clinical probability (score 2-6), or low-risk clinical probability (score <2) of PE. The outcome of CTPA was either positive or negative. Age-adjusted serum D-dimer was determined to be normal, elevated, or not ordered. The relationship between clinical probability, age-adjusted serum D-dimer, and CTPA results were compared. Descriptive analysis, including frequency, as well as, analytical statistics, were performed using SPSS (v. 26).

A proposed algorithm, using Well’s Criteria and serum D-dimer levels, was also created with the intent to guide provider decision making and reduce the number of CTPA performed in patients with suspected PE with low-risk clinical probability.

Results: 152 patients underwent CTPA for suspected PE. The prevalence of PE was 66% in the group of patients with high-risk clinical probability (p=0.004), and 1% in the group with low-risk clinical probability (p=0.000). In 104 (68%) of the performed CTPA, clinical probability for PE, based on Well’s criteria, was low. In the clinically low-risk probability group, serum D-dimer was ordered in 40 out of 103 (39%) cases. CTPA was inappropriately ordered in 23 out of 103 (22%) patients determined to have low-risk clinical probability and normal age-adjusted serum D-dimer level.

Conclusion: There is statistically significant evidence of excessive CTPA use and lack of adherence to recommended diagnostic evaluation of suspected PE. Implementing a stepwise clinical predictive model can assist provider decision making, and potentially limit inappropriate use of CTPA. Future work will focus on the implementation of our predictive model in our electronic medical record (EMR), followed by pre- and post-intervention analysis.

Emergency department chest X-ray severity in patients with COVID-19 is associated with hypoxemia and clinical outcomes

Daniel Kotok, Christine Girard, Jose Rivera Robles, Andrew Kim, Shruti Shettigar, Allen Lavina, Christopher D’Angelo, Samantha Gillenwater, Anas Hadeh

Background: Severity of radiographic abnormalities on chest X-rays (CXR) obtained in the emergency department (ED) in patients diagnosed with COVID-19 has been shown to be associated with outcomes, but studies are limited by different scoring systems, sample size, patient age and study duration. We sought to evaluate this question using a well-validated scoring system (the Radiographic Assessment of Lung Edema [RALE] score) using data over 6 months from a large, multi-hospital healthcare system including all adult (age >= 18) patients.

Methods: We collected CXRs, demographic, historic and clinical data from patients with a naso- and/or oropharyngeal swab positive for SARS-CoV-2 PCR visiting the ED for COVID-19-related complaints between March and September 2020. Two independent reviewers quantified radiographic edema using the RALE scoring system. Fraction of inspired oxygen (FiO2) was calculated using 1 liter per minute (lpm) supplemental O2 to 3% FiO2 conversion and capped at 15 lpm O2. We examined the association of radiographic edema with hypoxemia, need for hospital admission, ICU admission, need for mechanical ventilation within 7 days of admission and 30-day mortality.

Results: 453 patients met criteria for inclusion (median age 54, 51% female). Inter-rater agreement for RALE score was excellent (interclass correlation coefficient = 0.97, 95% CI 0.94 - 0.98, p < 0.0001). 99 patients had a normal (RALE = 0) CXR on ED visit. Median RALE score was 3. RALE scores negatively correlated with degree of hypoxemia as quantified by SpO2-FiO2 (SF) ratio (r = -0.34, p < 0.001). Patients admitted to the hospital had higher RALE scores than those who were discharged home (median 2 IQR [0, 6] vs 3 [10, 17], p < 0.001). Amongst 199 admitted to the hospital, RALE scores were higher in those requiring admission to the ICU compared to those who did not (7 [14,20], 2 [8,16], p = 0.007). Patients in the 3rd and 4th RALE quartiles were more likely to require mechanical ventilation and had higher 30-day mortality compared to those with RALE scores below the median, even after adjustment for age, SF ratio and history of diabetes (p < 0.02 for all).

Conclusions: The RALE score is highly reproducible and easily implementable in adult patients presenting to the ED with COVID-19. Its association with physiologic parameters and outcomes makes it a readily available tool for prognostication and early ICU triage, particularly in patients with severe radiographic edema as quantified by the RALE score.
SAMIScore Study (Symptoms, Admission, MICU, and Intubation) Associates Mortality with Different Phenotypes of COVID-19

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Introduction: Diverse presentations of SARS-CoV-2 infection exist, with some studies differentiating as many as five phenotypes. Each of the phenotypes describes varying symptoms, inflammatory markers, and lung physiology – many of which require invasive testing to diagnose. The two most common phenotypes, L-type and H-type, advance along a spectrum indicating an evolving illness. Recently, this physiology has been explained as a shift from an acute viral illness to progressive inflammatory response. The objective of this study is to identify differences in the SAMI Score between death and non-death cohort, from data collected in a large, multi-center healthcare system for adult (age >18) patients.

Methods: All patients enrolled in this retrospective study were identified by a positive nasal or oropharyngeal swab for SARS-CoV-2 PCR in the ED between March and September 2020. Symptomatic data was collected based on ED admission histories and prior medical records. The SAMI score was calculated based on duration of days from symptom onset to hospital admission (SA score), time to ICU admission (AM score), and time to intubation (MI score). Patient cohorts were separated by mortality.

Results: Out of 510 patients, 227 patients met inclusion criteria for enrollment. In the death cohort (43 patients, mean age 75, 53% female), the mean SA score was 5.6d while the AM score was 1.9d and the MI score was 1.9d. In the non-death cohort (43 patients, mean age 60, 49% female), the mean SA score was 6.3d while the AM score was 1.3d and the MI score was 6.0d. The average MI score was 2.3d and the SAMI score was 11.6d among those intubated. In the non-death cohort (184 patients, mean age 60, 49% female), the mean SA score was 6.3d while the AM score was 1.9d and the MI score was 1.9d. Overall, the mean MI score between the two groups (2.3d vs. 1.9d) was statistically significant. Similarly, the mean SAMI score between the two groups (11.6d vs. 6.0d) was also statistically significant. There was no significant difference between the average SA score (p = 0.63) or AM score (p = 0.37).

Conclusions: Patients who required rapid intubation after symptom onset (short SAMI score) are associated with less mortality than those requiring a prolonged time to intubation (long SAMI score). Physiologically, rapid intubation and a short MI score suggest a recoverable acute disease state. Conversely, prolonged time to intubation may be indicative of a progressive irreversible process. This research allows for further sub-group analysis to determine if inflammatory markers are higher in the group with longer SAMI scores.

Is it a bird or a plane or both? Organizing pneumonia with unusual cryobiopsy findings: A case report

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Introduction: Cryptogenic Organizing pneumonia (COP) may present with a variety of CT findings (1) and may rarely overlap with radiological findings characteristic of Sarcoidosis (2,3). Our case presents a challenging diagnostic scenario in which radiology and biopsy findings were not concordant.

Case Presentation: A 62 year old female was sent to our clinic to investigate abnormal findings noted on a CT calcium score by her cardiologist. The patient reported worsening dyspnea on exertion over the prior 2 months, insidious in onset. She had no personal or family history of pulmonary or autoimmune disease. She had no vocational or avocational exposures. The CT coronary calcium score revealed scattered airspace opacities with reverse halo sign with peripheral predominance (fig 1), typical for COP. Interval dedicated CT chest imaging showed improvement in the peripheral opacities. Pulmonary function testing revealed a moderately reduced DLCO. Labs were remarkable for mild peripheral eosinophilia and a mildly positive ANA at 1:160. Other autoimmune markers, ACE level, and calcium level were all normal. A transbronchial cryobiopsy of right middle lobe and right lower lobe revealed peri-bronchial non-necrotizing granulomas and pneumocyte hyperplasia with minimal to absent inflammatory infiltrates in both specimens. No fibrosis, necrosis, tissue eosinophilia, vasculitis or malignancy were seen. The granulomas were composed of multinucleated giant cells, histiocytes, and occasionally surrounded by a cuff of lymphocytes. There was no evidence of organizing pneumonia. Infectious work up for fungi, nocardia and mycobacterium were negative.

Discussion: Cryptogenic Organizing Pneumonia is a clinicopathological entity (1), however in our case, the clinicoroadiologic features were characteristic of COP but the biopsy revealed sarcoidosis with no evidence of organizing pneumonia. The case was reviewed by a multidisciplinary committee which unanimously agreed that the radiological features and clinical course was consistent with Organizing pneumonia. Considering COP has been known to masquerade as Sarcoidosis (2,3), albeit rarely, we question if our biopsy findings represent an uncommon phase in the evolution of COP or if it was Granulomatous Organizing Pneumonia or a case of Sarcoidosis. COP overlap or Biopsy proven Sarcoidosis (2). Our patient’s respiratory symptoms and radiological findings resolved without intervention over a period of 2-3 months. There was no hilar lymphadenopathy or extrapulmonary involvement with normal ACE level, reducing the likelihood of Sarcoidosis.

Conclusion: One of the unique aspects of Pulmonary medicine is that pathological findings may not always concur with clinicoroadiologic diagnosis. Our case highlights the value of multidisciplinary discussion and close surveillance. We hope that future research demystifies this unusual combination of clinicoroadiologic COP with non necrotizing granuloma.
Salmonella Empyema Presenting as Tension Pseudoneumothorax in a Diabetic Patient
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Introduction: Salmonella infection most often causes acute gastroenteritis that presents as fever, abdominal pain, and bloody diarrhea. Salmonella is most commonly acquired via oral ingestion of contaminated food products, such as eggs and poultry, and travels through the alimentary canal, where invasion of intestinal mucosa occurs. Although salmonella bacteremia can develop infection at any site, pleural empyema due to salmonella infection is extremely rare.

Case description: A 51-year-old Hispanic male with no known past medical history presented with a 5 day history of difficulty breathing, chest pain, and vomiting. On examination, he was found to have blood pressure of 222/110, pulse of 144 beats per minute, and respiratory rate of 44 breaths per minute, saturating 90% on 4L of oxygen via nasal cannula. Physical exam was remarkable for lethargy, oral thrush, and severe respiratory distress. Patient was subsequently found to have blood glucose of 718, glycosylated hemoglobin of 10.4, and potassium of 6.2. Work up for infectious etiology was positive for previous Hepatitis A infection, negative for hepatitis B and C, and negative for HIV. Immunoglobulin levels were unremarkable; however, absolute CD4 count was only 36. Initial chest x-ray demonstrated large right pneumothorax with leftward mediastinal shift, requiring an emergent chest tube thoracotomy, which drained a significant amount of turbid, brownish fluid. Both pleural fluid and blood cultures grew Salmonella enterica subspecies houtenae (IV). Esophagram and computerized tomography of the chest did not demonstrate any extravasation or leak. Robotic right thoracoscopic total pulmonary decortication was performed, which revealed a significant amount of fibrinous debris. Hospital course was complicated with nosocomial pulmonary infections by Novar Nab asiatica, pseudomonas aeruginosa, and aspergilous niger. Despite adequate antimicrobial therapy with imipenem, trimethoprim-sulfamethoxazole, and voriconazole, patient developed respiratory failure, requiring tracheostomy.

Discussion: Salmonella empyema is a rare cause of pulmonary infection, even within the spectrum of diseases affecting immunocompromised patients. It is estimated that approximately 1 percent of Salmonella gastroenteritis results in bacteremia. Only 39 cases of pleuropulmonary complications due to salmonella species have been reported until 2005, of which S. enterica ser. typhimurium was the most common non-typhi species associated with empyema. S. enterica subsp. houtenae is a rare Salmonella subspecies that is mostly found in reptiles, with blood as the most common site of extraintestinal infection. There is a case reported of Salmonella houtenae-induced empyema as a complication of chronic tuberculosis empyema; however, to the best of our knowledge, there has been no reported cases of pleuropulmonary manifestation due to S. enterica subsp. houtenae alone.

Invasive salmonellosis is most commonly reported in adults with immunosuppressed conditions, such as HIV/AIDS, diabetes mellitus, malignancy, as well as in children with malarial infection or sickle-cell anemia. It is hypothesized that in cases of uncontrolled diabetes, hyperglycemia provides a favorable environment for bacterial growth, leading to further hematemal spread of the infection. Hyperglycemic state also inhibits immune response through neutrophil dysfunction, resulting in increased susceptibility to and severity of infections in diabetic patients. The etiology and pathogenesis of salmonella empyema is poorly understood due to the lack of reported clinical cases. Salmonella empyema in immunocompromised patients, such as diabetics, is a rare presentation with high mortality that warrants further clinical investigation surrounding the pathogenesis, diagnosis, and effective treatment modalities.
Acute Limb Ischemia Following a Mild Case of COVID-19
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Introduction: Severe acute respiratory syndrome coronavirus 2, or better known as COVID-19, research has flourished as the year progressed, but a lot is still not known about the virus and all of its long-term complications. Hypercoagulability with the virus has risen as a well-known complication and is believed to be associated with more severe systemic inflammation and respiratory compromise. We present a patient who experienced mild respiratory symptoms, and following near resolution presented with acute limb ischemia involving majority of his right lower extremity arterial vessels.

Case presentation: A 53-year-old male with a past medical history of depression and previous alcohol abuse presented to the emergency department on day 12 of his COVID-19 infection with sudden onset severe right lower extremity pain which woke him from sleep at 2 AM that morning. His respiratory symptoms recently resolved at home in isolation with a 10-day course of steroids prescribed via a telehealth visit with his doctor after COVID PCR came back positive 12 days prior. He initially had a cough with intermittent headaches. The lower extremity pain was associated with numbness and muscle weakness. In the emergency department he was tachycardic, afebrile and his right lower extremity was cold, numb, had an increased capillary refill time of 10 seconds and pulses were not palpable. Bedside Doppler of the right foot revealed a non-dopplerable pulse in the dorsalis pedis. Arterial Doppler of his right lower extremity revealed extensive arterial thrombosis and vascular surgery was immediately consulted for emergent right lower extremity revascularization. He was found to have a clot extending from his external iliac down to his Tibioperoneal trunk which required emergent thrombectomy. The patient had no prior history of cloting, no significant comorbidities, no recent hospitalization and his only acute risk factor was his recent diagnosis of COVID-19. He was bridged to warfarin with heparin following his procedure with no residual deficits and discharged one week after admission once he was therapeutic.

Discussion: It has been found that the direct viral infection of endothelial cells with dense perivascular T cell infiltration along with aberrant macrophage activation, endothelial and inflammatory cell death, thrombotic microangiopathy, and angiogenesis all contribute to the hypercoagulability with the virus.1 Most complications have been reported causing myocardial infarction, ischemic stroke, and venous thrombo-embolism in hospitalized patients. The risk of major arterial vessel involvement outside the heart is not as heavily reported, especially in those individuals who do not require hospitalization or those who are not critically ill.2 The association between COVID-19 and acute ischemic limb has been minimally studied in literature. In a similar case published by Mietto et al, their patient presented without respiratory symptoms and acute onset pain with walking. He was found to have arterial thrombus from iliac artery to popliteal artery.3 Similar to our case, there was an absence of underlying atherosclerotic disease. Despite these low risk factors, COVID-19 likely acts as a procoagulant and activates the coagulation system resulting in thrombosis. Further research in the younger, non-hospitalized populations without significant comorbidities is necessary to assess the long-term complications and necessity for prophylaxis with this novel virus.

Recurrent Pneumothorax in the Setting of COVID-19
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Background: COVID-19 causes significant damage to the lungs, with acute respiratory distress syndrome (ARDS) being the most prominent complication.1,2 However, more recent studies have shown that spontaneous pneumothorax could also be a complication. Spontaneous pneumothorax occurs due to underlying pulmonary pathologies but there have been a small number of cases related to COVID-19, and most of which were mechanical ventilator associated. We present a case of recurrent pneumothorax secondary to COVID-19.

Case Presentation: 75-year-old male former smoker, non-oxygen dependent COPD who presented with hypoxia after testing positive for COVID-19. Patient presented with nonproductive cough, fever, hypoxia with saturation in the high 80’s. Labs were remarkable for elevated CRP, ESR, D-dimer, ferritin, and lymphopenia. Chest x-ray (CXR) revealed bilateral opacifications but no pneumothorax [Figure 1]. Patient completed treatment for COVID-19 and was discharged on 2L home oxygen. Ten days after discharge he was readmitted for worsening dyspnea and chest discomfort. He was found to have right sided pneumothorax and persistent bilateral parenchymal opacities on CXR [Fig 2]. A 12 French right sided chest tube was placed with full lung re-expansion. Serial CXR showed resolved pneumothorax [Fig 3], and patient was discharged after chest tube removal. Twelve days later, the patient again became hypoxic, unable to maintain oxygen saturation above 90%, requiring hospitalization. He was again found to have right sided spontaneous pneumothorax [Fig 4]. A 10 French right sided chest tube was inserted. Due to intermittent chest tube air-leak and worsening respiratory failure, a CT chest was obtained which revealed large right sided pneumothorax with left mediastinal shift, blebs, and fibrotic changes [Fig 5,6]. A 28 French right chest tube was then added with anterior approach. Ultimately, both chest tubes were removed, with no pneumothorax noted on the serial CXR, and the patient was discharged home.

Discussion: Since the onset of COVID-19 in early 2020, we have recognized new and different sequelas associated with the novel virus, of which the most prominent complication remains ARDS.1,2 Although we have a better understanding of possible mechanisms of COVID-19 related ARDS, our understanding of other reported complications are poor. Spontaneous pneumothorax can occur with underlying lung pathologies such as chronic obstructive pulmonary disease (COPD) with emphysema, cystic fibrosis, and lung cancer 3 however there are increasing numbers of COVID-19 associated pneumothoraces being reported. A retrospective case series study including 71 patients with pneumothorax in Europe did not show any correlation between pneumothorax and prior lung disease.4 The exact underlying pathophysiology of pneumothorax secondary to COVID-19 is unclear. It appears COVID-19 related severe lung parenchymal injury and destruction might be the culprit. Postmortem histopathological examination of the lung has revealed diffuse alveolar damage, intra-alveolar hemorrhage, hyaline membrane formation, bacterial superinfection, microthrombi and fibrin deposits.5,6,7 Formation of cyst which progresses to bullae has been noted radiologically with disease progression.4 Our patient’s recurrent, non-spontaneously resolving pneumothorax despite chest tube treatment could point at a necrotizing lung parenchymal damage. Although pathophysiology is unclear, we suspect multifactorial etiologies (infarction, viral and bacterial damage, inflammatory response, cyst formation) leading to parenchymal destruction and subsequently air in the pleural space. Our patient never required mechanical ventilation ruling out a possibility of barotrauma. While secondary pneumothorax related to COPD is a possibility, there was no obvious COPD related lung parenchymal pathology on imaging. Clinicians should be aware of pneumothorax as a COVID-19 complication, especially in patients with refractory hypoxia. Further studies are needed to characterize patients with pneumothorax and ascertain demographic and disease associations.
An uncommon presentation of pulmonary nocardiosis with N. transvalensis in a patient with neurocysticercosis

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**Intro:** Human infections with Nocardioides species are rare. N. transvalensis is one of the more unusual species and is not well described in the United States as a pathogen, since it is more common in Africa compared to the rest of the world. We present a case of pulmonary nocardiosis caused by N. transvalensis in a patient with neurocysticercosis with immunosuppression from steroid use.

**Case Presentation:** 79-year-old male presented to the ED with left facial droop, dysarthria and memory loss of 4 days. His NIH stroke scale was 4. Non-contrast CT head showed multiple left hemispheric lesions with edema and midline shift suggesting underlying mass. MRI brain confirmed a cystic, multiloculated left frontotemporal mass with dural extension. Decadron was started, with mild improvement in his symptoms. Biopsy of the mass with intraoperative histopathologic evaluation suggested neurocysticercosis, for which complete resection was not pursued. Once final pathology confirmed diagnosis, albendazole was started. He became febrile prompting repeat infectious work-up where his CXR now showed new opacities in the right lung lobes. Follow up CT chest showed multifocal areas of consolidation prompting treatment with Zoyn for suspected aspiration pneumonia. He continued to deteriorate. CT chest was repeated revealing interval worsening, with bilateral mass-like areas of consolidation. The antibiotics were escalated, and methylprednisolone was added for suspected bilateral obliterans organizing pneumonia. He continued to have intermittent fevers, with a labile respiratory status despite all sputum and blood cultures being negative. His last sputum culture eventually grew beaded, branching gram positive rods consistent with Nocardia. Bacitracin was immediately added. He slowly started to improve and was eventually discharged to a skilled nursing facility pending final sensitivities from the National Jewish Medical Center, which eventually did result as N. transvalensis.

**Discussion:** Pulmonary nocardiosis is a rare but severe infection caused by Nocardioides species. The first case of N. transvalensis was described in 1927. Since no environmental source for N. transvalensis has been identified, it is considered to be transmitted via inhalation. The CDC isolated N. transvalensis in 15 patients from January 1981 to January 1990, 75% of whom had an underlying immune disorder or were receiving immunosuppressive therapy. In their study, Tomas et al found that in patients with pulmonary nocardiosis 94% had specific risk factors, the most common of which was steroid treatment or immunosuppression. Our patient had pulmonary nocardiosis as a complication of steroid use for treatment of neurocysticercosis.

**Conclusion:** This case highlights the importance of increased awareness of various presentations of nocardiosis and how a high index of clinical suspicion can help with rapid diagnosis to improve survival in this otherwise fatal disease.

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An Atypical Presentation of Obstructive Shock

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**Background:** Circulatory shock is a common occurrence in the intensive care unit. Septic shock is the most common etiology for shock. Other types of shock, including cardiogenic and obstructive shock are less commonly seen; however, they still carry a high mortality. Atypical presentations of shock are rarely encountered in the ICU and when they occur, it may delay the diagnosis and result in high mortality. We present an atypical presentation of obstructive shock in a trauma patient.

**Case:** The patient is a 44-year-old male with no significant medical history who presented as a trauma alert. He had sustained a gun shot wound to the right chest as well as the right upper extremity. On arrival to our institution, he was hemodynamically stable. Imaging done included a CT of the chest and abdomen which showed a macerated right hepatic lobe with rapid active extravasation. He was placed on mechanical ventilation and underwent right hepatic artery embolization by interventional radiology (IR). An inferior vena cava (IVC) filter was placed on day one for prophylaxis of venous embolic event due to increased risk of bleeding. On day two he became hypotensive requiring vasopressor support. Concerns were raised for septic shock and he was taken to the operating room for exploratory laparotomy. Findings were unremarkable. Empiric antibiotic coverage was started and he was hydrated with intravenous fluids. Imaging of the abdomen and chest were repeated which showed a large right sided pleural effusion. Ventilatory requirements increased and he continued to require vasopressor support. On day 4 he developed severe pain in his left lower extremity and swelling. He was taken for fasciotomy due to concerns for compartment syndrome. Doppler ultrasound of the lower extremities showed extensive bilateral deep venous thrombosis. At this time obstructive shock secondary to Phlegmasia cerulea dolens due to IVC filter occlusion was suspected. IR was consulted for an inferior vena cava venogram which showed complete thrombosis of the IVC below the IVC filter. Bilateral rheolytic thrombectomy with angioplasty was done with good results. The shock state improved and the patient was weaned off vasopressors.

We present a case of obstructive shock secondary to extensive bilateral deep venous thrombosis and complete occlusion of the IVC filter. Phlegmasia cerulea dolens has been described as a rare complication of IVC filter placement in one case report. Furthermore, obstructive shock due to IVC filter occlusion is quite rare and limited literature exists documenting such complication. It is important for physicians to recognize IVC filter occlusion as a potential complication and cause of obstructive shock.
Necrotizing MRSA pneumonia causing simultaneous bilateral spontaneous pneumothorax: A rare and life-threatening clinical condition

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Introduction: Pneumothorax (PTX) is the presence of air in the pleural space causing compression of the lungs, leading to subsequent respiratory distress. Spontaneous PTX develops in the absence of trauma and is classified as primary or secondary if underlying lung disease is noted. Rarely, a patient can develop simultaneous bilateral spontaneous pneumothoraces, which can result in a life-threatening state requiring intubation or resuscitation. Some sources list this occurrence to be about 1-1.9% of spontaneous pneumothorax-related cases.

Case: A 38-year-old female with a history of Type 1 DM and ESRD on peritoneal dialysis, presented with a cough, fever, and significant dyspnea. CXR showed bilateral lung consolidation consistent with pneumonia. She was admitted to the ICU for acute hypoxia. Broad spectrum antibiotics were started. Blood and sputum cultures grew methicillin resistant streptococcus aureus (MRSA). Her blood cultures also grew VRE and the antibiotics were changed appropriately and PD catheter was removed. Despite overall clinical improvement, her respiratory status declined due to worsening hypoxia which was attributed to mucus plugging due to her inability to initiate a good cough reflex. Aggressive pulmonary toiletting resulted in no improvement. A repeat CXR was done and showed bilateral pneumothoraces significantly worse on the left side, without evidence of tracheal shift. Urgently, a chest tube was inserted on the left side and placed to suction, with follow up imaging showing improvement of the left PTX, but significant worsening of the right PTX. This prompted another chest tube placement on the right side. Repeat CXR showed improvement in both pneumothoraces. Despite this, she failed multiple attempts at discontinuing her chest tubes due to reaccumulating air. Invasive procedures were avoided due to her persistent pneumonia and critically ill condition. The patient and family decided to pursue comfort care measures.

In a Taiwan study of Spontaneous Secondary Pneumothoraces, a bacterial etiology was identified in about 11% of patients. The pathogenesis was postulated to be to be associated with migration of the bacteria into the pleural space, leading to empyema. It is hypothesized the patients developed the pneumothoraces secondary to bilateral necrotizing bacterial pneumonia. The causative bacterial agents were Staphylococcus, Klebsiella, Pseudomonas, Streptococcus Pneumoniae, and Anaerobic organisms.

Since our patient had MRSA pneumonia, it can be inferred that this was the culprit of her pneumothoraces as there was no other cause. Akcam et al reported a mortality rate of 54% in patients with SBSP within the first 6 months of follow-up. Hence, it is important to have a high suspicion for SBSP in patients who have respiratory decline after initial improvement.

Introduction: Methicillin-sensitive Staphylococcus aureus (MSSA) is a gram-positive aerobic cocci that frequently colonizes healthy adults. Infection may occur when there is breach of the mucosal or epidermal barriers. MSSA bacteremia can result in disseminated disease if there is a delay in diagnosis and treatment, which confers a high mortality.

Case Report: A 64 year-old Asian female with past medical history of type-2 diabetes mellitus presented to our institution with altered mental status. She was employed as a dumpling maker at a Chinese restaurant. One month prior to presentation she cut her left pollex and developed a pustule, which she manipulated with a needle. She was hypotensive, tachycardic, and unresponsive, thus, immediately intubated. She was Labs were significant for leukocytosis, lactic acidosis, hypokalemia, elevated renal indices, metabolic acidosis, hyperglycemia, and ketonemia. Chest computed tomography (CT) showed a large pericardial effusion. Brain CT revealed bilateral temporal and occipital subcortical hypodensities. She was admitted to the ICU and started on broad spectrum antibiotics, intravenous insulin, and fluids. Later that evening she went into cardiac arrest. Cardiopulmonary resuscitation (CPR) was initiated, with return of spontaneous circulation after eight minutes. Bedside echocardiogram demonstrated worsened pericardial effusion with complete collapse of the right ventricle. Emergent pericardiocentesis yielded 200 milliliters of milky-pink fluid. Lumbar puncture was consistent with bacterial meningitis. Cultures from blood, CSF, pericardial fluid, sputum, and urine were all positive for MSSA. Transesophageal echocardiogram (TEE) was negative for infective endocarditis (IE). The patient progressively developed acrocyanosis of the upper and lower extremities, with associated livedo reticularis. Magnetic resonance imaging of the brain showed multifocal areas of infarction and a hyper-intense left basal ganglia. Repeat chest CT showed new pulmonary lesions with cavitation. Blood cultures were persistently positive despite appropriate treatment with intravenous Nafcillin. Multi-organ failure and shock ensued, while neurologic exam was consistent with minimal brainstem activity. The patient unfortunately expired on hospital day seven.

Discussion: Our case details the clinical manifestations of disseminated MSSA infection acquired from a finger cut, which resulted in purulent pericardial tamponade, CNS infection, and diffuse septic emboli. We believe that CPR performed during cardiopulmonary arrest further propagated the embolic phenomenon. Although TEE was negative for IE, it is quite possible that the patient had valvular vegetations that were dislodged with chest compressions.
A Cryptogenic Case of Fungal Pneumonia
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Introduction: Pulmonary cryptococcosis is caused by inhalation of the encapsulated fungi Cryptococcus neoformans, which can then undergo hematogenous spread to other organs. Radiographic findings include solitary or multiple noncalcified nodules, hilar and mediastinal adenopathy, and pleural effusions. Asymptomatic pulmonary cryptococcosis in an immunocompetent host is rarely seen.

Case description: An 88-year-old Hispanic male with history of COPD, former smoker (30 pack-years), colon carcinoma status post hemicolectomy presented to the emergency department with general malaise, shortness of breath, and productive cough of yellow sputum for one week. He previously completed a 7-day course of oral Levaquin, with no improvement. Chest radiograph showed right lower lobe (RLL) pneumonia with a pleural effusion. Due to lack of clinical improvement, post-obstructive pneumonia was considered. Bronchoscopy showed edematous and erythematous mucosa. BAL cultures and cytology were negative. The patient completed a 14-day course of linezolid and meropenem, with resolution of symptoms. Follow up chest CT showed improvement of RLL pneumonia, but showed a new 1 cm cavitary lesion with associated nodules measuring 2.4 cm x 1.9 cm and 2.5 cm x 2.5 cm. CT-guided biopsy showed necrotizing granulomas in lung parenchyma and suspicious narrow-based budding yeast. Histopathologic specimens stained positive with PAS stain and mucicarmine, confirming the diagnosis of cryptococcosis. HIV and Quantiferon titers were negative. The patient was treated with fluconazole 400 mg daily for 6 months. Follow up Chest CT showed no significant changes.

Discussion: Pulmonary cryptococcosis represents a medical challenge since its symptoms and radiological findings are nonspecific. Treatment in an asymptomatic immunocompetent host is questionable but it warrants management when suspecting severe disease.

Bronchopleural Fistula secondary to Primary Streptococcus intermedius Empyema
Mohamad Hamade MD, Yonatan Ghiwot MD, Michelle Finkelstein DO

Case presentation: A 68-year-old woman with a 16-year smoking history presented for dyspnea on exertion and lightheadedness. The patient endorsed recent dry cough, night sweats, and headache but denied fever, chills, or chest pain. Vital signs on admission revealed oxygen saturation of 84% on room air and a heart rate of 102. The remainder of the physical examination was significant for diffuse crackles bilaterally, most notably at the right mid-lung zone, with obvious use of accessory muscles. CBC revealed a leukocytosis with neutrophil predominance and normocytic anemia. Initial chest X-ray showed a right basilar pneumothorax with associated effusion and atelectasis. Subsequent CT angiogram of the chest did not reveal any pulmonary embolism but confirmed a right basilar hydropneumothorax (approximately 25% in size) with adjacent right lower lobe consolidation and presence of a bronchopleural fistula (BPF). The patient underwent thoracostomy tube placement with drainage of purulent, milky fluid that was cultured and ultimately grew Streptococcus intermedius. She was started on intravenous ceftriaxone and had three days of intrapleural fibrinolytic therapy with tPA and Dornase alfa (recombinant human deoxyribonuclease, also known as pulmozyme) in order to dissolve the remaining septations and loculations. A repeat CT scan of the chest without contrast showed non-resolution of the empyema with hydropneumothorax and persistence of the bronchopleural fistula. Three more days of serial chest X-rays continued to show right lower lung zone hydropneumothorax with a persistent air leak (PAL) in the chest tube apparatus despite clamping. Thus, the patient underwent video-assisted thoracoscopic surgery (VATS) with decortication for the non-resolving hydropneumothorax and bronchopleural fistula. Bilateral chest tubes were placed intraoperatively and drained serosanguinous fluid for many days. Multiple water seal trials were attempted and failed, evidenced by the serial chest X-rays and a PAL secondary to the BPF. After a prolonged hospital course with her chest tube to suction, the patient was successfully weaned off and had a Heimlich valve placed. The patient was successfully discharged in stable condition.
A Case of Asthma, Elevated IgE with Multilobar Atelectasis

Alibel J. Bello, Amit Diwakar

**Introduction:** Eosinophilic bronchitis (EB) can occur in association with bronchial asthma, or in its absence. It contributes to inflammation, airway remodeling, and airway hyperresponsiveness. We report a case of a patient with clinically well controlled asthma with progressive atelectasis of multiple lobes.

**Case:** A 63-year-old female with asthma, allergic rhinitis, nasal polypectomy, and aspirin anaphylaxis presented two years ago with fever and nonspecific complaints. Chest X-ray showed a left mid-lung opacity. A CT-chest revealed focal bilateral bronchiectasis with patchy infiltrates on the left and a 2.8 x 4.6 cm mass-like opacity in the right lung causing narrowing of the right middle and lower lobes. Her asthma was well controlled with the Fluticasone/Salmeterol inhaler. Repeat CT-chest in six months showed progressive right lower lobe (RLL) atelectasis and complete collapse of the right middle lobe (RML). She had an elevated serum IgE 799 kU/L and a normal serum IgG. Aspergillus galactomannan antigen was negative. She returned a year later with an asthma exacerbation which improved with short course steroids. Repeat CT-chest demonstrated complete atelectasis of the RML and RLL with bronchial wall thickening and areas of mucoid impaction. Serum IgE increased to 912 kU/L with peripheral eosinophilia. Worsening airway obstruction without reversibility was noted on spirometry. Diagnostic bronchoscopy revealed inflamed mucosa throughout the airways with thick inspissated mucus. The RML was completely occluded with heaped up mucosa. RLL opening was narrow and inflamed. The lingular opening was also completely occluded with inflamed mucosa. Needle aspiration of the RLL mass revealed mixed inflammatory cells along with mucus and cellular degeneration. Lavage of the RLL grew *Moraxella catarrhalis*. Fungal smears and cultures were negative. The lack of central bronchiectasis and absence of fungus ruled out allergic bronchopulmonary aspergillosis. She was started on a long steroid taper for EB and levofloxacin for her superimposed bacterial pneumonia with plans for treatment with anti-IgE agents.

**Discussion:** Eosinophilic bronchitis in asthma has been well described. However, it is typically associated with symptoms of cough and difficulty to control asthma. (1-3) Our patient clinically had well controlled asthma on inhaled corticosteroids, yet had progressively increasing airway obstruction, IgE and mucosal inflammation causing advanced multilobar atelectasis. Furthermore, the growth of *Moraxella* in her lungs may also be contributing to her asthma exacerbations. (4) Treatment with systemic steroids and anti-IgE agents for her is aimed at resolution of inflammation and aeration of atelectatic lobes.

**Conclusion:** EB causing intense airway inflammation can cause progressive atelectasis despite clinically well controlled asthma.

Renal Cell Carcinoma Presenting with Hemorrhagic Pleural Effusion

Amira Ibrahim, Anneka Hutton, Daniel Gutman

**Introduction:** Renal cell carcinoma (RCC) comprises 85% of all primary renal neoplasms. Fifty percent of RCC is identified incidentally on radiographic imaging. Pleural effusion as the manifesting sign of RCC is exceedingly rare.

**Case Report:** A 53-year-old male presented to the emergency department due to 3 weeks of worsening dyspnea and non-productive cough. He had been treated for community acquired pneumonia without improvement of his symptoms. He had no significant past medical history and never smoked. He denied fevers, upper respiratory symptoms, or weight change. Vitals were stable with normal oxygen saturation on room air. Absent breath sounds were noted over the right hemithorax. Initial laboratories were unrevealing. CXR showed near-complete opacification of the right hemithorax. Chest CT confirmed a large right pleural effusion and revealed nodular deposits along the pleura and within lung parenchyma. Bulky mediastinal and axillary lymphadenopathy was evident. Thoracentesis yielded 2.6 L of grossly bloody fluid. Pleural fluid cytology was negative. Subsequent CT revealed improved lung inflation and identified a 9.4 cm solid right-sided renal mass with paraaortic lymphadenopathy suspicious for a primary renal malignancy. Biopsy from both lung parenchyma and pleural masses revealed poorly differentiated carcinomatous cells, positive for CA IX, MOC31, and CD10, confirming metastatic RCC. Cytoreductive right nephrectomy was performed. Pathology revealed clear cell predominant RCC. The patient was initiated on immunotherapy.

**Discussion:** RCC is referred to as the “internist’s tumor” due to its varied presentation. The classic triad of flank pain, hematuria and a palpable abdominal mass occurs in only 10% of patients. Fifty percent of patients have regionally advanced or metastatic disease at diagnosis. The most common site of metastasis is the lung (50-60%), presenting as multiple or solitary lung nodules. Rarely, RCC may result in malignant pleural effusion due to pleural metastasis. This is exceedingly uncommon as RCC accounts for 1-2% of all malignancy related pleural effusions. Pleural involvement appears to occur late in the disease process and was found in only 12% of autopsies in patients with metastatic RCC. Pleural metastasis is postulated to occur through lymphatic drainage of lung metastasis or hematogenously through renal veins or Batson’s venous plexus. As in our case, pleural effusions caused by RCC may be grossly bloody upon thoracentesis. This is likely due to the highly vascular nature of RCC itself. Prognosis in stage IV RCC is poor. Median mortality ranges from 12.5 with no treatment to 28.4 months with molecular targeted therapy such as vascular endothelial growth factor inhibitors. Early recognition may allow for earlier initiation of molecular targeted therapy and improve survival. Thus, we urge clinician awareness of this rare presentation of RCC.
Asymptomatic Saddle Pulmonary Embolism in a Patient with Poorly Differentiated Signet Ring Cell Adenocarcinoma

Jared M. Kelly MD; Lilibeth Jauregui MD; Mishah Azhar MD; Polina Gaisinskaya MD; Daniel Gutman MD

Saddle pulmonary embolism are visible thromboembolus straddling the bifurcation of the main pulmonary artery trunk with a 2 week mortality of 5.8% if not treated. At times, saddle pulmonary embolisms can be associated with a wide range of clinical presentations and hemodynamic instability can be relatively uncommon. Our patient is a 50 year old male with no significant past medical history who presented with heartburn and several months of indigestion, early satiety, decrease appetite, and weight loss. CT abdomen/pelvis was performed which showed severely distended stomach secondary to gastric outlet obstruction caused by mass lesion in the pylorus vs duodenal bulb, with bulky lymph nodes at the root of mesentery and retroperitoneum suspicious for metastatic disease. Patient was taken for endoscopy and biopsy. Biopsy was significant for poorly differentiated signet ring cell adenocarcinoma. CT chest/abd/pelvis done for staging and noted bilateral pulmonary filling defects consistent with saddle embolism. Patient was taken for EKOS and put on heparin drip, then bridged to warfarin. Patient was then started on chemotherapy and follows up at the FAU clinic for continuity of care. Incidental PE have been suspected to occur most commonly in patient with brain, ovarian, gastric and pancreatic cancers with the highest risk within 3-6 months after initial diagnosis. Despite being a rare occurrence in patient’s with signet ring cell adenocarcinoma, some studies have shown patient with cancer have more than 4-fold increase risk of dying after an acute thrombotic event than patient with out. Although treatment for Incidental PE is still not clear, most recommend LMWH for 3-6 months. Even so, most studies show no difference in 6 month mortality between cancer patient with IPE and cancer patient diagnosed with PE based on symptoms along with risk of major bleeding or reoccurrence when on treatment. Despite this, IPE, especially when they become symptomatic, are associated with a poor prognosis in cancer patient’s. With such uncertainty and potential risk, further research should be addressed with either earlier direction of VTEs or more appropriate management especially in cancers with high risks of developing VTE.

Large Pulmonary Masses in a smoker are always a concern for malignancy.

Kishankumar Patel MD, Vishal Singh MD, Christian Almanzar-Zorrilla MD, Jan Sambataro MD

Description: A 59-year-old female with medical history of hypertension, and smoker (27 pack years) presented to the clinic with intermittent dry cough. She commonly traveled to New Mexico. She denied any other symptoms. On chest x-ray revealed a peripheral 2cm lung lesion. Her laboratory workup was negative. She underwent CT-guided biopsy which revealed chronic inflammation without malignancy. VATS with wedge resection of the left lower lung lobe was pursued. The specimen showed a white, necrotic, irregular nodular mass. Histology showed necrosis, granulomatous inflammation, yeast cells. Staining was positive for GMS, PAS and Mucicarmine. Blood cryptococcal antigen was positive. Her absolute CD4 count was within normal limits, however the CD4% was low at 39.9%. CT scans of the brain, abdomen, and pelvis were negative for disseminated disease. This fit the picture of an isolated pulmonary cryptococcosis.

Discussion: Cryptococcosis in immunocompromised individuals is well documented. In both immunocompromised and immunocompetent patients, the fungus enters the respiratory system via inhalation of yeast spores, and commonly presents as a disease of the CNS. However, there are few documented cases of isolated pulmonary cryptococcosis in immunocompetent patients, which is hypothesized to be from impairment in lymphocyte response due to low CD4 counts. Treatment with fluconazole 200-400mg daily for 6-12 months is recommended. Surgical resection is necessary for histopathological diagnosis in pursuit of neoplasia. It should be recognized that cryptococcosis can present as a pseudotumor lesion and be confirmed with a biopsy.
COVID-19 Associated Submissive Pulmonary Embolism With the Use of Dabigatran
Zeeshan Chauhan, MD, Huda Asif, MD and Hector Vazquez Saad, MD

Introduction: COVID-19 infection is associated with a hypercoagulable state with higher incidence of VTE complications including pulmonary embolisms (PE). The use of anticoagulation therapy has been suggested to prevent these complications with COVID-19 Infection. We present a case of submissive PE while on dabigatran in the setting of COVID-19 infection.

Case Presentation: 69 y/o male with history of DVT, on lifelong dabigatran (PRADAXA), presented with worsening dry cough, dyspnea, chest pain, headache, nausea, vomiting and diarrhea for past 3 days. Patient denied fever or sick contact. He endorsed medication compliance with dabigatran 150mg twice-daily dose. Initial blood work noted for high D-dimer, inflammatory markers, troponins and pro-BNP with positive COVID-19 PCR. CTA Chest showed right lower lobe patchy ground-glass opacities as well as large filling defects within the bilateral main pulmonary arteries representing acute bilateral PEs with RV strain. Lower extremities doppler ultrasound also showed bilateral acute on chronic DVTs. He was started UF-heparin infusion for submissive PE. Given increased clot burden and evidence of right heart strain, he underwent successful catheter-directed thrombolysis by IR without complications. He also completed a course of remdesivir and decadron for COVID Pneumonia. With stable respiratory status and negative follow up COVID-19 PCR, he was discharged home on long-term Apixaban anticoagulation.

Discussion: Dabigatran has been associated with 92% reduction in incidence of VTE in general population. There is no data on the incidence of VTE while on direct thrombin inhibitors with COVID-19 infection. That leads to inquire the anticoagulation effect of direct thrombin inhibitors like dabigatran with COVID-19 infection.

Atypical Takotsubo Cardiomyopathy Secondary to Acute Chest Syndrome
Anneka Hutton MD, Navneet Kaur MD, Jared M. Kelly MD, Eli S. Levine MD, Aashish Neupane MD

Introduction: Takotsubo Cardiomyopathy (TCM) is characterized by transient left ventricular dysfunction with wall motion abnormalities extending beyond the vascular distribution of any single coronary artery in the absence of obstructive coronary disease on cardiac catheterization.

Case Presentation: A 57-year-old female with Hemoglobin SC disease presented with left sided pleuritic chest pain. She was febrile to 103°F, tachycardic, tachypneic and hypoxic to 78%. Physical exam revealed labored breathing and rhonchi over the left hemithorax. Cardiac examination was unremarkable. CBC revealed a leukocytosis of 29, hemoglobin of 6.8 below baseline of 10.8. CXR revealed patchy consolidation in right upper and left lower lobes. Acute chest syndrome (ACS) was suspected. Troponins were elevated at 4.7, EKG revealed ST elevations in leads III, aVF, V3-V5. Emergent cardiac catheterization revealed normal coronary arteries without flow limiting disease. Left ventriculography revealed distal apical and anterolateral hypokinesis with hyperdynamic basal wall motion. Atypical multi-focal TCM was diagnosed; ACE-I and beta blocker were initiated. Patient denied emotional stressors. Her ACS rapidly improved with blood transfusion, IV fluids and antibiotic therapy. Repeat echocardiography showed normalized wall motion and she was discharged on hospital day 5.

Case Discussion: ACS is a vaso-occlusive crisis caused by microvascular ischemia; RBC sickling occurs within pulmonary microvasculature resulting in occlusion and infarction. To our knowledge, we present the first reported case of TCM secondary to ACS. We postulate a multifactorial etiology: increased catecholamine release due to pain and hypoxia due to ACS with concurrent cardiac microvascular ischemia due to direct insult of RBC sickling and occlusion. We further theorize that diffuse cardiac microvascular ischemia played a role in the unique multi-focal nature of our patient’s TCM. This is reflected in her atypical ventriculogram with anterolateral wall hypokinesis with distal akinesis. Stress-related catecholamine release and microvascular ischemia have both been theorized to play a role in the development of TCM; however, further analysis is required to definitively identify causative pathophysiology.
An Interesting case of pulmonary embolism after kyphoplasty.
Gustavo Avila MD., Purva Sharma MD.

Introduction: Pulmonary cement embolism (PCE) refers to embolization of polymethyl methacrylate into the lungs. Patients are most often asymptomatic, but reports have been made were patients present symptomatically after PCE. We report a case of a 61-year-old man who had a vertebral kyphoplasty and presented 2 days later with acute onset respiratory distress and found to have a fatal PCE.

Case Presentation: 61-year-old male with medical history of uncomplicated kyphoplasty of T11, T12, L1 vertebrae, did well post-operative and was discharged. Patient presented back to the ER on same day of discharge with complaints of acute onset shortness of breath. Patient appeared in severe respiratory distress. His physical examination was remarkable for decreased breath and crackles sounds bilaterally. Patient was intubated and placed on mechanical ventilation. Initial CXR showed increased hyperdense perihilar opacities. The clinical presentation was concerning for embolic vertebroplasty material. CT angiography which reported extensive vertebroplasty cement embolism to the pulmonary arteries and enlargement of the pulmonary arteries. Patient was admitted to the ICU for mechanical ventilation. Management and open cardiac surgery to remove cement from the lungs was considered. Patients status continued to deteriorate in the following 24 hours. He was hemodynamically unstable requiring large doses of vasopressors and requiring immediate hemodialysis. Patient had an episode of PEA arrest and expired.

Discussion: In this case, a Chest X ray showed pulmonary infiltrates and an increase in perihilar opacities compatible with embolic vertebroplasty at the ER after 72 hours post-procedure. Although most patients remain asymptomatic according to literature, it has been reported cases in which patients develop symptoms months, and even until 10 years after the procedure. PCE after kyphoplasty is a complication that happens according to different series as low as 3.5% up to high as 28.6%. Percutaneous kyphoplasty has been reported with less possibility to develop Pulmonary cement embolism than vertebroplasty. The presence of comorbidities in a patient of the older age increased the possibilities of fatal outcome in this patient.

Adenocarcinoma Masquerading as Interstitial Lung Disease
Melaine Lanza, MD, Christine Girard MD, Samantha Gillewter MD and Nydia Martinez, MD

Intro: Lung adenocarcinoma is the leading cause of all cancer deaths in the United States with a relatively high prevalence and poor prognosis with delayed diagnosis. It is the most common primary lung cancer, representing approximately 40% of all WHO classified Malignant Epithelial Lung Tumors. At the time of diagnosis, patients with Non-Small Cell Lung Cancers (NSCLC) frequently have regional and distant metastases, resulting in a poor prognosis. Common presentations are nonspecific and include cough, hemoptysis, chest pain, or non-resolving pneumonia. Additionally, approximately 10% of patients with Lung Adenocarcinoma are asymptomatic at the time of diagnosis, further delaying early detection. In these cases, lung adenocarcinoma is frequently discovered as an incidental finding on radiographic imaging. The classic radiographic finding of this cancer is a discrete mass located centrally or peripherally. Less common radiographic presentations can include areas of consolidation or ground-glass opacities which are also seen in interstitial lung disease (ILD). In this case series, we present two cases of lung adenocarcinoma that are radiographically consistent with ILD.

Case 1: A 59-year-old man with 30-pack-year smoking history presented with new onset shortness of breath. He did not endorse any systemic symptoms and labs were unremarkable, including no leukocytosis. Autoimmune work up was negative. Radiographic chest imaging demonstrated peripheral and peribronchovascular consolidative ground glass opacities involving all lobes reflective of ILD. Full cardiac evaluation including ECHO and stress test were negative for any cardiac disease, including shunt. Several rounds of treatment with corticosteroids and antibiotics were administered without symptomatic improvement. Hospital courses were complicated by bilateral pneumothoraces that required multiple chest tube placements. He underwent a VATs procedure with right lower lobe wedge biopsy which was positive for invasive adenocarcinoma. Palliative chemotherapy was recommended, however therapy was not initiated secondary to his rapid decline. Hospice was recommended, and the patient expired.

Case 2: A 62-year-old man with 40-pack-year smoking history presented for worsening shortness of breath and cough. He had been hospitalized several times and treated for recurrent pneumonia with antibiotics and corticosteroids without clinical improvement. Chest CT scan was obtained revealing diffuse bilateral ILD consisting of peripheral/subpleural reticular and ground glass opacities. He continued to decline on traditional therapy. Bronchoscopy with biopsy revealed adenocarcinoma with mucinous and acinar components. Despite aggressive measures with both chemotherapy and radiotherapy he had progressive decline and ultimately opted to initiate comfort measures in hospice care.

Discussion: Lung adenocarcinoma may radiographically present as ILD or other infectious etiologies causing delays in diagnosis and treatment. Often patients fail multiple rounds of corticosteroid and antibiotic treatments before the diagnosis of pulmonary adenocarcinoma is considered. In both cases, their initial presentation masqueraded as an ILD, symptomatically and radiographically, but was rather lymphangitic spread of cancer. Biopsy was required to obtain tissue and ultimately establish the diagnosis. Both cases demonstrate the importance of considering malignancy in the context of failed traditional therapies for ILD or other infectious/inflammatory etiologies. Hence, clinical deterioration or worsening radiographic changes should not just be attributed to progression of ILD. Instead, malignancy should be kept on the differential and considered early in the diagnostic and treatment course. Ultimately, early diagnosis with invasive techniques allow for timely intervention with surgery, chemotherapy, and/or radiotherapy to prevent poor outcomes.
Hiding in Plain Sight – A Unique Case of a Pericardial Cyst Masquerading as Recurrent Acute Bronchitis

Carla Williams, MD; David Lindner, DO, MBA, FCCP, FAOCPI

Introduction: Pericardial cysts are benign, congenital encapsulated lesions arising from the pericardium with a low incidence of 1 in 100,000. These lesions are usually asymptomatic and discovered incidentally on imaging such as chest radiography, echocardiography, computed tomography (CT), and magnetic resonance imaging. The following case describes a patient with recurrent upper respiratory tract symptoms produced by a pericardial cyst.

Case Report: A 71-year-old woman with a past medical history of hypertension, paroxysmal atrial fibrillation, paroxysmal supraventricular tachycardia, and 35 pack-year smoking history presented to the emergency department (ED) complaining of recurrent dyspnea with cough, sore throat, congestion, palpitations, and subjective fever that worsened at night and when lying flat. She also reported one episode of hemoptysis after a bout of severe coughing. This was the patient’s seventh ED visit within the last year for similar complaints. The patient had been diagnosed with acute bronchitis and used Tussalon Perles, Mucinex, and antibiotics as prescribed; however, symptoms continued to recur. The patient worked as a pre-kindergarten teacher for the past two years and reported previous TB exposure without Isoniazid prophylaxis. Patient immunizations were up to date and included Prevnar, Pneumovax, and Influenza vaccines. Physical examination on admission was notable for vital T 36.8 °C, BP 154/81, HR 79/min, RR 18/min, and 99% oxygen saturation on room air. Her oral mucosa was moist, with no pharyngeal erythema or bleeding in the oropharyngeal tract. On auscultation, there were diminished vesicular breath sounds throughout, and an irregularly irregular heart rhythm. Laboratory results showed no leukocytosis and a negative Quantiferon-TB Gold Plus test. Pulmonary function tests demonstrated an FEV1/FVC ratio of 63%, consistent with GOLD (mild) obstructive lung disease without bronchodilator response, along with mechanical air trapping and increased airway resistance. Chest CT revealed hyper-expansion of lungs with scattered calcified granuloma, minimal linear scarring versus atelectasis at the right lung base, and a 4.2 x 2.4 x 2.3 cm fluid density mass-like structure with no internal septations at the right cardiophrenic angle. A detailed review of prior imaging studies indicated that this mass was present three years prior and was unchanged. The patient was diagnosed with a stable, simple pericardial cyst, and her respiratory symptoms managed conservatively. One year later, the patient is asymptomatic except for mild intermittent dyspnea on exertion and remains on Dilatazem. She continues to be monitored closely in Pulmonary and Cardiology clinics with routine surveillance of the pericardial cyst, but there is currently no indication for surgical intervention.

Discussion: Pericardial cysts pose a diagnostic challenge but can be differentiated from other lesions such as hematomas, thymic cysts, pericardial fat pads, diaphragmatic hernias, and pericardial effusions by cross-sectional imaging, demonstrating a non-enhancing lesion with transudative fluid contents. The right anterior cardiophrenic angle is the most common location of pericardial cysts (70%); however, only 25 – 30% of patients experience dyspnea, cough, and arrhythmias due to mass effect. This case describes an uncommon symptomatic presentation of a pericardial cyst and highlights the importance of a systematic and comprehensive approach to reviewing imaging, including close comparison with previous images when available.

Coughing it Up: A Case of Diffuse Alveolar Hemorrhage

M Gonzalez, MD; D Viamonte, MD; A Carter, MD; C Girard, MD; R Mired, MD; S Derosier, MD; D Koth, MD; S Gillenwater, MD; H Elzawawy, MD; S Gabreselassie, MD; I Alsheilli, MD

Introduction: Diffuse alveolar hemorrhage (DAH) is a potentially catastrophic syndrome that has various different etiologies. A broad differential must be used as treatment varies drastically depending on the underlying pathology.

Case Presentation: 68 year old male with a past medical history of renal cell carcinoma status post partial right sided nephrectomy who presented to our hospital with rust colored urine and weakness who subsequently developed hemoptysis. Six weeks prior he was admitted to another hospital for ophlopa, neck pain and right leg weakness. Computerized tomography (CT) and magnetic resonance imaging (MRI) scans of the brain were negative for acute stroke. Acetycholine receptor antibodies were negative. Three weeks later he was admitted again for abdominal pain, myalgias, malaise and night sweats. CT scan of the abdomen/pelvis showed peripheric fat stranding for which he was treated with empiric antibiotics. He was admitted a third time one week later with left arm numbness and right foot drop. MRI showed tiny foci suggestive of punctuate subacute and acute nonhemorrhagic infarcts. He had a brief episode of atrial fibrillation and was subsequently started on Apixaban. Transesophageal echocardiogram (TEE) was negative for atheroma or endocarditis. During this same admission he was found to have developed proteinuria, hypoaibuminemia and elevated creatinine levels. Renal biopsy showed vascular nephrosclerosis, intesitial fibrosis and segmental and global glomerulosclerosis as well as staining positive for IgA, kappa and lambda light chains. Intermitent hemodialysis was initiated. One week later he developed rust colored urine and presented to our emergency department. On admission to our hospital the patient had 1.3 mm nonpalpable petechiae on bilateral hips. CT scan of the brain was unremarkable. Initial CT of the chest showed asymmetric nodular infiltrate in the left lower lobe with a coalescence of several pulmonary nodules in the left lower lobe with a conglomeration of these nodules measuring 1.7 cm in maximal diameter. CT of abdomen/pelvis revealed peripheric collection in the left kidney consistent with a hematoma. Apixaban was stopped given hematuria. A few days into his admission, the patient developed hemoptysis. Repeat CT scan of the chest showed extensive consolidative and ground glass opacities throughout both lungs with lower lobe tree-in-bud opacities that were new compared to CT on admission. He underwent bronchoscopy that showed diffuse alveolar hemorrhage. Blood, sputum and cultures from the bronchoscopy were negative for infectious sources. Testing for human immunodeficiency virus (HIV) and hepatitis viruses was negative. Patient was found to have a positive c-ANCA however had a negative proteinase-3 antibody. ANA, RNP, SSA, SSB, Jo, ribosomal RNP, dsDNA and GBM antibodies were all negative. Serum immunoglobulins were all within normal levels. Bone marrow biopsy was performed that showed polytypic plasmacytosis but was negative for lymphoproliferative disorder or neoplasms. C3 was low at C4 and C4 was undetectable. Rheumatoid factor was elevated at 187. Serum light chains were very mildly elevated in a 1:1 ratio. Serum electrophoresis did not show an M spike. Urine protein electrophoresis showed an M spike. Quantitative cryoglobulin serum was 451. Patient was diagnosed with mixed cryoglobulinemia and started on pulse dose methylprednisolone. He subsequently underwent plasmapheresis for three sessions and then was started on Rituximab. He improved symptomatically.

Discussion: This patient initially presented with hematuria and renal failure. Initial laboratory testing was significant for a positive c-ANCA. Subsequent development of diffuse alveolar hemorrhage seemed to further indicate granulomatosis with polyangiitis. However undetectable C4 levels and positive rheumatoid factor levels are inconsistent with granulomatosis with polyangiitis. In this scenario the positive c-ANCA was of questionable clinical significance given discordance with negative proteinase 3 antibodies. Workup for infection was negative and patient did not respond to empiric antibiotics. In the setting of low complement levels, elevated rheumatoid factor and elevated cryoglobulins, the diagnosis of cryoglobulinemia is more likely. Although DAH is less commonly seen in mixed cryoglobulinemia than in ANCA vasculitides, it nonetheless should be evaluated in any patient presenting with DAH and other systemic manifestations.
Case: A 21-year-old man with a history of intravenous drug use and CD4 cell count <200 who was diagnosed with PCP by lung biopsy and commitment to ART to combat HIV infection. Clinical presentation and physical exam signs tend to be non-specific. As a result, the diagnosis is only suspected once characteristic radiologic findings, bilateral reticular opacities, granular opacities, pneumatoceles or septal thickening are identified in an immunocompromised host.

Discussion: Literature reviewed displayed a case of a single lung abscess in a 23 year old male with a history of intravenous drug use and CD4 cell count <200 who was diagnosed with PCP by lung biopsy and commitment to ART to combat HIV infection. Clinical presentation and physical exam signs tend to be non-specific. As a result, the diagnosis is only suspected once characteristic radiologic findings, bilateral reticular opacities, granular opacities, pneumatoceles or septal thickening are identified in an immunocompromised host.

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Efficacy of tezepelumab in patients with low and high bronchodilator reversibility in the phase 2b PATHWAY study
Jonathan Corren, Mark C Liu, Karin Bowen, Kinga Salapa, Gene Colice, Jean-Pierre Llanos-Ackert

Introduction: In the phase 2b PATHWAY study (NCT02054130), tezepelumab reduced annualized asthma exacerbation rates (AAERs) by up to 71% versus placebo in adults with severe, uncontrolled asthma. We evaluated the effect of tezepelumab on exacerbations in patients with low and high bronchodilator reversibility.

Methods: Adults with severe, uncontrolled asthma were randomized to tezepelumab (70mg every 4 weeks [Q4W], 120mg Q4W or 280mg every 2 weeks) or placebo for 52 weeks. AAER and the rate of exacerbations resulting in hospitalization or emergency room (ER) visits were estimated for patients with low (<20%) and high (≥20%) forced expiratory volume in 1 second (FEV1) reversibility at baseline.

Results: Of 550 randomized patients, 299 and 251 had low and high FEV1 reversibility, respectively. Tezepelumab 210mg (phase 3 dose) reduced AAER over 52 weeks by 70% (95% confidence interval [CI]: 41.85%) and 72% (95% CI: 32.88%) versus placebo in the low and high reversibility groups, respectively. For pooled tezepelumab doses, AAER was reduced by 69% (95% CI: 21.81%) and 60% (95% CI: 26.78%) in the low and high groups, respectively. Exacerbations resulting in hospitalizations or ER visits were reduced by 85% (95% CI: 21.97%) and 78% (95% CI: 32.96%) versus placebo in the low and high reversibility groups, respectively, for tezepelumab 210mg, and by 84% (95% CI: 51.94%) and 64% (95% CI: 18.89%) in the pooled tezepelumab group, respectively.

Conclusions: Tezepelumab treatment reduced AAER irrespective of baseline bronchodilator reversibility, further supporting its potential benefits in a broad population of patients with severe asthma.

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Effect of Dupilumab on Oral Corticosteroid Use in Severe Asthma Patients With Improving Lung Function
Jorge F. Maspero, David M.G. Halpin, David J. Jackson, Nicola A. Hanania, Mario Castro, Christian Domingo, Nadia Daizadeh, Michel Djindjic, Paul Rowe, Yamo Deniz

Introduction: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component of IL-4/IL-13, key and central drivers of type 2 inflammation. In phase 3 VENTURE (NCT02528214), add-on dupilumab 300mg every 2 weeks vs placebo reduced oral corticosteroid (OCS) use, reduced severe asthma exacerbations, and improved pre-bronchodilator forced expiratory volume in 1 second (FEV1) in patients with OCS-dependent, severe asthma. We assessed dupilumab’s effect on OCS use in patients with improved FEV1.

Methods: Patients were stratified by FEV1 improvement of ≥100mL or ≥200mL at Week 24. Percentage reduction from baseline in OCS dose at Week 24 was derived with an ANCOVA model, and percentage of patients with reduced OCS dose during the 24-week treatment period with a logistic regression model.

Results: ≥100mL ≥200mL improvements in FEV1 at Week 24 were observed in 97 (61 dupilumab/36 placebo) and 79 (49 dupilumab/30 placebo) patients. In dupilumab-treated patients with FEV1; improvements of ≥100mL or ≥200mL at Week 24, OCS dose vs placebo was reduced by 39.4%/39.9% (95% confidence interval [CI] 19.57–59.14 and 16.82–62.92) (both P<0.001). In patients with FEV1 improvements of ≥100mL or ≥200mL, odds ratios vs placebo were 6.4/6.6 (95% CI 2.06–15.09 and 1.98–21.78) (both P<0.01) for ≥50% OCS reduction; 5.6/5.9 (95% CI 2.06–15.09 and 1.93–18.13) (both P<0.01) for OCS reduction to <5mg/day; and 3.1/3.7 (95% CI 1.18–8.03 and 1.25–10.73) (both P=0.02) for OCS elimination at Week 24.

Conclusions: Dupilumab significantly reduced OCS dose while improving lung function in patients with OCS-dependent, severe asthma.

Funding: Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Dupilumab Long-Term Safety and Efficacy in Patients With Asthma: LIBERTY ASThma TRAVERSE

Introduction: Efficacy and safety of dupilumab in asthma have been demonstrated up to 52 weeks in phase 2/3 studies. TRAVERSE, an open-label extension (OLE) study (NCT02134028), assessed long-term safety and efficacy in patients who had completed a dupilumab asthma study (DRI, QUEST, EXPEDITION, or VENTURE).

Methods: 2,282 patients with moderate-to-severe asthma or oral corticosteroid-dependent severe asthma received add-on dupilumab 300mg every 2 weeks for up to 96 weeks. Treatment-emergent adverse events (TEAEs), annualized rate of severe asthma exacerbations (AER) during the treatment period, and change from parent study baseline (PSBL) in forced expiratory volume in 1 second (FEV1) and biomarkers up to Week 96 were assessed.

Results: TEAE rates were similar to those observed in the parent studies; between 10.2%-12.1% of patients experienced a serious TEAE. AER for dupilumab-treated patients during the parent studies DRI/QUEST and VENTURE ranged from 0.33 to 0.65, and from 0.33 to 0.35 across studies in the OLE. By Week 96 of the OLE, absolute mean FEV1 ranged from 1.89 to 2.07L across these studies (representing a 16.2-19.6 mean percentage change from PSBLs). Similar AER and mean FEV1 were observed in patients with a type 2 phenotype. By Week 96, blood eosinophils had decreased to below-PSBL levels in patients from DRI/QUEST and were near PSBL levels in patients from VENTURE; total IgE levels decreased by 82% (median % change from PSBL) in DRI.

Conclusion: Long-term use of dupilumab was well tolerated and showed sustained efficacy in asthma patients for up to 96 weeks.

Funding: Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Single inhaler triple therapy in patients with advanced COPD (FULFIL): exacerbation/pneumonia composite outcomes
Mark Dransfield, David MG Halpin, Helen Barnacle, Ruby Birk, Nouhniq Brealey, Chang-Qing Zhu, David Lipson

Introduction: FULFIL reported statistically significant improvements in lung function and health status with once-daily fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) 100/62.5/25µg via the ELLIPTA® inhaler vs twice-daily budesonide/formoterol (BUD/FOR) 400µg/12µg via the Turbuhaler® in patients with advanced COPD (Lipson DA et al. Am J Respir Crit Care Med. 2017;194(4):436-446). Given the clinical overlap of exacerbations and pneumonia, we analyzed composites of these outcomes to assess the overall benefit/risk of FF/UMEC/VI compared with BUD/FOR.

Methods: We performed post-hoc analyses in the ITT (24 weeks; FF/UMEC/VI, n=911; BUD/FOR, n=899) and extension (EXT; 52 weeks; FF/UMEC/VI, n=210; BUD/FOR, n=220) populations. There were two composite outcomes: time-to-first investigator-reported moderate (required antibiotics or oral/systemic corticosteroids)/severe (required hospitalization) exacerbation or pneumonia event (investigator reported by a prespecified list of preferred terms); and time-to-first severe exacerbation/hospitalized pneumonia event. Analyses were based on a proportional hazards model.

Results: For moderate/severe exacerbation or pneumonia, FF/UMEC/VI had a statistically significant reduction in risk vs BUD/FOR of 25% (ITT: 109 [12%] vs 130 [14%]; p=0.027) and 44% (EXT: 37 [18%] vs 63 [29%]; p=0.006). For severe exacerbation/hospitalized pneumonia, FF/UMEC/VI had a lower risk vs BUD/FOR of 17% (ITT: 22 [2%] vs 24 [3%]; p=0.541) and 65% (EXT: 8 [4%] vs 23 [10%]; p=0.010).

Conclusions: The results of these exacerbation/pneumonia composite outcomes support a favorable benefit/risk profile of once-daily FF/UMEC/VI compared with BUD/FOR in patients with COPD.

Funding: GSK (CTT116853)
Comparison between FF/UMEC/VI versus UMEC/VI and FF/VI and UMEC/VI versus FF/VI based on baseline exacerbation history and FEV1: Sub-analysis from the IMPACT trial

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Introduction: IMPACT is a 52-week, randomized, double-blind trial comparing fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) with FF/VI and UMEC/VI in 10,355 symptomatic COPD patients with a history of exacerbations. Primary endpoint was annual rate of on-treatment moderate/severe exacerbations. We compared FF/UMEC/VI vs dual therapies and UMEC/VI vs FF/VI based on exacerbation history in the previous year and FEV1 at screening.

Methods: Sub-analyses of annual rate and time-to-first (TTF, post-hoc) moderate/severe exacerbations were conducted in the following subgroups: FEV1<50%, <2 moderate/no severe exacerbations (group 1); FEV1≥50%, ≥2 moderate or ≥1 severe exacerbation (group 2); FEV1≥50%<80%, ≥2 moderate or ≥1 severe exacerbation (group 3).

Results: FF/UMEC/VI vs UMEC/VI significantly decreased annual moderate/severe exacerbation rates in all three subgroups (rate ratios (RR) range: 0.72-0.83), and significantly reduced TTF in group 2 (hazard ratio [HR] = 0.83 [95% CI: 0.73,0.92]) and group 3 (HR=0.87 [0.79,0.96]) compared to UMEC/VI vs FF/VI significantly reduced exacerbation rate in group 1 (RR=0.82 [0.72,0.92]) and group 2 (RR=0.82 [0.75,0.91]), and TTF in group 1 (HR=0.88, 95% CI: 0.81,0.95) and group 2 (HR=0.83; 95% CI: 0.75,0.92). UMEC/VI showed higher moderate/severe exacerbation rates vs FF/VI in group 2 (RR=1.13; 95% CI: 1.01,1.27) and group 3 (RR=1.31; 95% CI: 1.14,1.51). There were no significant differences in TTF between UMEC/VI and FF/VI for the three subgroups.

Conclusions: In IMPACT, regardless of disease severity, FF/UMEC/VI improved exacerbation outcomes vs both UMEC/VI and FF/VI. When comparing dual treatments, FF/VI significantly reduced moderate/severe exacerbation rates in subjects with more frequent or severe exacerbations vs UMEC/VI.

Funding: GSK [NCT02164513]

CAPTAIN Study: Evaluating the Efficacy of Once-Daily, Single-Inhaler Fluticasone Furoate/Umclidinium/Vilanterol (FF/UMEC/VI) Versus FF/VI in Inadequately Controlled Asthma Using Change in Asthma Control Questionnaire and the Relationship With Trough FEV1

Andrew Fowler, Hui K Jerzynski, Zelie Bailes, Maggie Tabberer, Neil Barnes, Guy Peachey, John Oppenheimer, Laurie Lee

Introduction: Despite inhaled corticosteroid/long-acting β2-agonist (ICS/LABA) therapy, some patients with moderate/severe asthma remain symptomatic and have poor disease control.

Methods: CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study in patients with uncontrolled asthma. Treatment: once-daily fluticasone furoate/vilanterol/FF (100/25, 200/25mcg) or FF/umeclidinium (UMEC/VI) (100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25mcg) via the Ellipta inhaler. The following pre-specified endpoints are reported: mean change from baseline (CFB) in asthma control questionnaire (ACQ)-7 score and proportion of ACQ-7 responders (minimal clinically important difference, MCID: ≥0.5) (Week 24). Logistic regression of trough FEV1, change and ACQ-7 response (Week 24) was performed post hoc.

Results: CFB in ACQ-7 score >MCID was seen in all treatment groups, with numerically greater improvements for FF/UMEC 62.5mcg/VI versus FF/VI (0.089 [95%CI: -0.156, 0.031]). Greater proportions of ACQ-7/6 responders were also seen with FF/UMEC 62.5mcg/VI, with higher odds of response versus FF/VI (odds ratios 1.43, 1.31, and 1.23 for ACQ-7/6, respectively). A modest correlation (-0.37) was observed between trough FEV1, and ACQ-7 scores across the study population (treatment independent); a greater CFB in trough FEV1 was associated with larger ACQ-7 improvements. An increase of 100 ml in FEV1 at Week 24 increased the odds of being an ACQ-7 responder by 26% (95%CI: 21.30) at Week 24.

Conclusions: FF/UMEC 62.5mcg/VI improved asthma control versus FF/VI as measured by ACQ-7 score CFB and ACQ-7/6 responders. ACQ-6/5 improvements and the modest relationship between trough FEV1 and ACQ-7 responder suggest improved control is not only driven by lung function changes.

Funding: GlaxoSmithKline (study 205715/NCT02924688)

CAPTAIN Study: Simultaneous Step-up to High-Dose Fluticasone Furoate and Addition of Umclidinium for the Treatment of Inadequately Controlled Asthma

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Introduction: For asthma patients uncontrolled on inhaled corticosteroid/long-acting β2-agonist (ICS/LABA), options include increasing ICS dose or adding long-acting muscarinic antagonist (LAMA). Effects of simultaneously doubling ICS dose and adding LAMA have not been examined.

Methods: CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study in adults with uncontrolled asthma. Treatment: once-daily fluticasone furoate/vilanterol (FF/VI) (100/25, 200/25mcg) or FF/umeclidinium (UMEC/VI) (100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25mcg) via Ellipta inhaler. Endpoints: trough FEV1; change from baseline (Week 24; primary); annualized moderate/severe exacerbation rates; proportions of asthma control questionnaire (ACQ-7) responders (Week 24). Data not adjusted for multiplicity.

Results: Increasing FF dose and/or adding UMEC was associated with trough FEV1 improvements versus FF/VI 100/25mcg: simultaneous step-up (to FF/UMEC/VI 200/62.5/25mcg) showed the greatest improvement (145ml, [95% CI: 100,187] vs FF/VI 100/25mcg). Increasing FF dose in dual therapy led to the greatest reductions in annualized rate of moderate/severe exacerbations versus FF/VI 100/25mcg (rate ratio: 0.65 [95% CI: 0.50,0.85]); effects of simultaneously adding UMEC were minimal. Increasing FF dose or adding UMEC increased the proportion of ACQ-7 responders versus FF/VI 100/25mcg; treatment changes were additive, with simultaneous step-up to FF/UMEC/VI 200/62.5/25mcg showing the greatest improvement (odds ratio: 1.71 [95%CI: 1.27,2.30]). Safety was similar in all groups.

Conclusions: Doubling FF dose and/or adding UMEC 62.5mcg led to numerical improvements in all endpoints, with additive effects on lung function and asthma control. Simultaneously increasing FF dose and adding UMEC represents a therapeutic option for patients inadequately controlled on FF/VI 100/25mcg.

Funding: GSK (study 205715/NCT02924688)
Repeat prescription claims for dual long-acting muscarinic antagonist/long-acting β2-agonist bronchodilators in patients with chronic obstructive pulmonary disease

Asif Shaikh, Elizabeth M. Garry, Jukka Montonen, Edward Yu, Marc Miravitlles

Introduction: We compared discontinuation of repeat prescription claims during a 1-year period in patients initiating tiotropium/olodaterol (tio/olo) versusumeclidinium/vilanterol (ume/vi) as maintenance therapy for chronic obstructive pulmonary disease (COPD).

Methods: Two cohorts were established using data from the IBM MarketScan US commercial claims database (November 17, 2015–March 31, 2018). Patients aged >40 years who had been diagnosed with COPD at or before cohort entry were followed for up to 1 year. The primary outcome was discontinuation of repeat prescription (tio/olo or umec/vi), defined as no refill claims within 60 days during follow-up. Propensity score matching (1:2) was used to account for differences in demographics, concomitant medications, comorbidities, respiratory-related covariates (as a proxy for disease severity) and COPD duration. Given the limitations of claims data, the cohorts could not be fully matched for disease severity, socio-economic factors, or medication supply route (pharmacy or mail order).

Results: The cohorts included 3,876 initiators of tio/olo and 7,420 initiators of umec/vi. Mean age was 65 years; 54% were male. The percentage of patients without evidence of repeat prescriptions was 64.2% (tio/olo) and 60.3% (ume/vi). The rate of discontinuation was 1.826 and 1.647 per 1,000 patient-years for tio/olo and umec/vi, respectively. The matched hazard ratio for discontinuation of repeat prescriptions with tio/olo versus umec/vi was 1.11 (95% confidence interval: 1.06–1.17), which varied with refill window length.

Conclusions: Discontinuation was high (~60%) in both cohorts. Repeat prescription claims were slightly lower in patients initiating tio/olo versus umec/vi.

Funding: Boehringer Ingelheim

Consistent effect of nintedanib on reducing decline in forced vital capacity (FVC) across interstitial lung diseases (ILDs)

Francesco Bonella, Toby M Maher, Vincent Cottin, Florian Voss, Susanne Stowasser

Introduction: The effect of nintedanib on the rate of FVC decline has been investigated in clinical trials across a spectrum of fibrosing ILDs. We assessed the consistency of the effect of nintedanib vs placebo on the rate of FVC decline across clinical trials in subjects with various fibrosing ILDs.

Methods: The effects of nintedanib were investigated in placebo-controlled trials in subjects with idiopathic pulmonary fibrosis (IPF) (INPULSiS-1 and -2), systemic sclerosis-associated ILD (SENSCIS) and progressing fibrosing ILDs other than IPF (INBUIld). In each trial, the primary endpoint was the annual rate of decline in FVC (mL/year) assessed over 52 weeks. We performed a meta-analysis based on the relative treatment effects of nintedanib vs placebo on the annual rate of decline in FVC (mL/year) to account for the different natural histories of these diseases, to estimate the combined relative effect and to test for heterogeneity across trials.

Results: Nintedanib slowed the annual rate of decline in FVC vs placebo in the combined analysis by 51.0% (95% CI 39.1, 63.0). The relative effect of nintedanib vs placebo on the rate of FVC decline was 52.2% (95% CI 32.4, 72.0) in INPULSiS-1, 45.2% (21.7, 68.8) in INPULSiS-2, 43.9% (3.2, 84.6) in SENSCIS, 60.7% (33.7, 87.8) in subjects with a ULP-like fibrotic pattern on HRCT in INBUIld, and 48.8% (10.3, 87.3) in subjects with other fibrotic patterns in INBUIld.

Conclusion: Nintedanib had a consistent effect on reducing the annual rate of decline in FVC across trials conducted in subjects with a range of fibrosing ILDs.

Funding: Boehringer Ingelheim

Outcomes of patients with combined idiopathic pulmonary fibrosis (IPF) and emphysema in the IPF-PRO Registry

Hyun J Kim, Laurie D Snyder, Megan L Neely, Thomas B Leonard, Daniel A Culver* on behalf of the IPF-PRO Registry investigators

Introduction: We used data from the IPF-PRO Registry, a multicenter US registry of patients with IPF, to examine associations between the presence of emphysema and clinical outcomes.

Methods: We defined emphysema on the basis of investigators prospectively recording the presence of “clinically significant emphysema” on an HRCT scan. Associations between emphysema at enrollment and times to death or lung transplant; hospitalization; and death, lung transplant or hospitalization follow-up were analyzed using Cox regression models.

Results: Of 934 patients in the analysis cohort, 119 (12.7%) had emphysema. In patients with and without emphysema, respectively, Kaplan–Meier rates of death or lung transplant at 1 year were 17.5% (95% CI: 11.7, 25.8) and 11.2% (95% CI: 9.2, 13.6), rates of hospitalization at 1 year were 21.6% (95% CI: 14.6, 29.6) and 20.6% (95% CI: 17.9, 23.5), and rates of death, lung transplant or hospitalization at 1 year were 30.4% (95% CI: 22.9, 39.7) and 26.3% (95% CI: 23.4, 29.5). Presence of emphysema at enrollment was not significantly associated with death or lung transplant (HR 1.07 [95% CI: 0.74, 1.54]), hospitalization (HR 1.18 [95% CI: 0.87, 1.60]), or death, lung transplant, or hospitalization (HR 1.02 [95% CI: 0.75, 1.37]), after adjusting for clinical risk factors at enrollment.

Conclusions: Approximately 13% of patients in the IPF-PRO Registry had clinically significant emphysema on HRCT at enrollment. There was no significant difference in the risk of death, lung transplant, or hospitalization between patients who did and did not have emphysema.

Funding: Boehringer Ingelheim
Effect of nintedanib in patients with progressive fibrosing interstitial lung diseases: subgroup analyses from the INBUILD trial

Martin Kolb, Kevin R Flaherty, Rainer-Georg Goeblnder, Rozsa Schlenker-Herceg, Athol U Wells on behalf of the INBUILD trial investigators

Introduction: In the INBUILD trial in patients with fibrosing ILDs and a progressive phenotype, nintedanib slowed the rate of decline in FVC (mL/year) versus placebo, with adverse events that were manageable for most patients. We assessed the effect of nintedanib on the rate of FVC decline across subgroups defined on baseline characteristics.

Methods: Patients with an ILD diagnosis other than IPF, features of diffuse fibrosing lung disease of >10% extent on HRCT, FVC >45% predicted, and DLCO >30%–<80% predicted, who had shown progression of ILD within the 24 months before randomization were randomized to receive nintedanib or placebo. ILD diagnoses were provided by the investigators based on their usual clinical practice. In pre-specified analyses, we assessed the rate of FVC decline over 52 weeks in subgroups of patients by sex, age (<65, ≥65 years), race (White, Asian, Black/African-American), FVC (>70%, >70% predicted), and ILD diagnosis (hypersensitivity pneumonitis, autoimmune ILDs, idiopathic non-specific interstitial pneumonia [NSIP], unclassifiable idiopathic interstitial pneumonia [IIP], other fibrosing ILDs) at baseline. Interaction p-values were calculated to assess potential differences in the treatment effect of nintedanib versus placebo across the subgroups.

Results: A total of 663 patients were treated. Nintedanib had a consistent effect on reducing the annual rate of decline in FVC (mL/year) across subgroups (treatment-by-subgroup-by-time interaction p<0.05).

Conclusions: In the INBUILD trial, nintedanib had a consistent effect on reducing the annual rate of decline in FVC in patients with progressive fibrosing ILDs, irrespective of demographic characteristics, lung function, or ILD diagnosis at baseline.

Funding: Boehringer Ingelheim

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Safety and tolerability of nintedanib in patients with fibrosing ILDs: a comparison of the INBUILD and INPULSIS trials

Fernando J Martinez, Ulrich Costabel, John A Belperio, Carl Coeck, Vincent Cotten on behalf of the INBUILD trial investigators

Introduction: The efficacy and safety of nintedanib in patients with idiopathic pulmonary fibrosis (IPF) and with other fibrosing interstitial lung diseases (ILDs) with a progressive phenotype were investigated in the INPULSIS and INBUILD trials. We compared the safety and tolerability profile of nintedanib in these trials.

Methods: Adverse events reported by the investigators, irrespective of causality, over 52 weeks of treatment and dose adjustments used to manage adverse events were assessed.

Results: In the INBUILD trial (n=663) and INPULSIS trials (n=1061), respectively, the proportions of patients who had a dose reduction were 33.7% and 27.9% in the nintedanib group, and 5.4% and 3.8% in the placebo group, while treatment interruptions occurred in 33.1% and 23.7% of patients in the nintedanib group in 10.3% and 9.0% of patients in the placebo group. Adverse events leading to discontinuation of trial drug occurred in 19.6% and 19.3% of patients treated with nintedanib, compared with 10.3% and 13.0% of patients who received placebo, in the INBUILD and INPULSIS trials, respectively. Diarrhea was the most frequent adverse event (reported in 66.9% and 62.4% of patients treated with nintedanib, compared with 23.9% and 18.4% of patients who received placebo, in the INBUILD and INPULSIS trials, respectively) and the adverse event that most frequently led to treatment discontinuation (in 5.7% and 4.4% of nintedanib-treated patients in the INBUILD and INPULSIS trials, respectively).

Conclusions: The safety and tolerability profile of nintedanib in patients with fibrosing ILDs other than IPF is similar to that in patients with IPF.

Funding: Boehringer Ingelheim

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Revefenacin Improves Lung Function Regardless of Baseline Symptom Status in Chronic Obstructive Pulmonary Disease: A Post Hoc Analysis of Phase 3 Trials

Thomas M. Siler, Gary T. Ferguson, David A. Lombardi, and Glenn D. Crater

Introduction: Revefenacin, a once-daily, long-acting muscarinic antagonist for nebulized inhalation, is approved by the US Food and Drug Administration for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Results from previous 12-week phase 3 trials demonstrated significant bronchodilation in patients with COPD in response to once-daily revefenacin 175 µg. We investigated whether COPD symptomatic status at baseline influenced the response to revefenacin 175 µg versus placebo in patients with moderate to very severe COPD.

Methods: A post hoc analysis of two randomized, 12-week, phase 3 trials (NCT02459080 and NCT02512510) was conducted. We assessed the impact of baseline symptomatic status (ie, COPD Assessment Test score ≥20, uncontrolled symptoms; <2, controlled symptoms) and St George’s Respiratory Questionnaire (≥2, uncontrolled symptoms; <2, controlled symptoms) on the response to revefenacin 175 µg versus placebo in patients with moderate to very severe COPD.

Results: Revefenacin significantly improved FEV1 and FVC versus placebo in patients with COPD regardless of baseline. Overall, patients with uncontrolled symptoms showed greater improvements in FEV1 with revefenacin treatment versus those with controlled symptoms. Interestingly, improvements in FVC were generally similar irrespective of baseline symptomatic status in revefenacin-treated patients.

Conclusions: The results of this post hoc analysis demonstrated that improvements in lung function occurred regardless of baseline symptomatic status following treatment with revefenacin 175 µg.

Funding: Theravance BioPharma

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A Time and Motion (T&M) Pilot Study of Nebulized Chronic Obstructive Pulmonary Disease (COPD) Therapy in US Inpatient and Long-term Care (LTC) Settings

Erwin De Cock, Grace Leung, Hemal Shah, Brooks Kuhn, Bryan Nichols

Introduction: Healthcare facilities devote substantial staff time treating COPD patients. In a T&M study, we quantified time and costs of nebulized COPD therapy at an inpatient and LTC site, and estimated efficiencies of once-daily therapy.

Methods: One healthcare professional (HCP) per site completed a survey describing center characteristics, COPD treatment, and nebulization workflow for albuterol (ALB) and ipratropium bromide/albuterol sulfate (IPR/ALB). Nebulization process time was recorded. Time and materials were translated to costs using local salary data and prices for materials.

Results: Inpatient observations included 3 ALB and 17 IPR/ALB. LTC observations included 5 ALB and 15 IPR/ALB (8 observations from cognitively impaired patients). Average process time (minutes) was 16.1 (95% confidence interval [CI], 14.5–17.8) for inpatient and 21.0 (18.8–23.2) LTC; 50% and 67% were nebulization time (NT). In LTC, CIs suggested differences by cognitive impairment: minutes mean 26.9 (21.3–26.9) if cognitively impaired vs 19.0 (16.1–21.8) if not. For inpatient, NT/admission was $7.8 h; a once-daily nebulized drug would require 23.9 h (~70%). In LTC, NT was $32.3 h; a once-daily nebulized drug would require 33.8 h (~75%). Average cost of HCP time and materials/nebulization was $38.33 inpatient and $31.82 LTC. Cost was $242/admission for current vs $572 for once-daily dosing (~70%) inpatient, and $1,880/mo for current vs $856 for once-daily dosing (~57%) LTC.

Conclusions: Nebulization involves quantifiable HCP time and cost. A switch from ALB or IPR/ALB to a once-daily nebulized drug could generate sizable time savings, depending on the setting of care and site characteristics.

Funding: Theravance BioPharma