Functional and anatomical characterization of a non-leaking bilateral cystoid macular edema induced by paclitaxel therapy for ovarian cancer: a case report

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Abstract
Abstract: Background: Paclitaxel is a member of the taxane family used for cancer therapy. Ovarian cancer is treated with Paclitaxel in first- and in second- line therapy. Cystoid macular edema without fluorescein leakage is a rare side effect of Paclitaxel treatment. Case presentation: We report the case of a 59-year-old female with ovarian cancer treated with paclitaxel. The patient received 21 cycles of adjuvant chemotherapy and was presented with bilateral gradual vision loss due to macular edema after paclitaxel treatment. Optical coherence tomography revealed a bilateral cystoid macular edema. Fluorescence angiography demonstrated the unusual finding of non-leakage in the late phases of the angiogram. Microperimetric findings of both eyes confirmed the visual deficits. After cessation of the paclitaxel therapy, vision, OCT and microperimetric findings returned to normal. Also, color vision testing demonstrated no persistent defect after therapy cessation. Conclusion: Paclitaxel induced bilateral maculopathy is a rare side effect of chemotherapy. Cessation of the Paclitaxel drug therapy leads to complete functional and anatomical resolution of drug induced side effects. Vision, microperimetric defects, color perception as also anatomical defects detected by OCT change to normal after drug cessation. Taxane induced bilateral maculopathy is a rare disease which should be known by ophthalmologists as also oncologists. Paclitaxel therapy must be counseled to report any vision problems during the treatment period because early recognition of a rare non leaking CME can facilitate appropriate intervention to reverse visual compromise and minimize any potential long-term ophthalmologic sequelae.

Background
Paclitaxel is a member of the taxane family used in various chemotherapeutical protocols for the treatment of ovarian cancer, lung cancer and breast cancer.[1] They are mitotic inhibitors, preventing normal reorganization of the microtubule network within cells [2]. Side effects of the drug are involving neurological disorders as also diseases of the eye. Bone marrow suppression, vomiting, alopecia and nausea have been described as systemic side effects. More rarely are ophthalmic side effects of the drug. A bilateral cystic macula edema with no leakage in fluorescence angiography is a rare side effect of Paclitaxel[3, 4]. Other retinal diseases demonstrating a cystoid macular edema
with non-angiographic leakage are juvenile X-chromosomal Retinoschisis, Goldman-Favre Syndrome, several forms of Retinitis pigmentosa as also Niacine toxicity of the macula[5-11]. Anatomical restauration and vision increase have been described after cessation of the drug, but also non-vision increase has been reported [1, 3, 4, 12-34].

**Case Presentation**

We report the case of 59-year-old female presenting with gradual bilateral vison loss. The patient was treated with adjuvant Paclitaxel chemotherapy for ovarian cancer and had received 21 cycles from 6/17 to 12/17. The cumulative dose of the drug was 2708 mg. Systemic diseases as diabetes and hypertension were not reported. Cataract surgery of both eyes was performed two years ago. Also, childhood strabism resulting in amblyopia of the right eye was reported.

Other diseases of the eye or surgeries were not reported. The visual acuity of both eyes was 0.5 at the initial presentation and did not improve through the use of lenses. No vision disturbing anomalies of the anterior eye section were seen on examination. Funduscopy of the retina revealed a macular edema (Fig.1). The eye pressure was in the normal physiologic range.

Spectral domain coherence tomography (OCT) (Heidelberg Spectralis OCT, Heidelberg GmbH, Heidelberg, Germany) scans revealed an increased bilateral macular thickness due to intraretinal fluid accumulation (Fig.4,5). Despite the OCT results demonstrating a cystoid maculopathy, the fluorescence angiography (FA) (Heidelberg Spectralis, Heidelberg GmbH, Heidelberg, Germany) (Fig.7-8) as also the indocyanine angiography (ICG) (Fig.9-10) showed no leakage and therefore no impairment of the blood retinal barrier. These results are consistent with the diagnosis of a cystoid macula edema without leakage. Fundus autofluorescence disclosed no pathologies (Fig. 6).

Microperimetry of both eyes (MAIA-microperimetry, Centervue, Padua, Italy) confirmed the visual deficits on a functional basis. Fixation problems of both eyes were detected as also a decreased sensitivity shift (Fig. 2,3).

Bilateral paclitaxel induced non-leaking maculopathy was diagnosed and chemotherapy treatment was discontinued. Five weeks after chemotherapy discontinuation, the vision increased to 0.6 on the right eye and 1.0 on the left eye. OCT disclosed the complete anatomical resolution of the previous
presented macular edema (Fig. 11). Microperimetry showed also the functional restauration of the fovea (Fig. 12, 13) as also a panel D-15 color test (Fig. 14). Microperimetry demonstrated an increased sensitivity of the fovea to the stimuli and a normal fixation performance. A later clinical control 9 weeks after chemotherapy cessation showed also a further vision increase of the amblyopic right eye to 0.8. The vision of the left eye stabilized at 1.0.

Discussion And Conclusions
The differential diagnosis for cystoid macula edema without angiographic leakage includes nicotinic acid- associated maculopathy, X-linked juvenile retinoschisis, various forms of retinitis pigmentosa and taxane-associated maculopathy [3, 6-11, 13, 14, 17, 22, 33, 34].

Taxane are a group of chemotherapeutic drugs that are used to treat several malignancies such as breast, lung and ovarian cancer. Paclitaxel (Taxol) is a microtubule-stabilizing agent which belongs to the Taxane family [35]. A bilateral, angiographically non-leaking cystoid macular edema is a seldom side effect of the drug especially after high cumulative doses. Imaging in Paclitaxel-related CME reveals fluid on ocular coherence tomography scan without leakage on fundus fluorescein angiography, which is in keeping with our findings. There are no recommended treatment guidelines for this condition because of the unclear mechanism of pathology. Treatment strategies have focused on Paclitaxel cessation, which appears to result in spontaneous resolution of CME and improvement in visual acuity [13, 15, 16, 22, 26, 32].

Color vision and microperimetric function of the fovea display other values characterizing foveal function. Until now, these parameters have not been evaluated after cessation of Paclitaxel.

Our group used for the first time microperimetry to evaluate the effects on paclitaxel on macular function. We were able to demonstrate fixation loss, loss of fixation stability as also macular sensitivity by Paclitaxel therapy for ovarian cancer. All parameters returned to normal after Paclitaxel cessation. These functional improvements demonstrate the importance to identify Paclitaxel maculopathy in early stages and initiate directly the cessation of the drug to improve vision and macular function.

Abbreviations
OCT: ocular coherence tomography, CME: cystoid macula edema, ICG: indocyanine green angiography

Declarations

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Authors’ contributions:

SH participated in the design of the study and wrote the manuscript. DG, PS, SM conceived the study and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Consent for publication:

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests:

The authors declare that they have no competing interests.

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Figures

Figure 1

Fundus photography of the right and left retina at first presentation
Figure 2

Microperimetry of the right eye at first presentation of the patient

Figure 3

Microperimetry of the left eye at first presentation of the patient
Figure 4

OCT of the right macula at first presentation

Figure 5

OCT of the left macula at first presentation
**Figure 6**

Autofluorescence of the right and left eye at first presentation of the patient

**Figure 7**

Fluorescence angiography of the right eye at first presentation of the patient
Figure 8

Fluorescence angiography of the left eye at first presentation of the patient

Figure 9

ICG of the right eye at first presentation of the patient
Figure 10

ICG of the left eye at first presentation of the patient

Figure 11

OCT of the right and left eye- 5 weeks after cessation of Paclitaxel
Figure 12

Microperimetry of the right eye; 5 weeks after cessation of Paclitaxel

Figure 13

Microperimetry of the left eye; 5 weeks after cessation of Paclitaxel
Figure 14

Color vision of the right and left eye (Panel D15); 5 weeks after cessation of Paclitaxel

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