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Paclitaxel may be a risk factor for retinal phototoxicity

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ABSTRACT

Purpose: To report the first case, to our knowledge, of suspected paclitaxel induced phototoxic maculopathy following vitrectomy surgery.

Observations: A 62-year-old phakic female receiving paclitaxel therapy for ovarian carcinoma presented with a best corrected visual acuity (BCVA) of 20/40 OD with an epiretinal membrane (ERM) and lamellar macular hole on spectral domain optical coherence tomography (SD-OCT). The patient underwent an uneventful pars plana vitrectomy with ERM peel using standard illumination and vitrectomy settings. Membrane Blue Dual (DORC, Netherlands) was used to stain the ERM. Two weeks post-operatively, the patient presented with a reduced BCVA of 20/200 in the operated eye. Fluorescein and indocyanine green angiography revealed right sided patchy hypofluorescence and hyperfluorescence secondary to retinal pigment epithelium changes with intact choroidal and retinal vasculature. SD-OCT and fundoscopy showed right sided loss of ellipsoid layer, increased reflectivity within the retinal pigmented epithelium and subretinal fibrosis without cystoid macular edema. Four months post-operatively her vision had stabilized to 20/160; unfortunately, the patient was palliated a month later due to ovarian carcinoma progression.

Conclusions: A number of drugs are known to increase photosensitivity to solar and artificial forms of radiation. Paclitaxel use has been widely reported to cause dermatological photosensitivity. We report a case of suspected paclitaxel induced phototoxic maculopathy following endoillumination during vitrectomy surgery.

1. Introduction

Although light is essential to the function of the eye, it has the potential to cause sight threatening photic injury through thermal, mechanical or chemical damage. During ocular surgery, photothermal and photomechanical damage can be minimized by modifying the light wavelength and reducing the duration of exposure.[1] Less can be done to prevent retinal photochemical damage as this can occur under ambient light conditions.[2] In the presence of pharmacological agents such as chloroquine and phenothiazine, small quantities of solar or artificial radiation can cause retinal photochemical damage as a result of reactive oxygen species release during interactions between light and deposits of the drug in the retina.[1,3] Patients exposed to photosensitizing agents are at particular risk of photic injury during ocular surgery.

We describe a case of unilateral vision loss following pars plana vitrectomy with epiretinal membrane peel in a 62-year-old female receiving paclitaxel chemotherapy. Cases of maculopathy caused by paclitaxel have previously been reported, notably featuring cystoid macular edema (CME).[4–9] To the best of our knowledge, we report the first case of suspected paclitaxel induced phototoxic maculopathy secondary to endoillumination.

2. Case report

A 62-year-old Caucasian female with active stage IIIA ovarian carcinoma first came under our care following a referral from an optometrist for a suspected lamellar macular hole. There was no other ocular history of note and intraocular pressure was within normal range bilaterally. Examination of the anterior segment revealed no visually significant findings including a clear cornea and clear crystalline clear lens. The patient had undergone 6 cycles of three weekly 175mg/m^2 systemic paclitaxel chemotherapy for ovarian carcinoma. She then received a further 3 cycles at a reduced dosage of 70mg/m^2 due to worsening peripheral neuropathy. The patient had a past medical

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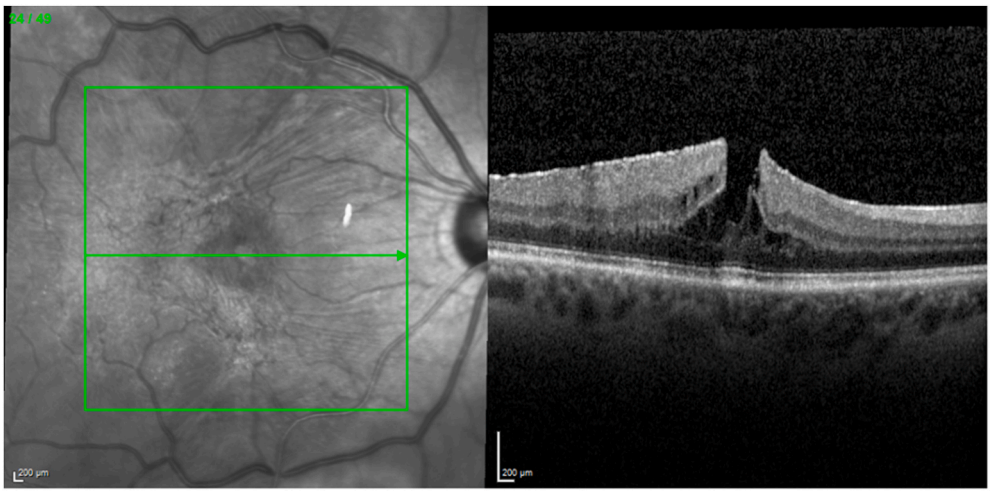

Fig. 1. Spectral domain ocular coherence tomography of the right eye showing a lamellar macular hole and epiretinal membrane baseline.

Table 1
Endoillumination settings used in our Center during vitrectomy surgery.

	Peak light wavelength (nm)	Luminous intensity (lm)
Blue light	465	0.21
Yellow light	656	8.89

history of guttate psoriasis and her regular medications were letrozole, indomethacin and pantoprazole. Following a dilated fundus examination and spectral domain ocular coherence tomography (SD-OCT), a diagnosis of right lamellar macular hole and epiretinal membrane (ERM) was confirmed. Since the patient was asymptomatic and had a best corrected visual acuity (BCVA) of 20/25 OU, further treatment was not indicated.

Six months later, the patient returned with increased distortion of vision in her right eye. Upon further assessment, her BCVA had worsened to 20/40 OD and 20/20 OS and SD-OCT demonstrated increased right eye ERM with distorted retinal architecture (Fig. 1). Surgical intervention was offered. Three months later, the patient underwent a 23-gauge pars plana vitrectomy using an Oertli OS 4, GoodLight LED light source with epiretinal membrane and internal limiting membrane peel using Membrane Blue Dual (DORC, Netherlands) staining for 1 minute and internal tamponade with SF6 gas. The surgery was carried out under sub-Tenon anesthesia and standard endoillumination setting were used (Table 1). The procedure was uncomplicated and was completed in less than 20 minutes.

Two weeks post-operatively, the patient presented with a reduced BCVA of 20/200 OD and 20/32 OS. Fundoscopy showed pigmentation in the inferior aspect of the macular in the right eye and no remarkable findings in the left eye (Fig. 2). Fluorescein and indocyanine green angiography revealed right sided areas of patchy hypofluorescence and hyperfluorescence secondary to retinal pigment epithelium changes (i.e., atrophy and pigment clumping) with intact choroidal and retinal vasculature (Fig. 3) and SD-OCT showed right sided loss of ellipsoid layer and increased reflectivity within the retinal pigmented epithelium (Fig. 4). Angiography of the left eye was unremarkable (Fig. 5). Subsequent assessment of BCVA showed minimal improvement and was last recorded as 20/160 OD and 20/32 OS 4 months post-operatively. One month later, palliative care was initiated and sadly the patient passed away from ovarian carcinoma.

3. Discussion

We describe a case of a 62-year-old female undergoing paclitaxel chemotherapy for ovarian carcinoma that presented with right sided maculopathy following pars plana vitrectomy and epiretinal membrane peel. It is suspected that the reported maculopathy is a result of photic injury that occurred during endoillumination due to retinal photosensitization following paclitaxel use.

Light can cause retinal photic injury during ocular surgery via mechanical, thermal or chemical damage. In this patient, phototoxic maculopathy due to photothermal and photomechanical damage is unlikely as surgical time was kept to a minimum and routine methods to reduce risk of light toxicity including minimizing macula exposure to the light source and the use of a central microscope filter when performing external aspects of the procedure were implemented. A more likely

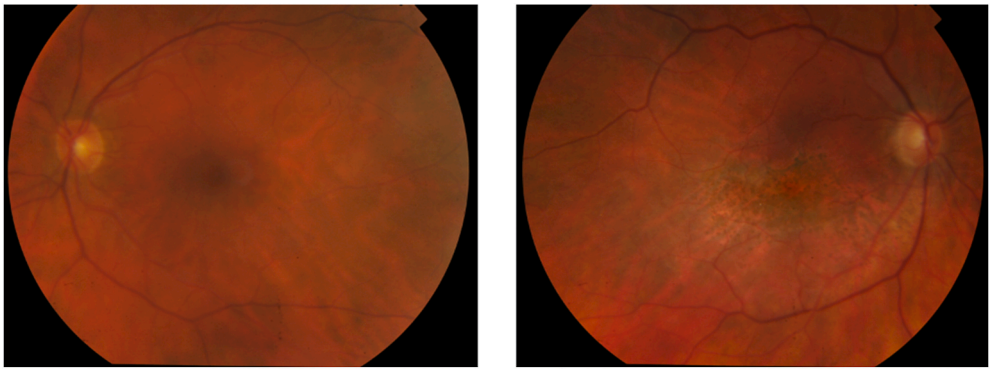

Fig. 2. Color fundus photos showing pigmentary changes of the inferior aspect of the macula in the right eye following the onset of symptoms. The left eye has normal appearances. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

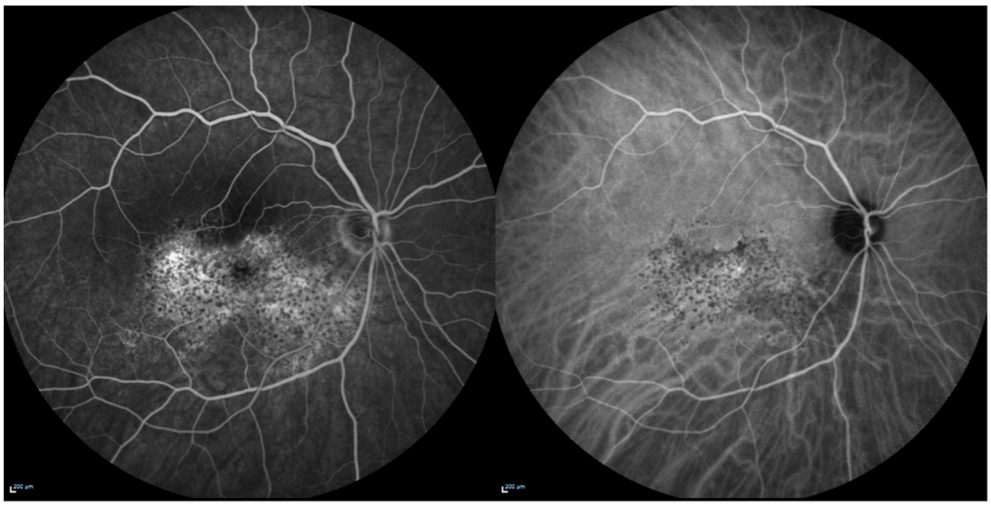

Fig. 3. Fluorescein and indocyanine green angiography of the right eye showing patchy hypofluorescence and hyperfluorescence secondary to retinal pigment epithelium changes with intact choroidal and retinal vasculature.

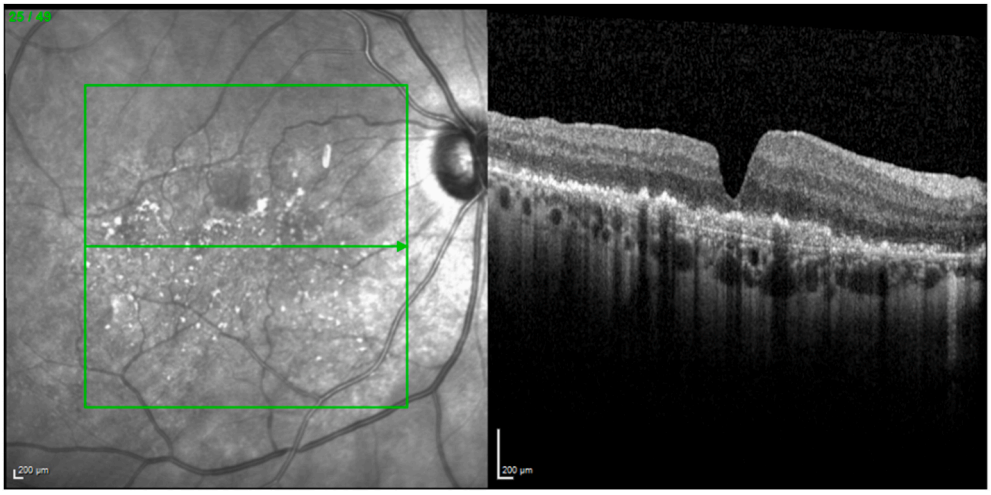

Fig. 4. Spectral domain ocular coherence tomography of the right eye 4 months post-operatively demonstrating retinal pigment epithelium hyperreflectivity, subretinal fibrosis and ellipsoid layer loss following the onset of symptoms. Cystoid macular edema was not present.

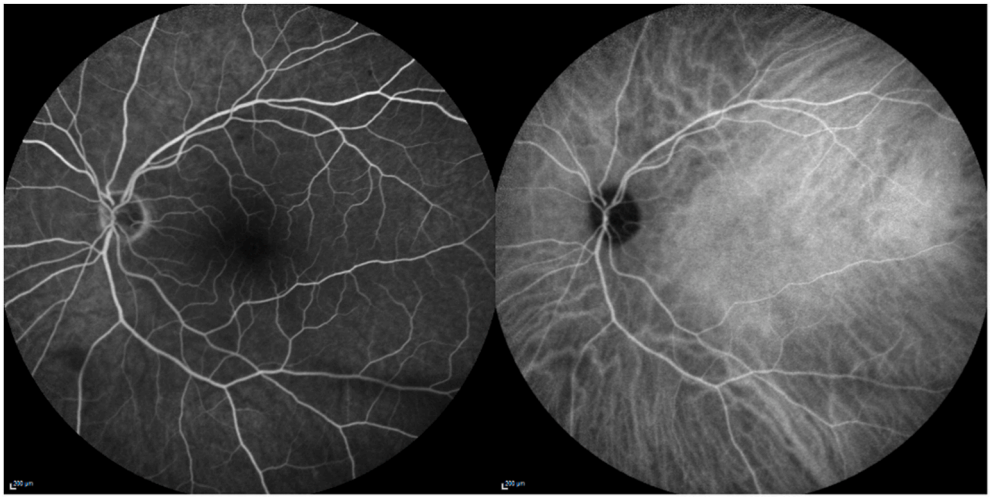

Fig. 5. Normal fluorescein and indocyanine green angiography of the left eye following the onset of symptoms in the right eye.

explanation is macular photochemical damage secondary to use of a pharmacological agent or an underlying disease.

To our knowledge, none of the patient's co-morbidities (guttate psoriasis and ovarian carcinoma) or current medications (letrozole, indomethacin, pantoprazole and paclitaxel) are known to be associated with retinal phototoxicity. Although phototoxicity secondary to Brilliant Blue G (BBG) staining during vitrectomy has been previously reported, typically following prolonged endoillumination, it was considered unlikely in this patient as compared to previous suspected cases of BBG phototoxicity surgical time was significantly shorter and Membrane Blue Dual dye containing only 0.025% BBG was used.[10–12]

In the absence of an alternative explanation, paclitaxel phototoxic maculopathy was considered the most likely cause as paclitaxel is known to induce maculopathy and the inferior distribution of maculopathy corresponded with the endoillumination probe entering superiorly.[4–9]

Paclitaxel belongs to the taxane class of chemotherapy drugs which act by disrupting intracellular microtubular reorganization. It is commonly used in the treatment of breast and ovarian carcinoma. Reported ophthalmic side effects include reduced visual acuity, scintillating scotomas, and abnormal visual evoked potentials.[4]

Paclitaxel induced maculopathy featuring CME is known to be a significant adverse effect of long-term paclitaxel use.[5] Although the exact mechanism of paclitaxel induced maculopathy remains unclear, several hypotheses have been proposed. Nakao et al. postulate that macular edema is a result of intracellular fluid accumulation provoked by Muller cell dysfunction, as supported by delayed and reduced B-wave amplitudes on ERG.[8] A case of irreversible paclitaxel induced maculopathy with CME has been previously reported with the authors proposing paclitaxel toxicity resulted in permanent cell damage.[9] To the best of our knowledge, we report the first case of paclitaxel induced maculopathy in the absence of CME.

Docetaxel is also a taxane and has previously been reported to cause non-edematous maculopathy.[13] However, there was no history of ocular surgery making phototoxicity a less likely cause.

Systemic paclitaxel use classically causes bilateral maculopathy; however, the current patient had unilateral signs.[5] A likely explanation is that paclitaxel photosensitizes the retinal pigment epithelium and photoreceptor cells, increasing the risk of photochemical damage during endoillumination. The mechanism for this may be related to taxane induced dermal photosensitivity, which is thought to be caused by porphyrin aberrations.[14] Since porphyrins have been linked to ocular injury including phototoxicity of the retinal pigment epithelium, it is feasible that porphyrin aberration due to paclitaxel use may cause retinal pigment epithelium photosensitization.[2] While it is possible that bilateral maculopathy would have subsequently developed as part of the natural history of the disease, future reports of phototoxic maculopathy following taxane use will provide further evidence for what appears to be a rare phenomenon.

4. Conclusions

To the best of our knowledge, this is the first case report of suspected paclitaxel induced phototoxic maculopathy. Given the observed effects of paclitaxel on the macula, concurrent use may contribute a guarded prognosis following similar operations.

Patient consent

Verbal consent was obtained from the patient for presentation of this case. The patient is now deceased. No personal identifiable information or images have been included in this report.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: JM, CW, JC and SS.

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