CLINICAL VIGNETTE

Diagnosis of Disseminated *Mycobacterium Chelonae* in a Renal Transplant Patient Presenting with Skin Rash and Arthralgias

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Case Report

A 59-year-old male with past medical history notable for end stage renal disease (ESRD) post deceased donor kidney transplant (DDKT) 10 months prior reported a sudden onset of multiple daily episodes of watery, non-bloody diarrhea unrelated to food intake 7 weeks ago. He denied abdominal pain, nausea, vomiting, decreased appetite, fevers, or chills. However, he reported a 10 lbs. weight loss since the onset of illness. Five weeks after developing diarrhea, and two weeks prior to presentation, the patient developed new onset bilateral knee and hand pain with a diffuse non-pruritic rash. His arthritis did not correlate with time of day or activity and denied having these symptoms in the past. His skin lesions initially developed as pustules before progressing to a necrotic center.

In addition to ESRD and DDRT, the patient's medical history included diabetes mellitus type 2, coronary artery disease, peripheral artery disease, hypertension, hyperlipidemia, and gout. In regards to his immunosuppression, the patient was induced with basiliximab and maintained on a combination of prednisone, tacrolimus, and mycophenolate mofetil. His other medications included insulin, nifedipine, atenolol, clonidine, bactrim, and folate. He was originally from Mexico and denied recent travel, tuberculosis risk exposure, outdoor exposure, gardening, or significant animal exposure. Patient denied tobacco, alcohol, or recreational drug use.

Physical examination revealed a well-developed, well-nourished male in no acute distress. Vitals signs were as follows: temperature 36.4 Celsius, pulse 78, blood pressure 129/76, respiratory rate 16, and oxygen saturation of 97% on room air. Other pertinent points of his exam included a non-tender, non-distended abdomen without organomegaly. Musculoskeletal exam revealed bilateral knee effusions without erythema or warmth. Skin exam was remarkable for multiple subcentimeter nodules on all four extremities with central necrosis without erythema, warmth, fluctuance, or purulence (Figure 1). The remainder of his exam was unremarkable.

Initial laboratory workup was remarkable for a WBC 12.5 (84% neutrophils), serum sodium 113, creatinine 1.4 mg/dL, and glucose of 253. Tacrolimus morning level was 32.0 ng/mL. Notablly, the patient had a history of supratherapeutic tacrolimus levels. Stool studies were sent and were negative for the following: bacterial culture, *Clostridium difficle* toxin, Giardia, ova and parasites (including *Coccicodies* and Cryptococcus). Cytomegalovirus (CMV) polymerase chain reaction (PCR) was negative. The patient also underwent arthrocentesis of the knee revealed yellow, viscous fluid with 236 white blood cells (WBC) without crystals, negative gram stain. The patient was admitted to the intensive care unit for hyponatremia management.

On hospital day 5, fluid aspirated from the left knee became positive for acid fast bacilli (AFB), a subsequent skin biopsy also revealed acid fast bacilli. The patient was empirically started on treatment for rapid growing mycobacterium with cefoxitin, moxifloxacin, and clarithromycin. Culture identification revealed *Mycobacterium chelonae*, at which point antimicrobial therapy was transitioned to imipenem, linezolid, and clarithromycin based on isolate sensitivities. *M. chelonae* was also isolated from acid fast blood cultures, and urine was positive for AFB on stains but not culture. Acid fast organisms were not found in the stool. Further workup revealed osteomyelitis of the left 4th finger (Figure 2) and right knee confirming significant disseminated disease. The patient was discharged to complete a prolonged course of antimicrobial therapy with imipenem, linezolid, and clarithromycin and transplant infectious disease follow up.

Discussion

Infections commonly occur in patients following renal transplantation and represent a major cause of morbidity and mortality. Several factors increase the risk for infection in the transplant patient[1,2] including: the level of immunosuppression, environmental exposure to pathogens in community or hospital settings, presence of immunomodulating infections such as human immunodeficiency virus and cytomegalovirus, metabolic abnormalities such as hyperglycemia, and presence of indwelling foreign bodies.

Traditionally, the approach to infections post-transplantation has been divided into three periods: post-operative (first month), early (one month to one year), and late (greater than one year).[2] Wound infections, urinary tract infections, and donor-transmitted agents are the predominant focus in the first month of transplantation. The early post-transplant period is notable for high levels of cumulative immunosuppression and as a result the occurrence of atypical infectious agents and reactivation of latent diseases (eg, tuberculosis, CMV, BK virus). Community acquired infectious agents are most common in the late period when immunosuppression can be minimized in the kidney transplant patient. The patient presented falls into the early post-transplant period and has a history of significant immunosuppression as noted by the tacrolimus trough of 32 ng/mL (goal 6-10 ng/mL). An atypical infection or reactivation should be suspected in this patient. Of note, his tacrolimus level may have been elevated by the presence of diarrhea, which inhibits enteric cytochrome P450, raising the serum levels of tacrolimus.

Nontuberculous mycobacteria (NTM) are a diverse group of organisms with greater than 100 different types speciated[3] and are commonly found in the environment including soil and water. They can be divided into two general categories: slow-growing mycobacteria (typically growing in culture after 14 days) and rapidly-growing mycobacteria (typically growing in culture within 7 days).[4] Slow-growing NTM include *M. avium intracellulare* (MAI), *M. kansasii,* and *M. marinum*, while rapid-growing NTM include *M. chelonae*, *M. fortuitum,* and *M. abscessus*. The distinction between slow-growing and rapid-growing NTM is important for the choice of empiric antimicrobial therapy. Although rare in the general population, immunocompromised patients with impaired cellular immunity have an increased risk for NTM infections. Solid organ transplant patients frequently are on maintenance therapy with calcineuron inhibitors and lymphocyte depleting agents to prevent organ rejection, putting them at higher risk for infections. Induction with lymphocyte depleting monoclonal antibodies including basiliximab and alemtuzumab have been associated with an increased risk of NTM infection.[5]
NTM as opportunistic infections in renal transplantation have an incidence of 0.16–0.38%.[6] Although this indicates that NTM is relatively uncommon in renal transplantation patients, it is important to include them as part of the differential especially in patients with higher levels of immunosuppression. Compared to lung and heart transplant patients, renal transplant patients may have a higher incidence of NTM infections.[4]

This case highlights several important points regarding recognizing this uncommon but important infection in transplant patients. In renal transplant patients, infectious skin rashes are most commonly due to viruses, followed by fungal infections and bacterial infections according to one series.[7] While appropriate workup should be done to rule out these causes, atypical infections should also be considered in patients with significant immunosuppression and unusual dermatological findings as seen in this case. One of the presenting symptoms of *Mycobacterium chelonae* in our case was a diffuse nodular rash, which is characteristic of M. chelonae infection.[8]

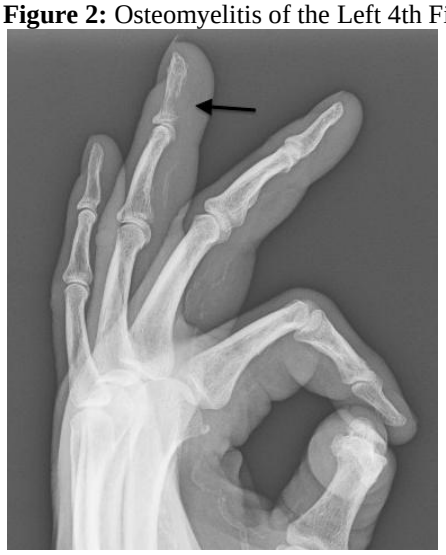
Septic arthritis is an important consideration in solid organ transplant in the setting of arthralgias. Septic arthritis in renal transplant patients generally present with synovial WBC of >30,000.[9] When our patient was initially evaluated, synovial fluid analysis revealed a WBC 236 consistent with a non-inflammatory picture. Bacterial, fungal, and viral studies returned negative, initially suggesting a non-infectious picture. However, NTM arthritis commonly presents with a bland synovial fluid analysis, emphasizing the importance of including NTM in the differential especially with suspected disseminated disease.[10]

After the diagnosis is made, it is important to thoroughly investigate for disseminated infection. Further workup done for our patient revealed multiple foci of disease including bacteremia, osteomyelitis, and urinary tract involvement. M. chelonae has been found to cause skin lesions, osteomyelitis, bacteremia, abdominal abscesses, and pericardial effusion in solid organ transplant recipients.[5,8,11,12] Echocardiogram in our patient did not show evidence of pericardial effusion, and CT imaging of the abdomen did not show evidence of intra-abdominal abscess or lymphadenopathy.

In our patient, markedly supratherapeutic tacrolimus levels documented on admission and months prior suggest prolonged over-immunosuppression that likely increased his risk for infection compared to the general transplant population. Maintaining patients within the narrow therapeutic window of immunosuppression is vital to minimize risk of infection and emphasizes the importance of patient education regarding close and consistent follow up.

Figure 1: Musculoskeletal Exam

Figure 2: Osteomyelitis of the Left 4th Finger



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