Case History

A 46-year-old man with a medical history significant for cadaveric renal transplant one year ago was evaluated in the emergency department for recurrent fevers and chills, progressive shortness of breath with exertion, increasing fatigue and a persistent non-productive cough. He stated that these symptoms had started a few weeks prior to arrival. He denied orthopnea, paroxysmal nocturnal dyspnea, chest pain or lower extremity edema. He had no night sweats, unintentional weight loss, hemoptysis, diarrhea, abdominal pain or melena. He also denied headaches, rashes, myalgias or arthralgias.

One week prior to presentation, the patient was hospitalized for similar complaints. A chest radiograph done during that admission was significant for right middle lobe and right lower lobe pneumonia and the patient underwent bronchoscopy and bronchoalveolar lavage. Results from the bronchoscopy were pending at the time of discharge three days later but the patient was discharged to home on levofloxacin and fluconazole for treatment of pneumonia. He did state that he got minimal relief of his symptoms while on antibiotics. He was also directed to the renal transplant clinic for close follow-up of his condition.

His medical history was significant for long-standing hypertension and end-stage renal disease. He had a renal biopsy in 1995 and was diagnosed with focal segmental glomerulonephritis. He began hemodialysis shortly thereafter. He was evaluated for kidney transplant in 2004. Pertinent pre-transplant evaluation was significant for the following: HIV antibody negative, CMV IgG negative, HBsAg negative, HBsAb negative, HBcAb negative; Hep C Ab, Hep C PCR negative; RPR – nonreactive; EBV Ab negative; a cardiac persantine stress test was also performed that showed global hypokinesis with an left ventricular ejection fraction of 26%. The stress test was negative for any reversible perfusion defects.

The patient underwent cadaveric renal transplant in 2005, one year prior to current admission. His initial immunosuppressive regimen consisted of prednisone, mycophenolate and cyclosporine. His initial post-operative course was complicated by significant lymphatic drainage from a left groin wound which was treated with incision and drainage. The patient recovered from this wound without further complication. He underwent a biopsy of his transplanted kidney two months later that was significant for some changes related to chronic rejection but did not show any changes related to acute rejection. At that point, the cyclosporine was discontinued and the immunosuppressive regimen was modified to prednisone, cellcept and sirolimus.

Past Medical History:
- End-stage renal disease due to focal segmental glomerulonephritis
- Cadaveric renal transplant 1 year ago
- Open heart surgery in 1975 for septal repair of the heart
- Long-standing hypertension
- Diabetes mellitus
- MRSA wound infection

Medications:
- labetalol 400mg twice daily
- doxazosin 2mg at bedtime
- minoxidil 7.5mg twice daily
- clonidine 0.2mg twice daily
- nifedipine XL 120mg daily
- isosorbide dinitrate 10mg three times a day
- glyburide 5mg daily
- omeprazole 40mg daily
- mycophenolate mofetil 1gm twice daily
- prednisone 10mg daily
- sirolimus 5 mg twice a day

Social History:
- Unmarried, lives with his girlfriend and children in the city of Richmond
- Works part-time as a painter
- Education – ninth grade
- Recently quit tobacco
- Denies recent alcohol or recent recreational drug use; admits to a past history of heavy alcohol use and cocaine use
- No sick contacts reported
- No recent travel reported
- Denies HIV risk factors

Physical Exam

General:	Generally healthy appearing, in mild respiratory distress
Vital signs:	Blood pressure 113/64 mm Hg, Pulse 53/minute and regular, Respiratory rate 22/min, Temperature 97.2° F, 90% oxygen saturation on room air
HEENT:	No scleral icterus or pallor noted; good dentition; no naso-pharyngeal lesions; no meningismus noted
Neck:	No evidence of jugular venous distention; no carotid bruits; no lymphadenopathy
CV:	Bradycardic with regular rhythm; normal S1 and S2; III/VI holosystolic murmur best heard at the apex
Lungs:	Increased respiratory effort; good air movement, bilateral rhonchi R>L

Abdomen: soft abdomen; non-tender to palpation; no masses, bruits or organomegaly
Extremities: Good peripheral pulses; no peripheral lymphadenopathy, edema, cyanosis or clubbing.
Neurologic: Alert and oriented to person, time and place; Cranial nerves intact, 5/5 upper and lower extremity motor strength; 2+ biceps and patellar DTR's

Laboratory Studies

Sodium 140 mEq/L, Potassium 5.4mEq/L, Chloride 110 mEq/L, Bicarbonate 23 mEq/L, BUN 48 mg/dL, Creatinine 3.04 mg/dL (baseline 2.5-2.8 mg/dL)

WBC 5.7 x 10^9/L, Hemoglobin 9.6 g/dL, Platelets 251 x 10^9/L

AST 33 U/L, ALT 41 U/L, AP 238 U/L, Total bilirubin 0.3 mg/dL

Arterial Blood gas analysis on room air: pH 7.43, pCO2 38, PO2 68

Hospital Course

The patient was admitted to the internal medicine service and started on empiric broad-spectrum anti-microbial and anti-fungal coverage. Despite the intravenous antibiotics, the patient showed minimal improvement of his symptoms. Blood and urine cultures were negative. Serum CMV antigen and urine Legionella antigen were negative. The sirolimus level was 11.2 ng/mL (5-15ng/mL).

A chest CT scan without contrast was then performed and revealed extensive focal consolidation with demonstrable air bronchograms involving the vast majority of the right middle lobe with concomitant involvement of the superior segment of the right lower lobe and anterior basal segment of the right lower lobe. There was also surrounding diffuse groundglass opacities and numerous sub-centimeter pulmonary nodules in the right lung. The left lung was relatively uninvolved.

The bronchoscopy results from the previous admission were reviewed. The BAL cytology was significant for 35% lymphocytes, 50% macrophages, 15% PMN. Further cytologic examination of the fluid with stains and cultures were negative for malignant cells, bacteria, acid-fast bacilli, *Pneumocystis* and fungi.

A diagnostic procedure was then performed.

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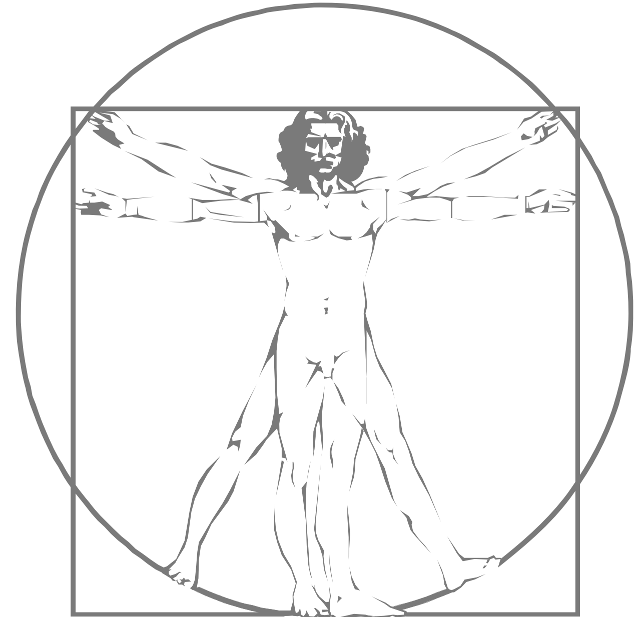
Protocol prepared by Venkat Ramachandran, MD

Department of Internal Medicine



Clinicopathologic Conference

November 2, 2006

A 46-year-old renal transplant patient with fevers and dyspnea

Discussant: Leonard Moses, MD
Associate Professor of Medicine, Department of Pulmonary and Critical Care Medicine

Radiologist: James Anthony Moore, MD
Department of Radiology

Pathologist: Margaret Grimes
Department of Pathology

Commentary: Eric Gibney, MD