A Unique Presentation of Bilateral Chorioretinal Atrophy

To the Editor:

Herein we report on a unique presentation of chorioretinal atrophy in a woman with a history of chemotherapy and cisplatin overdose. At 10 years of age, she underwent 17 cycles of chemotherapy involving adriamycin, cyclophosphamide, methotrexate, and cisplatin for osteosarcoma of the femur. During the first cycle, the patient was admitted to intensive care due to an unintentional cisplatin overdose. In addition, she experienced hearing loss shortly after the first cycle and cisplatin was subsequently discontinued. At the age of 23 she became aware of difficulties with night vision and underwent multimodal retinal imaging at age 28. The fundus showed an annulus of chorioretinal atrophy extending from the temporal retinal vascular arcades to the retinal mid-periphery and encircling the optic disks symmetrically in each eye (Figs. 1A, B). Pigment accumulation outlined a scalloped transition from the annulus to the far peripheral retina. Early (Figs. 1C, E) and late-phase (Figs. 1D, F) fluorescein angiography showed a window defect with late staining in the region of choroidal atrophy and no leakage in the macula. Early-phase indocyanine green angiography (Figs. 1G, H) of the upper quadrant revealed mid-peripheral chorioretinal atrophy and the presence of pigment overlying retinal vessels at the margins of atrophy, confirming that the pigment is at least partially intraretinal and suggesting photoreceptor loss prior to colocalized retinal pigment epithelium loss.1 An optical coherence tomography vertical scan passing through the fovea revealed preservation of retinal layering in the central macula and abrupt transition to full thickness retinal atrophy at the margin of the macular region (Figs. 1I, J). The left foveal clivus was partly flattened by a mild epiretinal membrane (Fig. 1J). The kinetic visual field testing of both eyes showed a central area of function maximum 50 degrees in diameter with the V4e target (Figs. 1K, L). In addition, the left eye also showed a far peripheral temporal area of function. Apart from the temporal visual field of the left eye, no vision could be detected in the far periphery by means of kinetic perimetry. The family history was negative and whole exome sequencing did not identify any variants having the characteristics of biallelic mutations associated with a Mendelian condition. One heterozygous variant in ADGRV1, a gene associated with Usher syndrome type II, was detected (NM_032119: c.367G>A, p.Gly1148Asp). This variant was classified in ClinVar as a “variant with conflicting interpretations of pathogenicity,” (4 submissions scored it as a variant of uncertain significance, 3 as likely benign, and 1 as likely pathogenic). However, we could not identify any additional coding variants with characteristics of a Mendelian mutation in the same gene, which would be necessary to explain a recessive/isolated condition, such as the one reported here.

Mitochondrial DNA analysis with coverage higher than 300× was also negative, with the exception of the chrMT:4024A>T, ND1:ENST00000361390:c.1257G>A, p. Thr240Ser variant, which was probably not related to this condition by virtue of its elevated frequency in the European population (around 1.5%). This unique funduscopic aspect, reminiscent of “posterior polar annular choroidal dystrophy,”2 has features suggestive of mitochondrial toxicity as has been reported after didanosine intake.3,4 There is some preclinical evidence that platinum-based drugs can retard mitochondrial function.5 We speculate that cisplatin in very high dosages can cause mitochondria-related retinal toxicity leading to a diffuse peripheral pattern of well-circumscribed chorioretinal atrophy similar to didanosine toxicity.

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The authors declare that they have no competing interests.

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