Perplexing Etiology of Acute Retinal Necrosis in a Renal Transplant Recipient

Sir,

Renal transplant recipients (RTRs) are prone to opportunistic infections, which at times can be difficult to diagnose due to perplexing etiology and atypical presentations. Disseminated varicella infection in a RTR is whimsical and consequent acute retinal necrosis (ARN) is even more inconspicuous,[1] especially if immunocompromised, with an incidence of 1.48% in post-transplant patients.[2] In this context, we describe a RTR who presented with acute onset blurring of vision, following cutaneous varicella infection and evaluation revealed ARN which responded to early preemptive antiviral therapy, reduction in immunosuppression, and prophylactic laser photocoagulation.

A 24-year-old male, who underwent a live related renal transplant in September 2018 (following dialysis vintage of 15 months with mother as a blood group compatible donor), with stable graft function (serum creatinine of 1.2 mg/dL) on triple immunosuppression therapy (tacrolimus, mycophenolate mofetil, and steroid) had presented 2 months post-transplant with cutaneous varicella infection. Although patient denied history of varicella eruptions in the past, he was exhibited antitubercular treatment for disseminated tuberculosis in July 2016 (ocular - bilateral anterior uveitis, lymph node–mediastinal, renal–granulomatous interstitial nephritis). Thereafter, he had complete resolution of symptoms with regression of mediastinal lymphadenopathy; however, progressed to an end-stage renal disease requiring initiation of hemodialysis. Current cutaneous varicella lesions recovered spontaneously over 1 week; but 2 weeks later, he developed acute onset bilateral blurring of vision. His visual acuity (VA) in the right eye (RE) was 6/36 and 3/60 in the left eye (LE). The ophthalmic evaluation suggested anterior uveitis in LE with keratic precipitates (KPs) in the left anterior chamber and multiple healed choroiditic patches, with no evidence of retinitis or ARN in either eye. MRI brain did not reveal any intracranial pathology and consequently, the patient was managed with prednisolone and atropine eye drops for left anterior uveitis. His vision improved in LE to 6/60, however, deteriorated in RE to 6/60 by the first week of January 2019. His anterior uveitis had flared up again and vision in RE further deteriorated to 2/60, along with KPs, 3+ cells, whereas vision in LE remained 6/60. Three weeks later, his vision deteriorated to finger counting at 1 m in RE with 3+ cells, 1+ flare, and ARN in RE. In background of recent varicella infection and evident eye-sight threatening infection, patient was preemptively managed with inj acyclovir for 2 weeks and prophylactic laser photocoagulation in both eyes to prevent retinal detachment (RD), along with supportive treatment and curtailed immunosuppression [Figure 1]. By February 2019, patient had improvement in vision to 2/60 with resolution of ARN in RE. His polymerase chain reaction (PCR) for varicella-zoster virus (VZV), herpes simplex virus (HSV I or II), and cytomegalovirus (CMV) were negative. IgM for toxoplasma and VDRL were also negative. Nevertheless, sampling form right aqueous humor was positive for VZV DNA PCR. Consequently, the patient received oral acyclovir for 6 weeks. He reported gradual subjective improvement and currently has VA of 6/60 in RE and 6/6 in LE with stable graft function (serum creatinine-1.2 mg/dL) on triple-drug immunosuppression.

ARN is usually secondary to infection with VZV or HSV (I/II) and can occur any time from 1 month to 60 months post-transplant as evident in index case who developed ARN after 4 months of renal transplant. ARN may not[3] be preceded by overt varicella eruptions, unlike our patient who had varicella eruptions 2 weeks before uveitis and 8 weeks before development of ARN.

The most common presentation of ARN is progressive vision loss (bilateral[2] in around 50%; suggesting hematogenous dissemination of VZV to the central nervous system) and may range anywhere from 20/40 to no light perception. The index patient had VA of 6/36P in RE and 3/60 in LE), which further deteriorated following ARN in RE. Other symptoms include acute onset ocular/periocular pain, redness, and photophobia.

Anterior chamber paracentesis or vitreous tap for PCR - herpes viruses (VZV, HSV, CMV, and EBV) and toxoplasmosis is more likely to delineate the etiologic agent[3] with sensitivity ranging between 80–90% for VZV[4] or HSV as was evident in the index case where PCR from aqueous humor was positive for VZV.

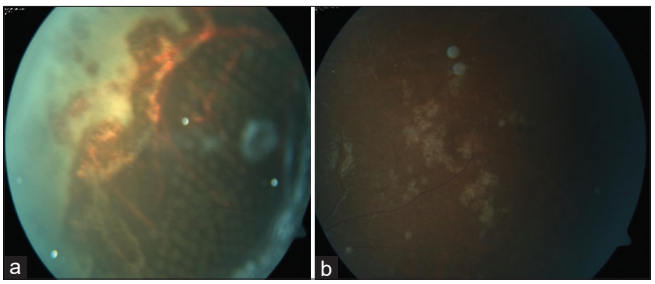

Figure 1: (a) Retinal picture of the right eye showing acute retinal necrosis. Also seen are laser photocoagulation marks (multiple round spots in the right half of retina). (b) The hypopigmented patches suggestive of healed areas of retinitis

The classical triad of ARN[5] includes firstly arteritis/phlebitis of retinal and choroidal vasculature, secondly confluent and necrotizing peripheral retinitis, and thirdly moderate-to-severe vitritis. Though PCR of ocular fluids supports the clinical diagnosis of ARN, treatment should not be delayed,[6] likewise our patient was preemptively exhibited inj acyclovir, pending laboratory confirmation to decrease the incidence of ARN in the fellow eye.[7] Acyclovir should be started at 10 mg/kg every 8 h or 1500 mg/m^2/day intravenously for 2 weeks; however, this may not be enough to clear the infection due to an initial plateau phase of VZ viremia in ARN followed by logarithmic reductions in VZV DNA levels after prolonged treatment with oral acyclovir 800 mg five times daily for 6 weeks[8] to 3 months. Even intravitreal foscarnet and other antivirals can be considered for progressive disease.[9]

Rhegmatogenous RD may occur in up to 75% of eyes with ARN within 3 months of the onset of symptoms. Prophylactic barrier laser photocoagulation posterior to active retinitis may be considered to wall off or prevent subsequent RD. Response to treatment has been variable from no light perception to 2/20. Propitious preemptive antivirals and prophylactic photocoagulation in both eyes to prevent RD resulted in considerable restoration of the vision in our patient.

To conclude, cutaneous varicella in a RTR should always be considered as a red herring for possible dissemination and warrants deliberation given an entirely different approach to diagnosis and management. ARN consequent to varicella infection in a RTR is rare, with higher mortality and morbidity; nevertheless, reversible if diagnosed early and adequately treated with prolonged antivirals, particularly in presence of anterior uveitis which may be a risk factor, and a harbinger of ARN particularly in the post-transplant setting.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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