ORAL CLINICAL VIGNETTES – 2018

1.	**Dr. Samuel Rosner** Johns Hopkins/Bayview	A Minimally Invasive Diagnosis of Malignancy
2.	**Dr. Bryan Broderick** Johns Hopkins/Broadway	Myeloprolifertive Neoplasm with Eosinophilia Transforming to Acute Myeloid Leukemia
3.	**Dr. Sunita Upreti** GBMC	When Fence Eats the Crop: Autoimmune Hepatitis Induced by Infliximab in a Patient With Crohn's Disease
4.	**Dr. Rasik Dhakal** MHIM	Sarcoidosis of the Spinal Cord: A Tale of a Seemingly Innocuous Fall
5.	**Dr. Evan O'Dea** MedStar Harbor	Post-Operative Pulmonary Embolism: Successful Thrombolysis Despite Relative Contraindication
6.	**Dr. Shyam Kolangara** Sinai Hospital	A Case of Strongyloides Stercoralis Superinfection Treated with Veterinary Ivermection Preparation
7.	**Dr. Hadi Elias** St. Agnes Hospital	Rivaroxaban Induced Hemopericardium
8.	**Dr. Kevin O'Malley** UMMC/VA	A Grave Matter: Autoimmune Thyroid Disease Following Immune Reconstitution
9.	**Dr. Benjamin McKinney** UMMC/Midtown	A Novel Use of Intrapleural t-PA/DNase Therapy for Loculated Chylothorax
10.	**Dr. John Curtin** Walter Reed National Military Medical Center	When Myositis Attacks The Lung

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Indicate your participation in research process (4 sentences or less):
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Tite: A Minimally Invasive Diagnosis of Malignancy
Authors: Samuel Rosner, Emily Insetta

An 87 year old female presents with 9 months of hemoptysis, shortness of breath, and night sweats. Patient has a history of 90-pack years smoking and a mother and daughter with fatal lung cancer. CT scan showed a cavitating lung mass in the left upper lung lobe, measuring 7 x 6.7 x 5.2cm, multiple other pulmonary nodules measuring up to 5mm, a large, multi-lobulated, hypo-attenuating liver mass, peri-hepatic ascites, and prominent abdominal lymphadenopathy. In discussion with the patient about the likelihood of cancer based on imaging, she was adamant that she wanted a more definitive diagnosis but would not want treatment if she were found to have malignancy. To honor her wishes, it was important to pursue a high yield diagnostic workup with low risk of patient harm. Instead of invasive bronchoscopy or CT-guided biopsy, two induced sputum specimens were sent for cytopathology. Both samples returned positive for squamous cell carcinoma. The patient expressed gratitude that her terminal illness had been defined. In line with her goals of care, she chose to pursue hospice and passed away peacefully two weeks later.

This case demonstrates a unique way to diagnose lung cancer while avoiding invasive procedures at the end of life and minimizing costs to healthcare systems. It is rare to encounter a diagnosis of malignancy via sputum cytology, given we are quick to pursue bronchoscopy or CT-guided biopsies, which carry significant risks. In the future, when the suspicion for primary lung cancer is high and diagnosis is not urgent, sputum cytology can be considered in the diagnostic workup.

Induced sputum cytology should be considered as an alternative way to diagnose lung cancer, as supported by a 1991 report in the *Lancet*. In this study, 67 patients who were suspected to have primary lung cancer based on clinical or radiographic findings were randomly assigned to expectorated or induced sputum collection for four days. Both groups underwent bronchoscopy with biopsy on the fifth day. The definitive diagnosis of malignancy was obtained from bronchoscopy or fine needle aspiration. In the induced sputum group, cytology identified 84% of 29 malignancies, which was not statistically different from bronchoscopy which identified 97% of cancers ($p<0.001$). Therefore, induced sputum cytology has a comparable yield to bronchoscopy and should be considered as a safe and affordable alternative to biopsy in the diagnosis of primary lung cancer.

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MYELOPROLIFERTIVE NEOPLASM WITH EOSINOPHILIA TRANSFORMING TO ACUTE MYELOID LEUKEMIA

The patient is a 68 year-old man who was in his usual state of health until he developed oral ulcers for which he was evaluated by his primary care provider. He otherwise felt well. The remainder of his exam at that time was unremarkable. His work up included a complete blood count, which revealed an absolute eosinophil count greater than 50 K/cu mm. He was admitted and underwent an extensive expedited work up for hypereosinophilia. A bone marrow biopsy revealed marked myeloid hyperplasia without evidence of morphologic dysplasia or increased blasts, consistent with myeloproliferative neoplasm (MPN) with eosinophilia. He was discharged on a steroid taper and then started on imatinib in the outpatient setting. Two weeks later, he presented to his outpatient hematologist's office with malaise and dyspnea on exertion. He had a temperature of 37.5C blood pressure of 153/65, heart rate of 103, respiratory rate of 20, and an oxygen saturation of 87% on room air. His exam was notable for a diffusely erythematous and excoriated oropharynx with shallow based oral ulcers and thrush, and rhonchi throughout his bilateral lung fields. He was admitted for further management. He had a white count of 155 K/cu mm, hemoglobin of 11.8 g/dL, platelets of 80 K/cu mm, and a differential notable for 42% eosinophils and left shift with 5% blasts. Other notable labs included a creatinine of 3.4 mg/dL (baseline 1.0 mg/dL), uric acid 20.3 mg/dL, troponin 0.30 ng/mL (reference <0.04 ng/mL), LDH 8,000 U/L, D-Dimer > 30.0 mg/L (reference 0.17-0.88 mg/L), and elevated coagulation studies. CT scan of the chest without contrast demonstrated bilateral centrilobular ground glass opacities. His presentation was consistent with MPN in blast phase complicated by leukostasis, tumor lysis syndrome (TLS), and acute disseminated intravascular coagulation (DIC). He was treated with emergent leukapheresis and cytoreduction in addition to supportive measures. A repeat bone marrow biopsy was performed and demonstrated myeloperoxidase positive blasts comprising approximately 25% of the cellularity. On further investigation, a gene panel revealed an FGFR1 translocation. He was reclassified according to the WHO classification system under the subgroup "Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, and FGFR1." The patient eventually began therapy with ponatinib, a tyrosine kinase inhibitor that binds to FGFR1.
This case exemplifies an uncommon cause of hypereosinophilia, illustrates the disease's natural course, and highlights the increasing role that specific genetic alterations are playing in the classification and treatment of a wide variety of cancers.

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When fence eats the crop: Autoimmune Hepatitis induced by Infliximab in a patient with Crohn's disease

Anti-Tumor Necrosis Factor (anti-TNF alpha) agents like Infliximab have been increasingly used to treat several pro-inflammatory autoimmune conditions. Despite their many benefits, serious side effects have often been encountered in clinical practice. Several case reports are found in which Liver toxicity or more commonly Drug Induced Liver Injury (DILI) has been encountered with the uses of anti-TNF alpha medications. However, a serologic and histopathologic evidence of Severe Autoimmune Hepatitis has rarely been reported with the drug. Here we discuss an autoimmune phenomenon induced while treating an immune mediated condition where the remedy appears to be worse than the disease.

A 34-year-old male with history of active perianal Crohn's disease who had been undergoing treatment with Infliximab presented to the emergency room with fatigue, severe weakness and dehydration. He was found to have severe hyperglycemia without ketoacidosis with markedly elevated liver enzymes. Patient had failed initial therapy for Crohn's disease and was started on Infliximab 6 months ago. He had been having mild elevation of liver enzymes since the initiation of the drug which was believed to be drug induced liver injury (DILI) however the therapy was continued as 'benefit outweighs the risk'. Upon admission to the hospital his LFTs were found to be 6 times the upper limit of normal. Acute hepatitis workup revealed no Viral hepatitis, normal acetaminophen levels and unremarkable ultrasound of the liver. An autoimmune workup revealed positive ANA, positive Anti-histone and Anti-smooth muscle antibodies. A subsequent liver biopsy characteristically showed prominent interface hepatitis consistent with severe form of AIH. Infliximab was discontinued, and patient's liver enzymes returned to the pretreatment levels in 8 weeks. A distal colectomy with colostomy for continued management of the Fistulous Crohn's disease was proposed.

AIH should be considered in any patient with unexplained elevated serum aminotransferases particularly if under treatment with Infliximab or any anti-TNF alpha agents. An early diagnosis and appropriate therapy can be of great value in suppressing disease activity. Untreated AIH universally leads to cirrhosis and its complications, including death, and there is a low but significant incidence of hepatocellular carcinoma. Establishment of correct diagnosis in a timely fashion may promote remission, both clinically and biochemically which is achieved by discontinuation of the drug.

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SARCOIDOSIS OF THE SPINAL CORD: A TALE OF A SEEMINGLY INNOCUOUS FALL

Rasik Dhakal MD, Erum Qureshi MD, Marc Shiffman MD; MedStar Health Internal Medicine, Baltimore, MD

Sarcoidosis is a multisystem granulomatous disorder with a wide range of clinical presentation. Neurologic involvement occurs in about 5% of cases[1]. Sarcoidosis of the spinal cord is even rarer with an incidence estimated at 0.43%[2].

A 36-year-old African American man with no past medical history fell at work landing on his left torso. X-ray done at an urgent care facility ruled out rib fracture. Ten days later, he came to the ED due to persistent pain. X-ray revealed diffuse bilateral faint miliary pattern. CT scan showed innumerable nodules and diffuse miliary pattern in both lungs along with bilateral hilar and mediastinal lymphadenopathy. The patient denied fever, constitutional or cardio-pulmonary symptoms; however, he reported numbness in his left leg for about 6 months that started in the dorsum of the foot and gradually progressed up to mid-thigh. He also noted some weakness in his left foot, especially with dorsiflexion. Examination was significant for diminished sensation in C6-C8 and L4-S1 distribution on the left side. Strength was 4/5 in knee flexor/extensor and ankle flexors. He had brisk reflexes in left biceps tendon and in bilateral patellar and Achilles tendons.

MRI showed diffuse cord swelling from the lower margin of the medulla to the level of T2-T3 with irregular nodular enhancement at the level of C5-C6 with similar abnormal swelling noted within the conus medullaris. Thoracic cord below T2-T3 was spared. MRI brain revealed abnormal nodular enhancement involving the hypothalamus. CSF analysis was significant for elevated protein and was negative for malignant cells. HIV, TB, fungal and bacterial infection were ruled out. Flow cytometry and paraneoplastic Ab panel were negative. SPEP, ANA, ANCA and ACE were normal. EBUS guided biopsy of mediastinal lymph nodes demonstrated noncaseating granuloma. FDG-PET scan further corroborated the diagnosis of neurosarcoidosis. Patient was treated with a five-day course of IV methylprednisone which resulted in improvement in cord swelling and neurologic symptoms.

Spinal cord involvement as an initial clinical manifestation of sarcoidosis is extremely rare. Imaging findings in neurosarcoidosis may mimic inflammatory processes such as multiple sclerosis, ADEM or NMO or neoplastic process such as lymphoma or primary CNS tumor. FDG-PET scan has emerged as a valuable alternative to biopsy in cases of isolated spinal cord involvement without systemic involvement[3]. In the presence of mediastinal lymphadenopathy, bronchoscopy and lymph node biopsy remains a safe option for diagnosis. The response to high dose steroids is usually dramatic. For long-term maintenance therapy, immunomodulating drugs can be used as steroid-sparing agents.

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POST-OPERATIVE PULMONARY EMBOLISM: SUCCESSFUL THROMBOLYSIS DESPITE RELATIVE CONTRAINDICATION

Thrombolysis with tissue plasminogen activator (tPA) is a potentially life-saving medical treatment for acute thrombotic events, but with possibly devastating adverse effects including intracranial hemorrhage and GI bleed. Thus significant effort has been made to establish clear criteria and contraindications for tPA since its approval by the FDA in 1996.

Case Presentation

A 75 year-old Caucasian man with no reported past medical history presented with perforated bowel and received emergent right colon resection and abscess drainage, after which he began thrombosis prophylaxis with sequential compression devices. On post-operative days (POD) 0 and 1 he also received prophylactic subcutaneous heparin, which was discontinued due to bloody stool in colostomy bag. His recovery was complicated by atrial fibrillation on POD 3 managed medically without anticoagulation, as well as atelectasis and pleural effusion. On POD 8 he restarted subcutaneous heparin, on POD 9 he had increasing oxygen requirements, and on POD 10 he further desaturated with hypotension to 72/52. CT angiogram (performed before acute decompensation) revealed large bilateral PE. The patient was intubated and given tPA followed by heparin infusion, with stabilization and gradual recovery. On POD 17, CT head was obtained for headache and showed subacute infarction, not seen on admission CT head. The patient had no focal neurologic symptoms at any time.

Discussion

This patient had two relative contraindications to tPA: recent major surgery (risk of bleed at surgical site), and age 75 (increased risk of intracranial bleed). However, given his acute hemodynamic instability the decision was made consistent with guidelines to administer tPA. Subsequent CT and MRI showed a subacute stroke with hemorrhagic component, but could not elucidate its exact timing or initial etiology (ischemic vs hemorrhagic). The stroke could feasibly have resulted from one or both of the atrial fibrillation and tPA.

Conclusion

PE with hypotension is a potentially fatal medical emergency that is most swiftly treated with tPA. This case illustrates the tenuous balance of risk and benefit in the presence of relative contraindications, and ultimately lends support to guidelines to consider tPA for cases of PE with hypotension.

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A CASE OF STRONGYLOIDES STERCORALIS SUPERINFECTION TREATED WITH VETERINARY IVERMECTIN PREPARATION

Shyam Kolangara MBBS[1], James Ladd MD[1], Jeremy Gradon MD[1]
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Introduction: Strongyloides stercoralis is a parasitic infection endemic to tropical countries, usually affecting the immigrant population in the United States. The cycle of autoinfection permits its presence for decades in an immunocompetent host with only minor symptoms. However, when the host becomes immunocompromised, such as in the event of a severe illness, a disseminated disease or hyperinfection syndrome can develop that often proves to be fatal.

Case presentation: A 77 year old man from Trinidad and Tobago presented with nausea, vomiting, poor appetite, abdominal pain and altered mental status. He also noted coffee ground emesis and melena. On examination, he was cachectic with marked epigastric tenderness and decreased bowel sounds. Patient's mental status deteriorated upon admission and he soon became unresponsive and hypotensive, which prompted a transfer to the intensive care unit for intubation, mechanical ventilation and vasopressor support. An esophagogastroduodenoscopy was done and biopsy revealed the presence of Strongyloides stercoralis. Albendazole and oral ivermectin were initiated through a nasogastric tube, but given the intestinal ileus, absorption was questionable. Therefore, measures were taken to obtain a veterinary subcutaneous ivermectin formulation and a request was submitted to the Food and Drug Administration (FDA) for compassionate use. Following the FDA approval, oral preparation was discontinued, and the subcutaneous formulation was administered along with oral albendazole. A lumbar puncture was unrevealing, but the patient was given empiric meropenem for suspected concurrent gram-negative meningitis. Since the patient remained intubated for 21 days, a tracheostomy and percutaneous gastrostomy tube placement were performed. He was eventually weaned from ventilator and vasopressor support, and was subsequently transferred to the acute care floor.

Discussion: Critically ill patients infected with Strongyloides stercoralis can develop hyperinfection syndrome, which is dangerous and challenging to treat, especially if concomitant intestinal malabsorption is present. Since parenteral ivermectin is not approved in humans, an unorthodox approach may be needed with the use of a veterinary formulation of subcutaneous ivermectin, which will require FDA approval. Thus, when dealing with a patient population at risk for Strongyloides infection, it is prudent to have different formulations of antiparasitic agents readily available and seek early FDA approval for the use of veterinary preparations.

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RIVAROXABAN INDUCED HEMOPERICARDIUM

Introduction: Rivaroxaban is a direct oral anticoagulant with a favorable safety profile when compared to warfarin in respect to bleeding. During postmarketing surveillance intracranial and retroperitoneal bleeds have been reported; however, hemopericardium has not been frequently reported. We present a case series of spontaneous hemopericardium associated with rivaroxaban.

Case 1: A 66-year-old African American male with venous thrombo-embolism (VTE) 6 mon before presentation,on rivaroxaban, presented with pleuritic chest pain for 2 weeks. Patient had undergone cardiac catheterization 2 weeks prior due to chest pain which revealed clean coronaries. Physical examination was significant for fever, tachycardia, moderate respiratory distress, elevated JVP and pulsus paradoxus. Laboratory investigations revealed leukocytosis, elevated ESR/CRP and elevated creatinine (2.1mg/dl). Echocardiography revealed a large pericardial effusion with evidence of tamponade physiology. 350 mL of hemorrhagic fluid were drained on pericardiocentesis.

Case 2: A 65-year-old Ghanian female with non-ischemic cardiomyopathy (EF 25%) and atrial fibrillation (AF) on rivaroxaban presented with intermittent chest pain and dyspnea for 2 weeks. Her physical examination was unremarkable except for irregularly irregular pulse. Laboratory investigations were unremarkable except for elevated BNP (1570 pg/ml). Echocardiography revealed a large pericardial effusion without evidence of tamponade physiology. Pericardiocentesis yielded 1100 mL of hemorrhagic fluid.

Case 3: A 77-year-old female with coronary artery disease (CAD), on dual antiplatelet therapy, and AF on rivaroxaban presented with worsening dyspnea for few days. On examination she was found to be hypotensive and in moderate respiratory distress. Laboratory findings were notable for elevated creatinine (2.2mg/dl). Echocardiography revealed a large pericardial effusion with evidenced of tamponade physiology. Emergent pericardiocentesis revealed 650 mL of hemorrhagic fluid.

Discussion: Hemopericardium is a rare but emerging and serious life threatening complication of direct oral anticoagulant therapy. Predisposing factors include impaired kidney function, concomitant use of antiplatelet agents, herbal supplements, and CYP3A4 inhibitors as these have been demonstrated to affect its metabolism and clearance. In this case series, rivaroxaban is thought to have been the causative agent, potentiated by the patients' underlying diseases and/or medications. This case series suggests that rivaroxaban- induced hemopericardium might not be as rare as initially thought.

Conclusion: Clinicians should be aware of the possibility of such life-threatening adverse events in patients taking rivaroxaban and should consider it in their differential diagnosis.

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A GRAVE MATTER: AUTOIMMUNE THYROID DISEASE FOLLOWING IMMUNE RECONSTITUTION. **O'Malley K, MD. The University of Maryland School of Medicine and VA Medical Center, Baltimore, MD.**

The development of Graves' disease following the initiation of anti-retroviral therapy in individuals with Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) is a rare phenomenon. It can be observed following CD4 repopulation and is described as an Immune Reconstitution Inflammatory Syndrome (IRIS).

A 62 year-old-man with HIVand AIDS presented to the emergency department with chest pain and palpitations. He appeared malnourished with poor hygiene. He had an irregularly irregular rhythm on auscultation. He had no proptosis, goiter, thyroid tenderness, or palpate thyroid nodule. Electrocardiogram demonstrated atrial fibrillation with rapid ventricular response. He was given IV Diltiazem with conversion to sinus bradycardia on repeat electrocardiogram.

On further history, over a year ago the patient had a CD4 T-cell count of 54 cells/μL and HIV RNA level 140,000 copies/mL. He was started on anti-retroviral therapy with Abacavir, Dolutegravir and Lamivudine (Triumeq). Seven months later he demonstrated immunologic and virologic response with CD4 T-cell count of 394 cells/μL and undetectable HIV RNA level. He was also noted to have evidence of hyperthyroidism with TSH <0.02 mIU/L and free thyroxine (T4) 3.13 ng/dL. At that time he was lost to follow-up reportedly due to a relapse of alcohol use disorder. Previously thyroid function testing was normal.

He had laboratory testing revealing thyroid stimulating hormone <0.02 mIU/L, total triiodothyronine (T3) 210 ng/dL, free T4 2.0 ng/dL, thyroid peroxidase antibody level 26.4 IU/mL and thyroid stimulating immunoglobulin level 306% above basal activity. Ultrasound of the neck with doppler revealed thyroid parenchymal heterogeneity with mild increased vascularity and no focal lesions and nuclear medicine radioactive iodide uptake scan demonstrated homogeneously increased tracer activity in the thyroid gland. He was diagnosed with Graves' disease thought to be triggered by IRIS.

The development of Graves' disease following immune reconstitution is a rare complication. Clinicians who care for patients with HIV must be vigilant for consideration of this phenomena.

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A Novel Use of Intrapleural t-PA/DNase Therapy for Loculated Chylothorax

Chylothorax is frequently encountered in clinical practice, but loculated chylothorax is rare and optimal management remains unclear. We describe the first known case of loculated chylothorax successfully treated with intrapleural t-PA and DNAse.

A 37-year old man with history of well-controlled HIV (CD4 603, undetectable viral load at admission), recurrent tricuspid valve endocarditis with bio-prosthetic valve replacement 3 years prior to admission, and gunshot wound 17 years prior presented with shortness of breath. He was normotensive and afebrile, with oxygen saturations of 88% on non-rebreather mask. Lung sounds were diminished at the bases bilaterally without wheezing. Initial laboratory findings showed a normal white blood cell count. CT scan of the chest demonstrated large, loculated pleural collections bilaterally, while bedside thoracic ultrasound revealed septations and fibrin stranding within the fluid collections. Broad-spectrum antibiotics were started empirically for presumed empyema thoracis and a 14-French pigtail catheter was placed on the left side with subsequent drainage of yellow, cloudy fluid. Pleural fluid analysis revealed an exudate with no organisms seen on gram stain, WBC count of 944 per mcL (94% lymphocytes) and a triglyceride count of 310 mg/dL. Fluid culture was negative. On day 2, pleural fluid drainage was minimal, but repeat bedside ultrasound showed persistent septated fluid pockets. Deoxyribonuclease (5 mg) and t-PA (10 mg) were instilled into the pleural space twice daily for four days, with marked increase in fluid drainage and dramatic improvement in the patient's dyspnea.. Prior to discharge, a surgical pleural biopsy was considered for definitive diagnosis. Due to concern about his comorbidities, however, outpatient thoracic imaging and pulmonary follow-up was favored.

While intrapleural fibrinolytic therapy is well-described for empyema, its use in chylothorax has been reported only once previously (streptokinase). To our knowledge, this is the first description of t-PA and DNase for treatment of non-draining loculated chylothorax. Intrapleural fibrinolytic therapy should be considered as a therapeutic option in this clinical scenario, although further study is required to determine safety and effectiveness.

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WHEN MYOSITIS ATTACKS THE LUNG

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Dermatomyositis (DM) is a relatively rare rheumatologic disorder, typically characterized by symmetric proximal muscle weakness and a variety of distinctive cutaneous findings. However, DM is also a heterogenous disorder that can involve many different organ systems, with a spectrum of subtypes and manifestations.

A 50 year-old Filipino woman presented with complaints of tingling in her hands and a red rash on her fingers. Hand radiographs were normal, but over the next month she developed a chronic dry cough accompanied by fevers, night sweats, facial erythema, hand swelling, muscle aches, oral ulcerations, and weight loss. A biopsy of the hand rash showed non-specific lichenoid dermatitis with papillary dermal edema, and a basic infectious workup was negative. Focused physical exam was notable for distinct weakness in the bilateral hip flexor and hamstring muscles. Initial laboratory investigations revealed mild, non-specific elevations in the ESR, CRP, AST, ALT, and CK. Aldolase was normal, and a myositis panel with anti-Jo-1 and anti-Mi2 antibodies was ordered. MRI of the thighs and high-resolution chest CT scan showed diffuse, proximal, bilateral myositis and pulmonary interstitial thickening. Interval laboratory evaluation returned negative for rheumatoid factor, anti-CCP, ANA, anti-dsDNA, anti-Smith, anti-RNP, anti-SSA/SSB, and anti-Scl70 antibodies. As the patient's condition deteriorated, she was given an intravenous corticosteroid pulse followed by high-dose oral prednisone. DM with anti-synthetase syndrome was considered, however her myositis panel returned negative. Serial pulmonary function testing revealed a decline in her respiratory status despite high-dose steroids. Given her overall clinical picture, an anti-MDA-5 antibody was requested and returned positive. She was diagnosed with Clinically Amyopathic Dermatomyositis (CADM) associated with interstitial lung disease.

This case describes a rare, severe variant of dermatomyositis. CADM with MDA-5 positivity is not well studied, and carries a poor prognosis due to association with severe, rapidly progressive pulmonary disease. No formal treatment guideline yet exists for this syndrome, however novel therapies such as rituximab may have a role. Further case descriptions such as this may help in defining an approach to faster diagnosis and increasingly effective management.