Correspondence

Optical Coherence Tomography Angiography Quantitative Assessment of Choriocapillaris Blood Flow in Central Serous Chorioretinopathy

REPLY

WE WOULD LIKE TO THANK SOUSA AND ASSOCIATES FOR their insightful observations regarding our study.[1] We agree with their remark about the potential existence of other latent pachychoroid spectrum disorders among fellow eyes in patients with unilateral central serous chorioretinopathy (CSC). Thereby, the term "unaffected" was voluntarily chosen in our study, in contrast with the "healthy" eyes in the control group. As noted, a significant proportion of these unaffected fellow eyes could be categorized as uncomplicated pachychoroid (UCP) or pachychoroid pigment epitheliopathy (PPE), in opposition to strictly normal eyes. These asymptomatic findings would represent early stages of the same condition, involving a primary choroidal vasculopathy that tends to be bilateral, potentially corroborating our results. Retinal pigment epithelium (RPE) changes can be observed in PPE and in different subtypes of CSC, especially after serous retinal detachment (SRD) resolution. B-scan and en face OCT images were both reviewed in all cases, as it is described in our methods section. Whereas segmentation artifacts in case of pigment epithelial detachment were systematically corrected, other RPE modifications were deliberately not taken into account for optical coherence tomography angiography (OCTA) interpretation as they were absent in a majority of unaffected eyes. On the contrary, the presence of SRD in active forms and major RPE clumping in severe forms of CSC, excluded from our analysis, can be responsible for noisy or low OCT signal underneath.[2] We assume that these potential attenuation artifacts are quite marginal in our study, especially regarding unaffected fellow eyes of CSC patients. However, we acknowledge that the use of swept-source OCTA could be more suitable for CC flow assessment.[3]

Whereas flow signal cannot usually be properly assessed in medium and large choroidal vessels with OCTA, several recent studies support the hypothesis of a CC hypoperfusion in CSC patients using this imaging modality.[4,5] These findings are consistent with areas of CC hypoperfusion detected by indocyanine green angiography (ICGA). Furthermore, areas of CC thinning can be observed with enhanced depth imaging (EDI) OCT, colocalizing with pachyvessels in ICGA and flow signal voids in OCTA, that is not suggestive of an increased blood volume with slower blood velocity within the CC.[5,6] We hypothesize that a chronic ischemic insult at the CC level along with an increased hydrostatic pressure originating from the underlying congested choroidal vessels may lead to RPE–Bruch membrane complex damage, outer blood-retinal barrier breakdown, and subsequent SRD.

As 2 eyes were incorporated in CSC patients, we chose to include both eyes in healthy individuals and the 2-way repeated measures ANOVA in this within-subjects approach showed a negligible impact on our statistical analyses. The multivariate model was not conducted because most of the selected variables were not significant in the univariate analysis ($P > .2$).

In conclusion, we appreciate these thoughtful suggestions, which will help promote further discussions in the field of blood flow dynamics in CSC and other pachychoroid spectrum disorders. Additional studies and advancements in quantitative flow imaging will help to accurately interpret inner and outer choroidal vascular disturbances and their relationship with RPE damage.

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CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

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Long-term Outcomes of Globe-Preserving Surgery with Proton Beam Radiation for Adenoid Cystic Carcinoma of the Lacrimal Gland

EDITOR:

WOLKOW AND ASSOCIATES DESCRIBE THEIR RETROSPECTIVE experience in 18 patients with lacrimal gland adenoid cystic carcinoma (LGACC) who had globe-preserving surgery with high-dose mixed radiation beams of protons and photons.[1] The title is slightly misleading, since only 1 patient received proton therapy alone and the remainder received a combination of protons and x-ray therapy. The authors used passive scattering proton beams with x-ray therapy. The "modern" technique of proton therapy uses active scanning proton beam delivery and intensity-modulated proton therapy (IMPT) that eliminates the need for photon therapy for skin sparing. The ocular late toxicities can be reduced by limiting the radiation dose to 64 CGE, ensuring the cornea receives less than 35 CGE, limiting the maximum dose to the optic nerve to 60 CGE, and ensuring the optic chiasm remains less than 54 CGE. Although the timing of delivery of radiation, the exact radiation technique, the operating surgeons, and the approach to surgery were varied among the 18 patients collected over a 27-year period, the authors state that this is the "first," "largest," and "most uniform" series of patients with LGACC treated with eye-sparing multidisciplinary approach. Such claims are not necessary to make this manuscript worthy, nor are they accurate given all the other publications using a very similar approach.[2–4] We congratulate the authors on publishing their data with a relatively long follow-up time, which is additive to previous publications. The Discussion briefly mentions previous reports and downplays their significance but should instead emphasize just how similar the authors' findings are to all the other previous publications. The current report confirms the conclusions from previous reports that local control rates and disease-specific survival with eye-sparing surgery and radiation are very similar to same outcomes in patients with LGACC after orbital exenteration and radiation. Wolkow and associates report that 4 out of 18 patients experienced local recurrences (22%), very similar to the 18% local recurrence reported in 37 patients in Woo and associates' paper published in 2016.[4]

We thank the authors for referencing our data published in 2004 as one of their "historical data treated with conventional therapy"[5]; these data are historical indeed, but are also dated and also importantly limited to patients with locally advanced tumors, often with cranial involvement. The authors have failed to reference 2 more recent manuscripts from M.D. Anderson on outcomes in patients who had orbital exenteration followed by radiation (published in 2006 and 2010)[6,7]; these 2 later manuscripts contained a more diverse group of patients and showed much better survival rates than the paper published in 2004. It should be noted that we at M.D. Anderson Cancer Center started to offer eye-sparing multidisciplinary treatment to our patients with LGACC in 2007, and only to a subset of patients in whom we thought gross total resection of the lacrimal gland mass was possible without sacrifice of the eye and important orbital structures such as extraocular muscles and in whom the tumor had not already entered the central nervous system at presentation. At our center, eye-sparing surgery is usually followed by concurrent chemotherapy with weekly cisplatin and proton therapy to doses of 60-64 CGE (unless there are specific contraindications to chemotherapy). We published our data for the first 11 patients with lacrimal gland carcinoma using this approach in 2016[2]; the majority of patients had adenoid cystic carcinoma. We are pleased that since the publication of our manuscript, additional reports of a very similar approach have been surfacing from throughout the world, including this current report from Boston.[1,3,4]

One question for the authors: since you have so nicely provided both tumor size and AJCC T category at presentation in your table of 18 patients, why not report the correlation (or lack thereof) between tumor size and local recurrence, distant metastasis, and disease-free survival? Even with 18 patients it is possible to find significant trends (or lack of significance). Also, was there a correlation between T category at presentation and local recurrence, distant metastasis, and disease-free survival? Even a nonsignificant *P* value should be provided.

We agree with the authors that multicenter clinical trials are acutely needed for patients with adenoid cystic carcinoma of the lacrimal gland. However, we believe the main issue is not so much variations on the theme of eye-sparing surgery and radiation but rather finding effective treatments for metastatic disease for which we have nothing to offer at the moment. As data emerge on local/-regional control rates for eye-sparing approaches that seem to be at least as good as orbital exenteration, the next steps are to design clinical trials for treatment of patients with metastatic LGACC.