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Common things are common even in the uncommon patients: a case of rampant necrotizing sinusitis in a kidney transplant recipient

A. Dejman[1], L.A. Shimose[2], C. Sidani[3], W. Kupin[4], G. Guerra[4], L. Abbo[2]

[1]Nephrology, [2]Infectious Disease, [3]Radiology and Neurosurgery; Jackson Memorial Hospital, University of Miami, Miami, FL, USA
[4]Transplant Nephrology, Miami Transplant Institute, Miami, FL, USA

ABSTRACT:

Bacterial infections account for one of the most important causes of morbidity and mortality after solid organ transplantation. Though the timeline is not fixed, infections may follow a probable outline after transplant. However, being exposed to highly vigorous anti-rejection therapies increases the risk of invasive disease in this special patient population. It may alter the typical clinical presentation and the expected course, leading to misuse of unnecessary treatment regimens that further render antibiotic resistance and medication side effects and interactions. Conversely, common infections may occur mimicking those that are known to be life threatening. It is of difficult management and there must be a fine balance between appropriate antibiotic therapy and immunosuppression to avoid graft rejection. We present the case of a patient who became severely ill resulting from a necrotizing sinusitis initially with cavernous sinus involvement shortly after acute rejection therapy.

Keywords: Solid organ transplant, Immunosuppression, Necrotizing sinusitis, Cavernous sinus thrombosis.

INTRODUCTION

Kidney transplantation is the most common solid organ transplantation performed worldwide. It is cost-effective and associated with lower mortality compared to long term dialysis[1], providing patients with a better quality of life[2]. With time, the release of new immunosuppressive drugs, improvement of the standard of care and implementation of new protocols have increased graft survival[3]. Nevertheless, up to 6% of kidney transplant recipients experience a life-threatening complication that requires ICU admission, mainly in the late post-transplant period (≥6 months)[1]. Additionally, mortality of kidney transplant recipients is significantly higher than that of the general population[4]. This is a consequence of the cumulative long-term risk of post-transplant induction therapy and maintenance immunosuppression which predisposes patients to a higher incidence of infections, malignancies and drug toxicities[1].

The purpose of this case report is to review a life threatening infection caused by an increasingly common organism, emphasizing on the increased susceptibility of this patient population and the importance of the fine balance between immunosuppression and infections.

CASE PRESENTATION

A 68-year-old man with a history of End Stage Renal Disease (ESRD) secondary to Autosomal Dominant Polycystic Kidney Disease (ADPKD) had undergone a deceased donor kidney transplant 12 months prior to presentation. His post transplant course was complicated by acute allograft antibody-mediated rejection (AMR) rejection and mild T-cell mediated rejection (11 months post-transplantation). He underwent therapy with our standard AMR protocol of rituximab (375 mg/m^2) x 1 dose, four sessions of plasma exchange with immediate bortezomib sub-cutaneous injection and 4 doses of intravenous immune globulin (IVIG) 2 g every 72 hours. Maintenance immunosuppression regimen was changed from sirolimus to prograf (3 mg twice daily). Chronic steroids (prednisone 10 mg daily) and mycophenolate mofetil (540 mg twice daily) were continued. A week after being treated for rejection, the patient complained of fatigue, weakness and was noted to have a new vesicular rash on the right cheek and around the nose. The patient was empirically treated with valacyclovir.

Two weeks later, he presented to the emergency department with confusion, purulent nasal discharge,

Corresponding Author: Adriana Dejman, MD; e-mail: adriana.dejman@jhsmiami.org

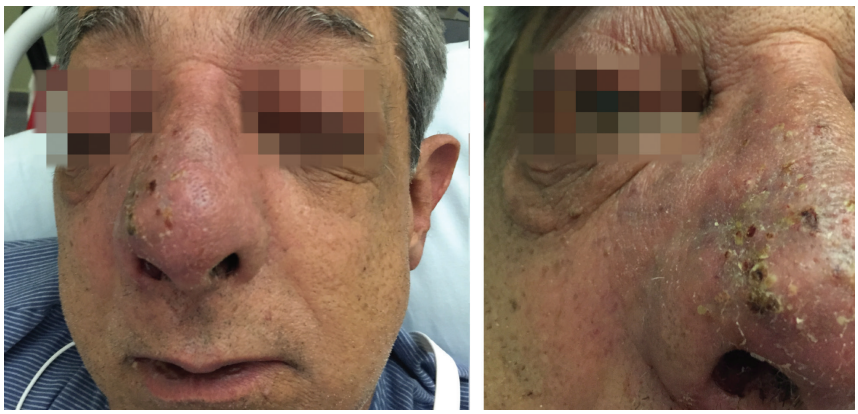

Figure 1. Deforming bilateral orbital edema, proptosis and decreased abduction and supraduction of the left eye with decreased corneal sensation.

deforming bilateral orbital edema, proptosis and decreased abduction and supraduction of the left eye with decreased corneal sensation (Figure 1). Ancillary data was pertinent for a White blood cell count of 35.000 cells/mcL (97% neutrophils, 6% bands) and acute on chronic kidney injury, stage 1 per Acute Kidney Injury Network (AKIN) as creatinine was 2.6 mg/dL from baseline 2 mg/dL.

A non-contrast computed tomography (CT) of the sinusis (Figure 2) showed sinusitis with post-septal cellulitis significant thickening of the nasal and facial soft tissues consistent with necrotizing cellulitis. There was dilation of the right superior ophthalmic vein raising the possibility of cavernous sinus thrombosis. Magnetic resonance imaging (MRI) with contrast confirmed these findings and confirmed involvement of the right orbital apex and bilateral cavernous sinus thrombosis (Figures 3).

Empiric antibiotic therapy was started with piperacillin/tazobactam 3.375 mg IV twice daily, vancomycin 1 g IV daily and liposomal amphotericin B 475 mg IV daily.

The patient was emergently taken to the operating room for nasal cavity debridement and septectomy. The necrosis extended to the septum nasal floor bilaterally, inferior turbinates, as well as the ethmoid sinuses bilaterally. Shortly after debridement, the physical exam revealed the involvement of left eye and necrosis of his palate, consistent with a rapidly progressing necrotizing lesion suggestive of invasive fungal sinusitis versus aggressive bacterial process, even though all pathology from the OR did not indicate either.

Within 12 hours of admission two sets of blood cultures were positive for *Staphylococcus aureus*. ENT strongly recommended a second debridement; however, patient refused and only accepted a palate biopsy, which further yielded presence of methicillin-susceptible *S. aureus* (MSSA) and no evidence of fungal infection in cultures or pathology from sinus biopsies.

Upon culture results, antimicrobial therapy was de-escalated to oxacillin 12 g IV daily through continuous infusion. The patient was successfully discharged home to complete a 2-month course of oxacillin and anticoagulation therapy for the management of bilateral cavernous sinus thrombosis.

DISCUSSION

It is well known that bacterial infections are one of the most important causes of morbidity and mortality after solid organ transplantation (SOT) in particular within the first six months post-transplantation, when patients receive potent immunosuppression to avoid graft rejection[5]. In addition, it is also known that treatment for rejection with highly potent immunosuppressive agents increases the risk of serious infections. According to Medicare claims data collected by the U.S. Renal Data System, the rate of infections in renal transplant recipients (RTRs) in the initial 3 years after kidney transplantation is estimated to be 45.0 per 100 patient-years of follow-up[6]. Improved prophylactic, diagnostic, and treatment strategies have decreased the negative effect of infection on transplant outcomes[7]. In fact, post-transplant infections may follow a predictable pattern with regard to timing after transplant[5]. Traditionally early infections (within the first month post SOT) tend to be nosocomially

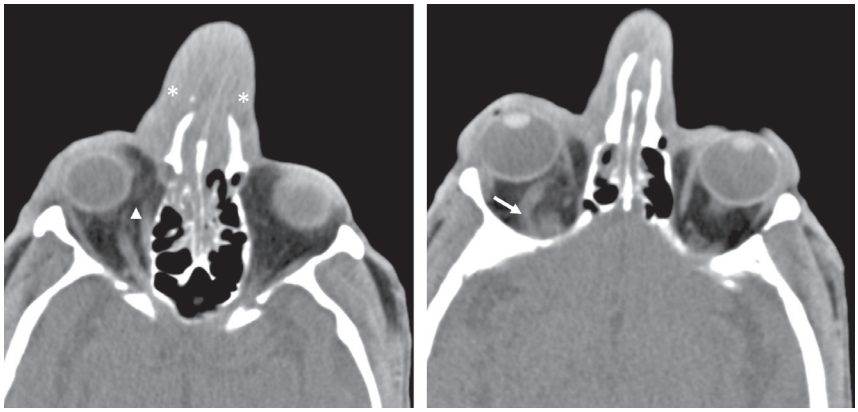

Figure 2. Axial non contrast CT of the face *(A)* caudal to *(B)*. *A*, Diffuse thickening of the nasal and soft tissues (asterisks). There is stranding of the post-septal fat planes (arrow head) consistent with post septal cellulitis. *B*, Enlargement of the superior ophthalmic vein (arrow) raising the possibility of cavernous sinus thrombosis.

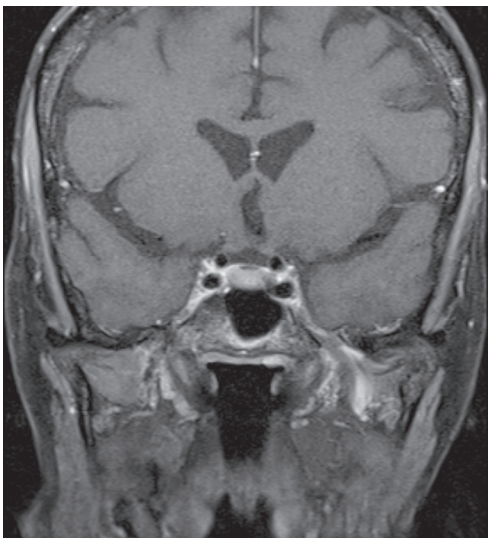

Figure 3. Coronal T1W post contast MRI at the level of the cavernous sinus confirms bilateral cavernous sinus thromsosis .

acquired pathogens, surgical site infections, and donor-derived infections. Opportunistic pathogens occur later, reflecting the greater impact of immunosuppressive therapies. Late infections, after six months, may be secondary to opportunistic pathogens or conventional ones; opportunistic pathogens are more frequently seen in patients who require greater immunosuppression or who have specific environmental exposures[5,7]. It is important to distinguish that the timeline is not fixed, the pattern and timing of infections may be significantly altered by the choice of immunosuppressive agents that affect the net state of immunosuppression at different time points. As seen in our case, the patient presented with a life threatening infection very shortly after potent immunosuppression for the management of AMR.

Acute rhinosinusitis is defined as the inflammation of the mucous membranes of the nose and one or more paranasal sinuses[8]. In the general population, it is most often caused by a community-acquired viral infection, followed by bacterial and fungal infections[8]. Reported rates[9] of morbidity and mortality in non-immunosuppressed patients with complications of sinusitis range from 5 to 40%. The two most common sequelae of sinusitis are orbital infections and intracranial complications[10]. Orbital infections have been classified into five stages: *periorbital cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess,* and *cavernous sinus thrombosis* (CST), with the latter being the most devastating.

Cavernous sinus thrombosis (CST) is a potentially lethal illness, which is infrequently seen by clinicians these days given the institution of appropriate antibiotics, better imaging modalities, and advancements in surgical interventions[11,12]. In the general population the most frequently identified pathogen in cases of CST is *S. Aureus* and less commonly, *Streptococcus pneumonia*, Gram-negative bacilli, and anaerobes. In immunocompromised patients, cases of CST related to fungal infections such as aspergillosis and mucor have been reported[13,14].

Conclusions

As physicians and health care community members, we should remind each other that "common things are common" even in the uncommon patients that may present in an unusual way mimicking those that are known to be usually fatal. Especially given that aggressive and unnecessary treatment regimens may be complicated by antibiotic resistance, drug interactions, fearsome side effects and that during infection there continues to be the need to maintain immunosuppression to avoid allograft rejection.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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