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MacTel Type 2: A Misnomer?

Dr. Elliott:
This is CME on ReachMD. I'm Dr. Dean Elliott, and here with me is my esteemed colleague, Dr. Charles Wykoff.

Charlie, macular telangiectasia, or Mac-Tel, is named for the vascular pathologies that characterizes the disease, but is this an accurate name given the neurodegeneration that occurs?

Dr. Wykoff:
Dean, thank you. Great to be here with you. And I think you're right. I think the title of this episode is correct. Mac-Tel is a misnomer, given our more recent understanding of its pathogenesis.

It's fascinating. Classical features of Mac-Tel were originally named for the prominent vascular changes that are often observed, including vascular telangiectasias, right-angled venules, blunt and dilated venules, often with cystic spaces, temporally and mild leakage on fluorescent angiography. But if we take a closer look, we have learned that the underlying pathology is more likely related to dysfunction and atrophy of the outer neurosensory retina, itself. And consistent with that, other findings on examination and imaging include foveal cavitation with ellipsoid zone loss, retinal cavitation on the more inner layers of the outer retina, in particular, variable loss and disorganization of the outer retinal layers on OCT. Pigment migration and what appear to be hard exudates that may be crystalline deposits.

Overall, these atrophic retinal processes are hypothesized to be related to Muller cell dysfunction and depletion, longitudinally. The thought process is that as Muller cells die, this lack of trophic support and atomic physical support to photoreceptors and other retinal cell layers leads to atrophy and disorganization, predominantly, of the outer retina.

Dr. Elliott:
Excellent point, surely. The vascular involvement that the disease is named for is really a secondary characteristic. Leakage observed with fluorescein angiographies not due to retinal edema, but a partial breakdown of the blood-retinal barrier. And subretinal neovascularization can develop in some cases, but this is a late phenomenon.

Here, you see a image that has some pigment proliferation and crystalline deposits, but there's a small amount of subretinal hemorrhage, as well. When you look at the OCT, there's some subretinal hyper-reflective material with some retinal thickening, and the OCT-A shows a flow void in the capillary plexus.

Roger Goldberg and Tom Albini discussed in a previous episode how the treatments we use for retinal vascular diseases and our anti VEGF meds really don't work for Mac-Tel. So, Charlie, how should we treat Mac-Tel since it's a neurodegenerative disease?

Dr. Wykoff:

We do have one FDA-approved treatment now. It's basically a system that's producing CNTF. So, what is CNTF, or ciliary neurotrophic factor? This is inherently, endogenously produced by Muller cells, and multiple preclinical studies have shown photoreceptors to be able to be rescued with intravitreal injections of CNTF.

The key problem though, is that CNTF itself has an extremely short half-life, so it's not amenable to repeated bolus injections as we give our anti-VEGFs because the half-life of this medication, when given exogenously as a bolus injection, is simply 1 to 3 minutes. And therefore, revakinagene taroretcel, or NT-501, was developed in order to allow sustained therapeutic delivery of CNTF intraocularly. This uses encapsulated cell therapy. Basically, it's genetically modified RPE cells that overproduced CNTF inside of a semi-permeable membrane. These cells produce the biological protein, CNTF, which then diffuses out of the semi-permeable membrane while oxygen and nutrients can diffuse in. Importantly, the cells that are placed inside the vitreous cavity in this membrane are sequestered from the immune system, and this whole ECT platform is placed into the vitreous cavity and anchored to the overlying sclera with a proline suture.

Dr. Elliott:
Thank you, Charlie.

So, Mac-Tel is primarily a neurodegenerative disease caused by Muller cell loss. CNTF is a powerful neural protector that can reduce photoreceptor loss. CNTF can now be delivered to the retina of adult patients with idiopathic Mac-Tel using an encapsulated cell therapy implant.

Thank you to our audience for joining us. And thank you, Charlie, for being here today.

Dr. Wykoff:
Thank you very much, Dean.