Letter to the Editor: Characterization of Choriocapillaris and Choroidal Abnormalities in Alport Syndrome

Bosnar, Damir; Knežić Zagorec, Mira; Bušić, Mladen; Cigić, Valentina; Zagorec, Nikola; Nikuševa Martić, Tamara; Galešić Ljubanović, Danica

Source / Izvornik: **Translational Vision Science & Technology, 2023, 12**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1167/tvst.12.5.25

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:372641

tvst

Letters to the Editor

Letter to the Editor: Characterization of Choriocapillaris and Choroidal Abnormalities in Alport Syndrome

We have read with great interest the research paper titled "Characterization of Choriocapillaris and Choroidal Abnormalities in Alport Syndrome" by Cicinelli et al.[1] We would like to congratulate the authors on their excellent work. However, we discussed several questions that have arisen from the paper. Here are our comments and suggestions.

Angiotensin II acting via type I receptors leads to chorioretinal vasoconstriction.[2,3] Therefore, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may have a significant effect on choroidal thickness. Accordingly, Temel et al.[4] found a statistically significant increase in choroidal thickness at 1 month after perindopril treatment initiation compared with baseline in treatment-naïve hypertensive patients. Furthermore, Gross et al.[5] showed that early treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers delays the onset of end-stage renal disease in Alport syndrome (AS). In the absence of specific gene therapy, these agents remain the gold standard treatment owing to their renoprotective effects in patients with AS. Although confounding is common in observational studies, baseline imbalance between transplanted and nontransplanted AS subgroups in angiotensin-converting enzyme inhibitors or angiotensin receptor blockers treatment history is a potential source of bias that may contribute to significant distortion, which modifies an association.

Moreover, patients with AS were divided into two subgroups on the basis of the history of kidney transplantation. Although preemptive kidney transplantation is the preferred renal replacement therapy in end-stage renal disease, only approximately 2.5% of patients in the United States undergo a kidney transplant as an initial treatment modality.[6] The vast majority of patients undergo pretransplant dialysis treatment. The survival of the patient and the post-transplant graft is significantly impacted by longer waiting times on dialysis.[7] Burton et al.[8] demonstrated that repetitive myocardial injury with consequent fibrosis and reduced left ventricular systolic function can be induced by hemodialysis (HD). A presumed underlying pathophysiological mechanism is ischemia owing to microvascular dysfunction.[9] Some clinical studies suggest that the choroid, and retina to a lesser extent, significantly thins after HD.[10] The cause of this is not yet understood fully. Some possible explanations include changes in blood pressure, serum osmolarity, and body fluid distribution.[11] Hence, we are of the opinion that the dialysis type (HD or peritoneal dialysis) and modality (e.g., ultrafiltration), as well as total duration of dialysis, must be taken into account in the analysis of choroidal and choriocapillaris parameters. In addition, in patients with no history of kidney transplantation, who are currently undergoing intermittent HD, the time interval between the last HD session and optical coherence tomography measurements may be of utmost importance.

Last but not least, potential adverse effects of immunosuppressive treatment in transplant recipients cannot be excluded, as the authors pointed out in the discussion. Gass et al.[12] reported different chorioretinal changes in four patients after kidney transplantation and in one patient after heart–lung transplantation taking prednisone, cyclosporine, and azathioprine. Numerous retinal abnormalities with subfoveal choroidal thickness changes were observed in asymptomatic renal transplant patients on low-dose corticosteroid therapy.[13] It is worth noting that similar findings were reported in a patient after liver transplantation for chronic hepatitis C virus infection taking tacrolimus with mycophenolate mofetil for 3 years.[14] Although these findings may be related to underlying disease,[15] the type, dose, and duration of immunosuppressive treatment should be described in sufficient detail owing to its potential association with various chorioretinal changes.

Damir Bosnar[1–3], Mira Knežić Zagorec[1,2], Mladen Bušić[1–3], Valentina Cigić[1,2], Nikola Zagorec[4], Tamara Nikuševa Martić[5], and Danica Galešić Ljubanović[6,7]

[1] Department of Ophthalmology, Reference Center of the Ministry of Health of the Republic of Croatia for Pediatric Ophthalmology and Strabismus, University Hospital "Sveti Duh," Zagreb, Croatia
[2] Faculty of Dental Medicine and Health Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia
[3] Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia
[4] Department of Nephrology and Dialysis, Dubrava University Hospital, Zagreb, Croatia
[5] Department of Medical Biology and Genetics, School of Medicine, University of Zagreb, Zagreb, Croatia
[6] Institute of Pathology, School of Medicine, University of Zagreb, Zagreb, Croatia
[7] Department of Nephropatology and Electron Microscopy, Dubrava University Hospital, Zagreb, Croatia.
e-mail: mira.knezic94@gmail.com

References

1. Cicinelli MV, Ritter M, Tausif H, et al. Characterization of choriocapillaris and choroidal abnormalities in Alport syndrome. *Transl Vis Sci Technol.* 2022;11(3):23.
2. Rockwood EJ, Fantes F, Davis EB, Anderson DR. The response of retinal vasculature to angiotensin. *Invest Ophthalmol Vis Sci.* 1987;28(4):676–682.
3. Senanayake PD, Miura S, Karnik S, Hollyfield JG. Angiotensin II and its receptor subtypes in the human eye. *Invest Ophthalmol Vis Sci.* 2003;44(13):436.
4. Temel E, Aşıkgarip N, Örnek K, Kıvrak A. Short-term effect of angiotensin converting enzyme inhibitor on choroidal vascularity. *Photodiagnosis Photodyn Ther*. 2021;36:102569. Epub October 3, 2021.
5. Gross O, Licht C, Anders HJ, et al. Early angiotensin-converting enzyme inhibition in Alport syndrome delays renal failure and improves life expectancy. *Kidney Int.* 2012;81(5):494–501.
6. Ashby VB, Kalbfleisch JD, Wolfe RA, Lin MJ, Port FK, Leichtman AB. Geographic variability in access to primary kidney transplantation in the United States, 1996–2005. *Am J Transplant*. 2007;7(5 Pt 2):1412–1423.
7. Meier-Kriesche HU, Port FK, Ojo AO, et al. Effect of waiting time on renal transplant outcome. *Kidney Int*. 2000;58(3):1311–1317.
8. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced repetitive myocardial injury results in global and segmental reduction in systolic cardiac function. *Clin J Am Soc Nephrol.* 2009;4(12):1925–1931.
9. Sigrist MK, McIntyre CW. Vascular calcification is associated with impaired microcirculatory function in chronic haemodialysis patients. *Nephron Clin Pract*. 2008;108(2):c121–c126.
10. Farrah TE, Dhillon B, Keane PA, Webb DJ, Dhaun N. The eye, the kidney, and cardiovascular disease: old concepts, better tools, and new horizons. *Kidney Int.* 2020;98(2):323–342.
11. Chang IB, Lee JH, Kim JS. Changes in choroidal thickness in and outside the macula after hemodialysis in patients with end-stage renal disease. *Retina.* 2017;37(5):896–905.
12. Gass JD, Slamovits TL, Fuller DG, Gieser RG, Lean JS. Posterior chorioretinopathy and retinal detachment after organ transplantation. *Arch Ophthalmol*. 1992;110(12):1717–1722.
13. van Dijk EHC, Soonawala D, Rooth V, et al. Spectrum of retinal abnormalities in renal transplant patients using chronic low-dose steroids. *Graefes Arch Clin Exp Ophthalmol*. 2017;255(12):2443–2449.
14. Abalem MF, Carricondo PC, Pimentel SL, Takahashi WY. Idiopathic organ transplant chorioretinopathy after liver transplantation. *Case Rep Ophthalmol Med.* 2015;2015:964603.
15. Zegans ME, Anninger W, Chapman C, Gordon SR. Ocular manifestations of hepatitis C virus infection. *Curr Opin Ophthalmol*. 2002;13(6):423–427.