Clinical Case Report

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Impaired retinal pigment epithelium in paclitaxel-induced macular edema

A case report

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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 anticancer effect by restricting the mobility of microtubules and hence leading to

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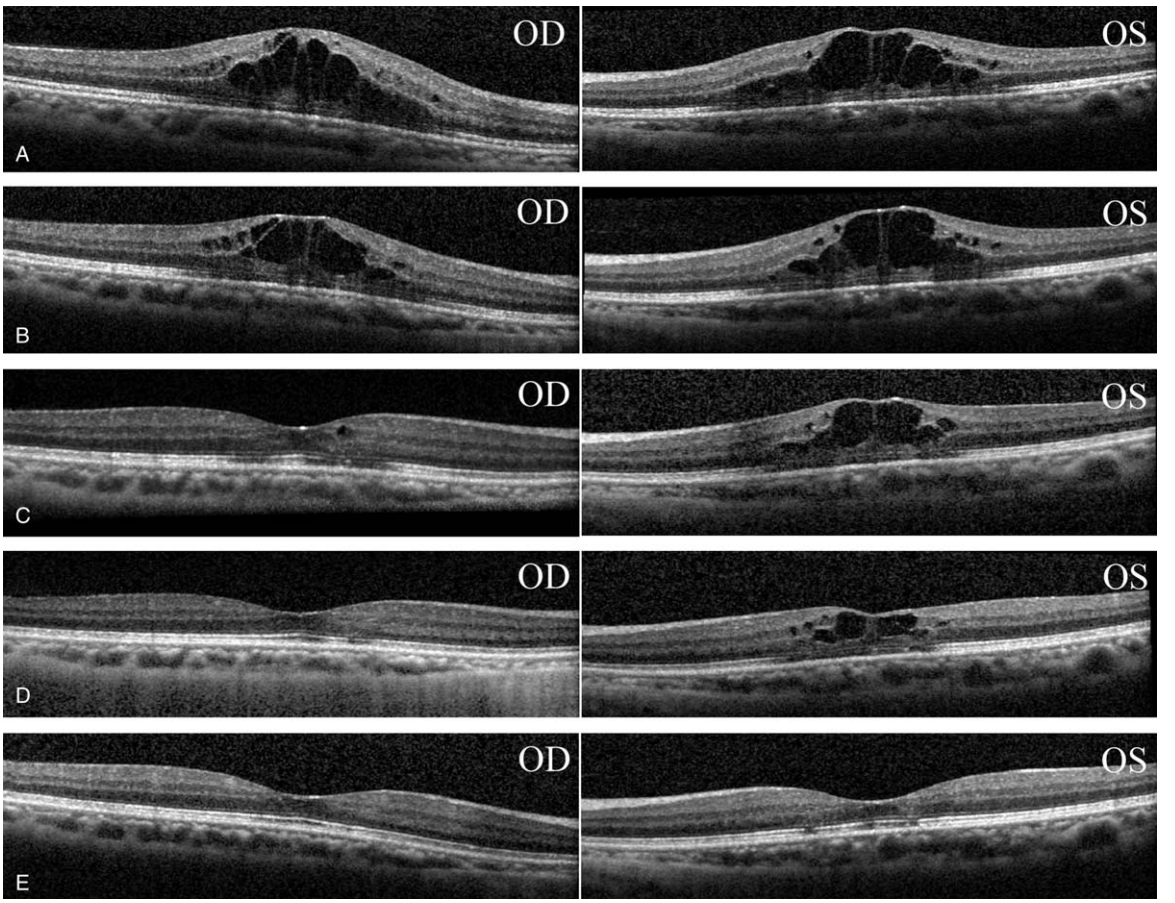

Figure 1. Serial images of optical coherence tomography (OCT) of this 60-year-old female patient after receiving paclitaxel. On first visit, OCT revealed prominent cystoid macular edema, and decreased choriocapillaris at subfoveal area in both eyes (A). One month later, there was still prominent macular edema (B). Two months later, the macular edema significantly decreased in the right eye (C). The macular edema almost resolved in the right eye by the end of third month, but there was still some extent of fluid spaces at macula in the left eye (D). Six months after cessation of paclitaxel treatment, the macular edema completely resolved in both eyes. The thickness and density of choriocapillaris at subfoveal area increased compared to that at disease onset (E). OCT = optical coherence tomography.

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.
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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.

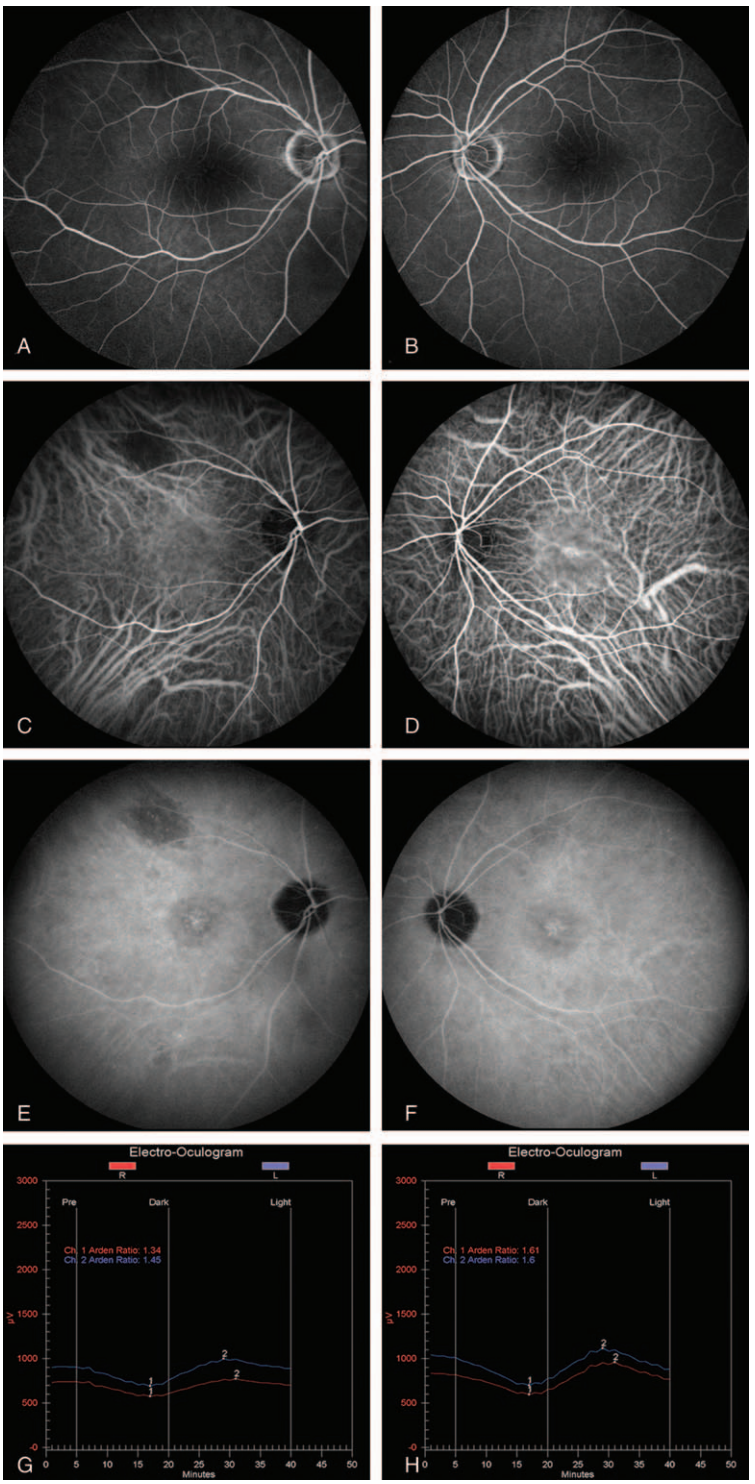

Figure 2. Angiography and electro-oculogram on attack of macular edema after paclitaxel treatment. Fluorescein angiography showed weak petaloid pooling in the macular region, but failed to detect any source of leakage in both eyes (A, B). Indocyanine green angiography revealed revealed an area of hypofluorescence of choroid at temporal upper fundus in the right eye and parafoveal areas in both eyes. Late petaloid pooling at fovea was also 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).

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