Impaired retinal pigment epithelium in paclitaxel-induced macular edema
A case report
Chia-Hsin Shih, MDa, Yuan-Chieh Lee, MD, PhDa,b,c,∗

Abstract
Rationale: Cystoid macular edema (CME) is a rare complication of the paclitaxel. However, the pathophysiology was unknown.

Patient concerns: A 60-year-old female presented with bilateral blurred vision due to cystoid macular edema after taking 12-course paclitaxel for her breast cancer. Optical coherence tomography (OCT), fluorescein angiography (FAG), indocyanine green angiography (ICGA), electroretinogram (ERG) and electrooculogram (EOG) were performed.

Diagnoses: Paclitaxel-induced macular edema.

Interventions: Paclitaxel was discontinued and supportive treatment with pentoxifylline was given.

Outcomes: The OCT showed bilateral cystoid macular edema. Impaired filling of choriocapillaries was noted on the ICGA; while EOG revealed decreased Arden ratio. The visual acuity, cystoid macular edema and decreased Arden ratio improved slowly over six months.

Lessons: Paclitaxel rarely causes cystoid macular edema. The damage of choriocapillaries and retinal pigment epithelium might be the underlying cause. Immediate discontinuation of the drug helps visual recovery.

Abbreviations: CME = cystoid macular edema, EOG = electrooculogram, ERG = electroretinogram, FAG = fluorescein angiography, ICGA = indocyanine green angiography, OCT = optical coherence tomography.

Keywords: choriocapillaries, cystoid macular edema, electrooculogram, indocyanine green angiography, paclitaxel, retinal pigment epithelium

1. Introduction
Bilateral cystoid macular edema (CME) is a rare complication of the taxane class of drugs, such as docetaxel or paclitaxel.1,2 Taxane-related maculopathy can be confirmed by optical coherence tomography (OCT) scans, but fluorescein angiography (FAG) fails to demonstrate the source of leakage in affected individuals.3–6 Here we report a case of paclitaxel-induced macular edema to suggest its possible mechanism. Consent for the publication of this case and any additional related information was taken from the patient involved in the study.

2. Case report
A 60-year-old female presented with bilateral blurred vision for 1 month. She had been diagnosed with stage IIA breast infiltrating ductal carcinoma, and had received paclitaxel per week for 12 courses (120 mg for 2 courses, 115 mg for 5 courses, and 110 mg for 5 courses). She had no diabetes, hypertension, major eye diseases, and had not received any intraocular surgery. Her family history was negative for congenital X-linked retinoschisis, Goldmann–Favre syndrome and retinitis pigmentosa. On examination, the best-corrected visual acuity was 20/40 in the right eye and 20/100 in the left eye. Biomicroscopic examination showed negative finding, but the fundus examination revealed decreased foveal light reflex. The OCT showed bilateral CME with a central foveal thickness of 530 μm in the right eye and 532 μm in the left eye (Fig. 1A). The FAG showed weak petaloid pooling in the macular region, but failed to detect any source of leakage in both eyes (Fig. 2A and B). Indocyanine green angiography (ICGA) revealed an area of hypofluorescence of choroid at temporal upper fundus in the right eye and parafoveal areas in both eyes. CME with late petaloid pooling at fovea was also noted (Fig. 2C–F). The OCT imaging of those areas showed dropout of choriocapillaris (Fig. 1A and B). While electroretinogram (ERG) showed normal b-wave implicit time and amplitude in both eyes; electrooculogram (EOG) indicated an Arden ratio of 1.41 in the right eye and 1.37 in the left eye (Fig. 2G).

Under the impression of paclitaxel-induced CME, the drug was discontinued and pentoxifylline 400 mg QD was prescribed. The CME decreased slowly over 6 months (Fig. 1B–E). The visual acuity improved as well. The EOG done at 2 months after discontinuation of paclitaxel showed an Arden ratio of 1.61 in the right eye and 1.60 in the left eye (Fig. 2H). The visual acuity improved to 20/25 in both eyes in 6 months.

3. Discussion
Paclitaxel, a member of the taxane family, exerts anticaner effect by restricting the mobility of microtubules and hence leading to

Editor: N/A.
The authors have no conflicts of interest to disclose.

a Department of Ophthalmology, Buddhist Tzu Chi General Hospital, 707 Sector 3 Chung-Yung Road, Hualien, 97002 Taiwan (e-mail: yuanchieh.lee@gmail.com).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc.
This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2018) 97:26(e11229)
Received: 17 March 2018 / Accepted: 21 May 2018
https://dx.doi.org/10.1097/MD.0000000000011229

1. Introduction
Bilateral cystoid macular edema (CME) is a rare complication of the taxane class of drugs, such as docetaxel or paclitaxel.1,2 Taxane-related maculopathy can be confirmed by optical coherence tomography (OCT) scans, but fluorescein angiography (FAG) fails to demonstrate the source of leakage in affected individuals.3–6 Here we report a case of paclitaxel-induced macular edema to suggest its possible mechanism. Consent for the publication of this case and any additional related information was taken from the patient involved in the study.

2. Case report
A 60-year-old female presented with bilateral blurred vision for 1 month. She had been diagnosed with stage IIA breast infiltrating ductal carcinoma, and had received paclitaxel per week for 12 courses (120 mg for 2 courses, 115 mg for 5 courses, and 110 mg for 5 courses). She had no diabetes, hypertension, major eye diseases, and had not received any intraocular surgery. Her family history was negative for congenital X-linked retinoschisis, Goldmann–Favre syndrome and retinitis pigmentosa. On examination, the best-corrected visual acuity was 20/40 in the right eye and 20/100 in the left eye. Biomicroscopic examination showed negative finding, but the fundus examination revealed decreased foveal light reflex. The OCT showed bilateral CME with a central foveal thickness of 530 μm in the right eye and 532 μm in the left eye (Fig. 1A). The FAG showed weak petaloid pooling in the macular region, but failed to detect any source of leakage in both eyes (Fig. 2A and B). Indocyanine green angiography (ICGA) revealed an area of hypofluorescence of choroid at temporal upper fundus in the right eye and parafoveal areas in both eyes. CME with late petaloid pooling at fovea was also noted (Fig. 2C–F). The OCT imaging of those areas showed dropout of choriocapillaris (Fig. 1A and B). While electroretinogram (ERG) showed normal b-wave implicit time and amplitude in both eyes; electrooculogram (EOG) indicated an Arden ratio of 1.41 in the right eye and 1.37 in the left eye (Fig. 2G).

Under the impression of paclitaxel-induced CME, the drug was discontinued and pentoxifylline 400 mg QD was prescribed. The CME decreased slowly over 6 months (Fig. 1B–E). The visual acuity improved as well. The EOG done at 2 months after discontinuation of paclitaxel showed an Arden ratio of 1.61 in the right eye and 1.60 in the left eye (Fig. 2H). The visual acuity improved to 20/25 in both eyes in 6 months.

3. Discussion
Paclitaxel, a member of the taxane family, exerts anticaner effect by restricting the mobility of microtubules and hence leading to
cell-cycle arrest and apoptosis. CME as an adverse reaction of taxane group drugs has been reported, but the underlying pathophysiology is not clear. The proposed possible mechanisms include fluid accumulation caused by toxicity to Müller cells,[2,7] fluid retention from increased capillary fluid filtration,[3,4] breakdown of blood retinal barrier due to dysfunction of retinal pigment epithelium (RPE) from loss of microtubules function.[8] Observing delayed implicit time and reduced amplitude of b-wave of full-field ERG, Nakao et al suggested that paclitaxel could cause certain toxicity to retinal Müller cells with subsequent CME. However, the ERG of our patient showed normal cone b-wave implicit time and amplitude. In contrast, the EOG of our patient showed decreased Arden ratio, which implied impaired RPE function. Besides, the ICGA in our case showed focal choroid hypoperfusion. The enhanced depth imaging of optical coherence tomography of choroid also revealed decreased choriocapillaris. Haider et al also described central macular hypofluorescence of FAG and RPE hyperpigmentation associated with nab-paclitaxel therapy. Decreased choroidal perfusion and hence impaired function of RPE might lead to CME.

Pentoxifylline, an alkylxanthine derivative, has been reported to increase submacular choroidal blood flow.[9,10] In our patient, macular edema resolved after cessation of paclitaxel and application of pentoxifylline. The thickness and intensity of choriocapillaris layer on OCT, and Arden ratio of EOG also reversed. However, this is only a case report. Whether pentoxifylline helps recovery of paclitaxel-induced macular edema needs more studies to clarify.

In summary, CME is a complication of paclitaxel, possible due to impairment of choriocapillaries and RPE. Physician should be aware of visual complaints when prescribing paclitaxel. Prompt diagnosis and discontinuation of the drug help visual recovery.

**Author contributions**

**Conceptualization:** Yuan-Chieh Lee.

**Data curation:** Chia-Hsin Shih.

**Formal analysis:** Yuan-Chieh Lee.

**Investigation:** Yuan-Chieh Lee.

**Methodology:** Yuan-Chieh Lee.

**Supervision:** Yuan-Chieh Lee.

**Validation:** Yuan-Chieh Lee.

**Writing – original draft:** Chia-Hsin Shih.

**Writing – review & editing:** Yuan-Chieh Lee.
**References**

[1] Teitelbaum BA, Tresley DJ. Cystic maculopathy with normal capillary permeability secondary to docetaxel. Optom Vis Sci 2003;80:277–8.

[2] Joshi MM, Garretson BR. Paclitaxel maculopathy. Arch Ophthalmol 2007;125:709–10.

[3] Telander DG, Sarraf D. Cystoid macular edema with docetaxel chemotherapy and the fluid retention syndrome. Semin Ophthalmol 2007;22:151–3.

[4] Baskin DE, Garg SJ. Abraxane-induced cystoid macular edema refractory to concomitant intravenous bevacizumab. Can J Ophthalmol 2011;46:200–1.

---

**Figure 2.** Angiography and electro-oculogram on attack of macular edema after paclitaxel treatment. Fluorescein angiography showed weak petaloid pooling in the macular region, but failed to detect any source of leakage in both eyes [A, B]. Indocyanine green angiography revealed an area of hypofluorescence of choroid at temporal upper fundus in the right eye and parafoveal areas in both eyes. Late petaloid pooling at fovea was noted (C–F). Electro-oculogram showed an Arden ratio of 1.34 in the right eye and 1.45 in the left eye (G). Two months after cessation of paclitaxel treatment, the Arden ratio increased to 1.61 in the right eye and 1.6 in the left eye (H).
[5] Georgakopoulos CD, Makri OE, Vasilakis P, et al. Angiographically silent cystoid macular oedema secondary to paclitaxel therapy. Clin Exp Optom 2012;95:233–6.

[6] Kuznetcova TI, Cech P, Herbold CP. The mystery of angiographically silent macular oedema due to taxanes. Int Ophthalmol 2012;32:299–304.

[7] Nakao S, Ikeda Y, Emi Y, et al. Possibility of Müller cell dysfunction as the pathogenesis of paclitaxel maculopathy. Ophthalmic Surg Lasers Imaging Retina 2016;47:81–4.

[8] Haider A, Bababeygy SR, Lu SY. Cystoid macular edema and macular pigmentation associated with nab-paclitaxel therapy. Retin Cases Brief Rep 2015;9:220–2.

[9] Flower RW, Lim JI. An ICG angiogram-based clinical method for characterizing the choroidal circulation used to assess the hemorrheologic effects of pentoxifylline. J Fr Ophtalmol 2000;23:756–62.

[10] Kruger A, Matulla B, Wolzt M, et al. Short-term oral pentoxifylline use increases choroidal blood flow in patients with age-related macular degeneration. Arch Ophthalmol 1996;114:27–30.