Mycophenolate Mofetil (Cellcept) Induced Pneumonitis:  
Case Report and Review of Literature

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LEARNING OBJECTIVES
• Recognize the clinical features of medication-induced pneumonitis
• Assess for the use of anti-inflammatories masking early symptom presentation

ABSTRACT
Mycophenolate is used to treat several disease conditions. Several side effects have been reported in several reported cases; however, a few other side effects have been underreported, for example, post-transplant pneumonitis. This case demonstrates suspected mycophenolate-associated pneumonitis, which was masked by the concurrent immune-modulatory drugs that the patients were taking. The pneumonitis became evident after the withdrawal of the immune drugs. This seldomly reported pneumonitis and mycophenolate association calls for further vigilance and a high index of suspicion by physicians when pneumonitis develops in patients taking this valuable medication.

Keywords: mycophenolate; pneumonitis; medication

INTRODUCTION
Mycophenolate Mofetil (Cellcept) has been reported to cause a vast number of adverse effects, including reactivation of latent TB, increased susceptibility to recurrent infections, sepsis, increased risk of lymphoma, leukopenia, pulmonary hypertension, etc. (Hosohata et al., 2018, Behrend M, 2001). The adverse effect of Mycophenolate Mofetil (Cellcept), least spoken about, plausibly because of its rarity, is drug-induced pneumonitis. We report a case of pneumonitis associated with Mycophenolate use after kidney transplantation.

CASE
A 45-year-old African American female with a history of hypertension and end-stage renal disease presented to the clinic status-post-living-donor renal transplant for a follow-up visit. During this visit, she reported nasal congestion, shortness of breath on exertion, cough, and wheezing. She denied chest pain, palpitations, fevers, or chills.

The patient was started on Mycophenolate Mofetil (Cellcept) three weeks earlier post-surgically and denied having these symptoms prior to starting medical therapy. Her other medications included Bactrim and tapering doses of both Tacrolimus (Prograf) and Prednisone, which were also started post-surgically. Her baseline medications included Albuterol sulfate as needed for seasonal allergies and Lisinopril. Immunizations were up to date, including the pneumococcal and influenza vaccine received earlier in the year.

On physical examination, there were crackles, “pops, and squeaks” on lung auscultation with accompanied wheezing. Cardiologic, abdominal, and neurologic examinations were all unremarkable.

Pulmonary function tests, 2D Echo, and high-resolution CT scan of the chest without contrast were ordered. The chest CT revealed; restrictive lung pattern with moderately reduced DLCO, subtle bilateral ground-glass mosaic attenuation with an incidental sub-centimeter lung nodule in the right upper lobe, the ECHO showed; mild pericardial effusion and an ejection fraction of 55%. After a review of patients presenting symptoms, clinical signs, and CT scan imaging features, a diagnosis of pneumonitis was made with mycophenolate highly suspected as a causative factor. The patient was started on Fluticasone-Salmeterol and Mycophenolate was discontinued. During the subsequent two-week clinic visit, she reported moderate relief of the pulmonary symptoms, which further supported the diagnosis. A six-month follow-up was recommended to monitor the sub-centimeter lung nodule for progression in size.

DISCUSSION
This patient was diagnosed with Mycophenolate mofetil (Cellcept) induced pneumonitis. The symptoms presenting three weeks after initiation of Mycophenolate and a tapering dose of prednisone indicate that the anti-inflammatory effect of prednisone blunted the pulmonary
effects of the medication. As the dose of prednisone was slowly tapered in the subsequent weeks, there was a paradoxical increase in the severity of this patient’s pulmonary symptoms.

Cases of Mycophenolate induced pneumonitis have been previously reported, but extensive clinical trials and research accessing its incidence are currently unreported. (Pocivalnik et al., 2013, Gross et al., 1997). Pneumonitis is a broad term that refers to inflammation of lung tissue. Technically, pneumonia is caused by a series of pneumonitis caused by infections. Pneumonitis, however, is typically used to refer to the noninfectious etiology of lung inflammation. Difficulty breathing, commonly accompanied by a nonproductive cough, is a frequent symptom of pneumonitis. Other common symptoms are fatigue, cough, loss of appetite, and weight loss. Treatment focuses on avoiding irritants and reducing inflammatory triggers like discontinuation of offending medications and chemicals.

Development of various interstitial lung diseases in patients on Mycophenolate is another rarely reported side effect, with only a few isolated case reports available. (Abelleira et al., 2018, Reynolds et al., 2008). Medication-induced pneumonitis has been reported to be caused by various chemotherapeutic agents, antibiotics, immunosuppressive agents, and anti-arrhythmic medications, especially amiodarone.

Medication-induced pneumonitis is a diagnosis of exclusion made after other differential diagnoses have been screened for and excluded. Patients normally improve after medication cessation, reduction of offending medication dosage, or a trial of glucocorticoid therapy.

CONCLUSION
Mycophenolate induced pneumonitis symptoms may present late in some patients due to simultaneous use of anti-inflammatory agents like prednisone, that mask symptoms and delay clinical presentation. Patients taking Mycophenolate should be closely monitored for symptoms of pneumonitis after drug initiation. Once symptoms are identified, dosage should be reduced or stopped to avoid further deterioration of lung function.

CONFLICTS OF INTEREST
None declared

AUTHOR CONTRIBUTIONS
Ibor Udoete, MD: assisted with patient care postsurgically during follow-up clinic visits and wrote the manuscript. Ngozika Orjioke MD, FCCP: provided postsurgical pulmonary clearance for the patient, Okelu Edwards Okobi, MD, M.Sc: article review and summary, Chinwendu Angel Onuegbu, MD: article review, referencing, and summary.

ETHICAL APPROVAL
Consent was gained from the patient on whom this case is based.

REFERENCES