Necrotizing herpetic retinopathy in kidney-transplanted patients on mycophenolate mofetil☆

Retinopatía necrosante herpética en trasplantado renal con mofetil micofenolato

Dear Editor,

A 73-year-old male, with a kidney transplant in December 2006, and treated with mycophenolate mofetil (MMF) 500 mg/d and tacrolimus. In April 2012, he was admitted to another hospital for diffuse cutaneous varicella, which progressed favourably with oral acyclovir; source of infection unknown. In December 2012, he attended A&E at our hospital for one-week of history of floaters and decreased vision in the left eye. An ophthalmologic and funduscopic examination revealed retinitis of the affected eye with a visual acuity (VA) of 20/100 and an intraocular pressure of 18 mmHg with a normal contralateral eye (Fig. 1A and B). PCR and viral serologic testing (IgG and IgM), and then a test for the varicella zoster virus (VZV), were negative (negative pre-transplant). A sample of aqueous humour from the anterior chamber for an analysis of viral DNA was obtained, and intravenous acyclovir was prescribed (the patient refused immediate intravitreal treatment). The patient's clinical progress was satisfactory, with rapid improvement after 11 days (Fig. 2), and initiation of a complete regression of lesions was evident. The PCR of aqueous humour confirmed that it was a VZV infection, and the rest of tests was negative. 360° laser photocoagulation of the retina was performed, while continuing with oral acyclovir. The patient was discharged 20 days after admission, with VA 20/32. Twelve weeks later, he presented with rhegmatogenous retinal detachment, which, despite a successful replication by *pars plana* vitrectomy with scleral buckling and silicone oil, failed to achieve more than 20/200. Three years later, he has a VA of just light perception and residual inferior retinal detachment.

The incidence of VZV in the general population increases with age after, the age of 50. However, disseminated varicella is a rare presentation even in immunosuppressed patients, and when it occurs, it is usually during the first year after transplantation.[1] This patient presented with clinical symptoms 9 years post-transplant with minimal doses of immunosuppression and without steroid therapy. His pre-transplant serology was negative, and so a primary infection due to varicella zoster was assumed; but he remained negative after 9 months of the cutaneous episode, which can be explained by the anergy of immunosuppression. To date, peri-transplant prophylaxis with acyclovir is not indicated in seronegative cases, but vaccination for VZV in waitlist patients, done at our centre since 2010, may reduce the incidence of this infection.

The time elapsed between the skin symptoms and the onset of retinopathy indicates virus latency in neurons. Primary VZV infection typically occurs in childhood, infecting the epidermal cells and causing the characteristic skin rash. Subsequently, the sensory nerve terminals of mucocutaneous tissue are infected reaching through axons the sensory roots of the dorsal root ganglia, where it remains dormant in neuronal bodies. Reactivation occurs with new virions in sensory neurons that migrate again through the axons to the epidermis (neuropathic pain and rash). It is known that cellular immune suppression plays an important role in this reactivation, such that these patients will present with VZV more often, with a prevalence between 3% and 14%.

Routine ophthalmologic examinations should be considered in patients with opportunistic viral infections. Retinal complications are rare,[2] and amongst their most common causes is external progressive acute retinal necrosis (ARN), retinitis caused by cytomegalovirus (CMV) and toxoplasmosis. Necrotizing herpetic retinopathies are caused by VZV, herpes simplex virus I and II, CMV, and rarely, Epstein–Barr virus.[3] Their most common presentations are decreased vision, pain and photophobia.[4] On examination, multifocal yellowish-white patches are typical, which tend to coalesce in diffuse areas of full-thickness retinal necrosis. Other signs of ocular inflammation, such as vitritis, vasculitis, optic disc swelling, keratic precipitate and posterior synechiae, may accompany them. ARN is an ophthalmological emergency in which antiviral treatment should be started early, as it leads to blindness due to retinal scarring, retinal detachment or optic nerve atrophy. In addition, one-third of patients develop bilateral involvement within the first month of presentation.

DOI of original article:
http://dx.doi.org/10.1016/j.nefro.2016.03.007.

☆ Please cite this article as: Morión Grande M, Martín-Gómez MA, Quereda Castañeda A, López Jiménez V, Cabezas Fernández T. Retinopatía necrosante herpética en trasplantado renal con mofetil micofenolato. Nefrologia. 2016;36:575–577.

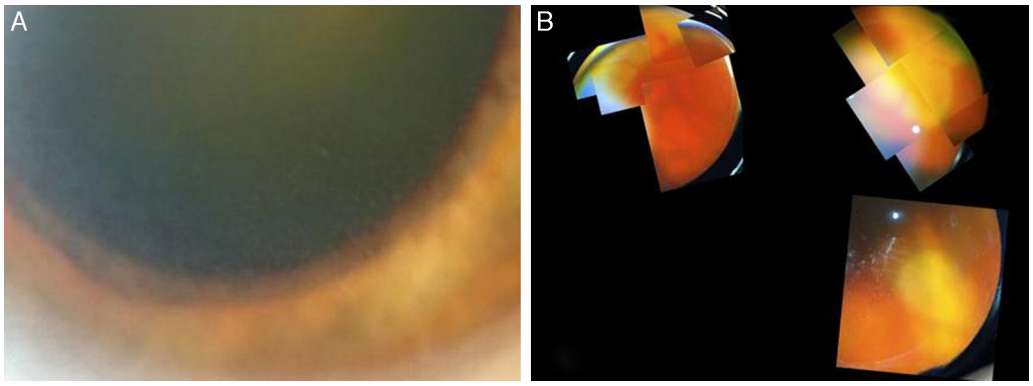

Fig. 1 – (A) Inflammatory reaction in the anterior chamber with thin retrokeratic precipitate, also discrete ciliary injection and a dense grade 5 cataract, LOCS II. (B) Funduscopy: moderate vitritis, optic nerve swelling and white-yellowish lesions in the upper and lower temporal nasal retina.

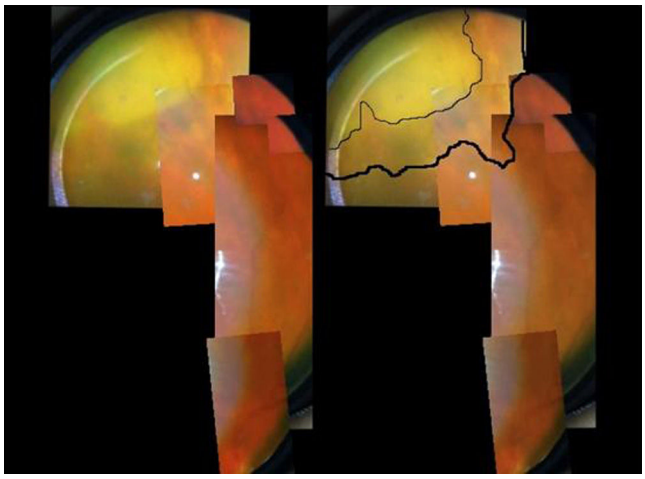

Fig. 2 – Upper nasal lesion with sharper edges and start of pigmentation in areas in resolution.

The development of VZV in the transplant population has been associated to MMF[5–7] This is due to viral thymidine kinase, which replaces the inosine monophosphate dehydrogenase inhibited by mycophenolate, thus allowing the cell to continue its life cycle. However, the specific involvement in this disease is not clear if compared with other immunosuppressants in clinical trials.[8] In addition, MMF has been shown to play certain role in enhancing the antiviral activity of acyclovir.[9] Thus the role of MMF in this type of viral infection or in this patient is not clear, especially when considering the low dose used. Clinical practice suggests that once disseminated disease presents, it makes sense to reduce the immunosuppressive burden, given the high morbidity and mortality of this disease.[10]

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Social disparities, risk factors and chronic kidney disease☆

Disparidad social, factores de riesgo y enfermedad renal crónica

Dear Editor,

The term "health disparities" refers to those differences in health status experienced by different demographic groups that occur in the context of social or economic inequality. Health disparities affect access to services and quality of care, which is reflected by the increase in the morbidity and mortality of chronic diseases.[1]

In countries where medical care for chronic kidney disease (CKD) is not universal, treatment for this disease represents a devastating medical, social and economic problem for patients and their families; thus, the costs of treating this disease are considered as "catastrophic health expenditures." A catastrophic health expenditure can be defined as one where the whole family spends more than 30% of their income to pay for the family's healthcare.[2]

In industrialised countries, CKD disproportionately affects socially disadvantaged groups, such as ethnic minorities and people with a low socioeconomic income.[3] Multiple studies conducted in the United States and Canada have shown a strong association between low socioeconomic status and higher incidence and prevalence and more complications related to CKD. Crews et al.[4] showed that people with a lower socioeconomic status had a 59% greater risk of developing CKD. This association was higher in the black population. Also, residence in poor neighbourhoods was found to be strongly associated with an increased prevalence of CKD.

In Europe, the relationship between socioeconomic status and CKD has been less studied; however, studies in Sweden, the UK and France have also found this association.[5,6]

Unfortunately, there are few studies in industrialising countries like India and Mexico. In these countries, there is a high prevalence of the disease in the socioeconomically disadvantaged population.[7] In Central America, particularly in Nicaragua and El Salvador, there have been reports of a new kidney condition called Mesoamerican nephropathy, which occurs mainly in poor workers who toil in suboptimal working conditions at extreme ambient temperatures and experience long periods of dehydration.[8]

Poverty also adversely affects some of the most important social determinants of health, such as developing healthy habits, getting healthcare in a timely manner and suffering environmental exposure to nephrotoxic agents such as lead, cadmium and arsenic (Table 1).

A higher prevalence of births with low birth weight promotes not only less development in terms of renal mass but also an increased risk of hypertension and CKD; the association of post-streptococcal GN with CKD has also been reported as a risk factor in some populations. Depression, anxiety and increased exposure to addictions also promote the activation of the sympathetic nervous system and an increased release of cytokines that can directly influence the pathogenesis of kidney damage (Fig. 1).[9]

An increased intake of sodium, sweetened beverages and foods with phosphorus has also been reported in this population. In addition, the chances of receiving proper treatment to slow the progression of kidney damage are lower in this population.[10]

A clearer understanding of the situations of vulnerable populations and risk factors in people in the lower socioeconomic strata might allow for designing better public health measures to reduce the burden of kidney disease in this population, since growth of national income per capita does not necessarily mean that the poorest members of society get better access to quality health services.

DOI of original article:
http://dx.doi.org/10.1016/j.nefro.2016.03.007.

☆ Please cite this article as: Robles-Osorio ML, Sabath E. Disparidad social, factores de riesgo y enfermedad renal crónica. Nefrologia. 2016;36:577–579.