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Case of Pneumocystis Pneumonia 6 Years Post-Renal Transplant while on Everolimus

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Learning Objectives

- Presentation of *Pneumocystis jirovecii* pneumonia >1 year post-transplant
- Role of immunosuppression and prophylaxis in post-transplant patient

Introduction

- *Pneumocystis jirovecii* pneumonia (PCP) is a rare cause of pulmonary infection that primarily affects the immunosuppressed (1).
- Populations at risk include: HIV patients with low CD4 counts, hematopoietic stem cell and solid organ transplant patients, cancer patients, and patients with long-term glucocorticoid or immunomodulator use
- Continued debate on best duration for prophylactic therapy. Currently is center dependent and tends to range between 6-12 months (2).
- Prophylactic regimen: First line is trimethoprim/sulfamethoxazole (TMP/SMX), for those with sulfa allergy use atovaquone

Case Description

- **Our patient**: Ms. P is a 73 year old female who presented to the Emergency Department with 2 weeks of SOB and generalized weakness
- She received an iron transfusion 2 days prior to presentation for newly discovered iron deficiency anemia but had no symptomatic relief.
- **Past Medical History**: Significant for Chronic Kidney Disease. First kidney transplant in 1996 was from sister. Due to signs of rejection, she received second kidney in 2012 from daughter. Also, she has a left lateral neck lesion newly discovered to be squamous cell carcinoma.
- **ED course**:
  - IV fluids
  - CXR: no acute process
  - CT chest: no PE, but evidence of emphysematous change
- She continued to require oxygen and was admitted to the general medical unit
- On **arrival to the floor** she was tachypneic and had significant wheezing. She was started on bronchodilators, glucocorticoids, and empiric antibiotics.

Case Description

- Patient's current **immunosuppresion regimen**: tacrolimus 1 mg q12, prednisone 5mg qDay, and newly substituted everolimus 0.75 mg q12 for mycophenolate mofetil. Change occurred due to recent skin cancer diagnosis.
- Concern for everolimus drug-induced pneumonitis versus infectious process led to holding everolimus and starting infectious work up
- Viral respiratory panel from nasal swab came back negative, sputum sample for *Pneumocystis jirovecii* negative, CMV DNA not detected. Proceeded with Bronchoalveolar Lavage a week later as patient continued to experience hypoxia requiring oxygen.
- Repeat CT showed ground-glass opacities with some nodularity.
- **Prior to discharge**: continued hypoxia requiring 4L NC. Left on prednisone taper and off of everolimus with follow up scheduled at Infectious Disease (ID) Clinic and Transplant Clinic.
- At **ID clinic**, Ms. P's lab results were all in and led to the final diagnosis of *Pneumocystis jirovecii*. She was started on TMP/SMX q8 PO for 3 weeks
- At **3 week follow up** appointment to ID clinic, patient reported symptomatic improvement with normal oxygen saturations on room air. She was instructed to continue TMP/SMX three times per week for 3 months as prophylaxis against PCP.
- **Immunosuppresion regimen set by Transplant** to tacrolimus 0.5 mg qDay and prednisone 5 mg qDay.

Images

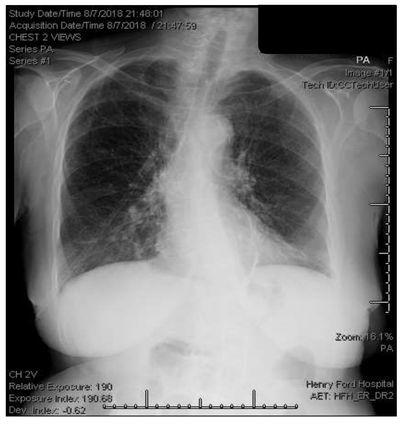

Figure 1. Ms. P's CXR in ED which showed no consolidation, pleural effusion, or vascular congestion

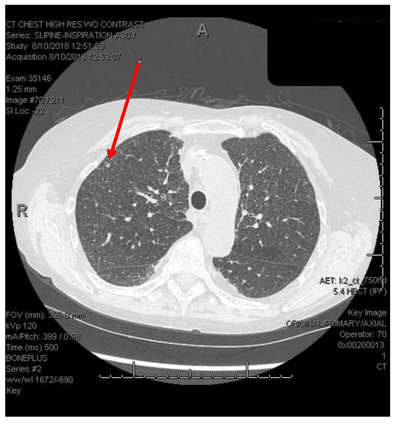

Figure 2. Ms. P's CT prior to discharge which shows a node in right upper lobe as well as scattered ground glass and nodular opacities

Labs

Labs Upon Admission 8/8	
WBC	11.9 (↑)
Neutrophil %	89
Lymphocyte %	4
Monocyte %	4
Eosinophil %	3
Basophil %	0
ANC	10.59 (↑)
Hgb	12
Platelet	319

Labs Upon Discharge 8/17	
WBC	5.9
Neutrophil %	87
Lymphocyte %	6
Monocyte %	7
Eosinophil %	0
Basophil %	0
ANC	5.2
Hgb	11.2 (↓)
Platelet	303

Labs at ID Clinic Visit 8/23	
Bronchoalveolar Lavage for PCP	DETECTED (!)
Respiratory Culture	No growth x 2 days

Conclusion

- Typical radiographic findings for PCP are **diffuse bilateral, interstitial infiltrates**. When x-ray plain film shows no abnormalities, CT may show ground glass opacities or cystic lesions. Findings for everolimus pneumonitis are similar with ground glass opacities, focal consolidations, nodular opacities, reticulation (1).
- Both PCP and everolimus drug-induced pneumonitis tend to present with nonspecific symptoms: dyspnea, dry cough, fever, fatigue, **hypoxia**, and hemoptysis (3)
- Patients not treated with prophylaxis are **most vulnerable during the first 6 months after transplant** (4). With the incorporation of PCP prophylaxis, incidence of PCP within the first year is quite rare**.** Greater immunosuppression increases risk of infection.
- Clinical suspicion of PCP is based on symptoms and radiographic changes. It is then confirmed with a positive PCP PCR assay. Of note, co-infection with CMV may increase risk of PCP infection (2).
- Although rare, this case demonstrates PCP can occur >1 year post-transplant.

References

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(3) Willemsen AE, Grutters JC, Gerritsen WR, Erp NPV, Herpen CMV, Tol J. mTOR inhibitor-induced interstitial lung disease in cancer patients: Comprehensive review and a practical management algorithm. *International Journal of Cancer*. 2015;138(10):2312-2321. doi:10.1002/ijc.29887.
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