Bilateral macular oedema secondary to docetaxel treatment

Francesc March de Ribot, Patchara Jirapanyayut, Anna March de Ribot

Chemotherapeutic agents can have side effects on the retina, causing cystoid macular oedema (CME). Docetaxel is a taxane class of drugs widely used to treat a range of malignancies including prostate cancer. We present a 67-year-old male patient who was referred with vision loss after receiving three cycles of docetaxel as palliative treatment for advanced prostate cancer. On presentation, visual acuity was 6/12 (0.3 LogMAR) bilaterally with significant CME on fundoscopy and optical coherence tomography (OCT) in both eyes. Chemotherapy was discontinued following three cycles of docetaxel with insufficient response. Visual acuity improved to 6/7 (0.1 LogMAR) bilaterally, along with a resolution of the CME. We recommend an ophthalmological examination in patients with visual complaints receiving docetaxel chemotherapy. Every patient therapy must be individualised to optimise the best outcomes.

Background

CME is characterised by the increase of retinal thickening and the formation of cyst-like spaces in the macula. CME is due to the disruption of the normal blood-retinal barrier that leads to fluid leakage from the perifoveal retinal capillaries into the intra-cellular space of the retina, primarily affecting the outer plexiform layer of the retina.[1] Several chemotherapeutic agents, such as tamoxifen, interferon, trametinib, imatinib, cytarabine and taxanes have been reported to be associated with CME, but uveitis, optic neuritis, optic oedema and retinal vein and artery occlusions can also be associated.[2–4] BRAF inhibitor drugs, such as vemurafenib, have been associated with CME secondary to uveitis.[5,6] Additionally, all mitogen-activated protein kinase (MEK) inhibitor drugs, such as refametinib, selumetinib and cobimetinib, are associated with varying degrees of retinopathy effects. MEK inhibitors cause the accumulation of subretinal fluid, altering the retinal pigment epithelial (RPE) permeability.[7]

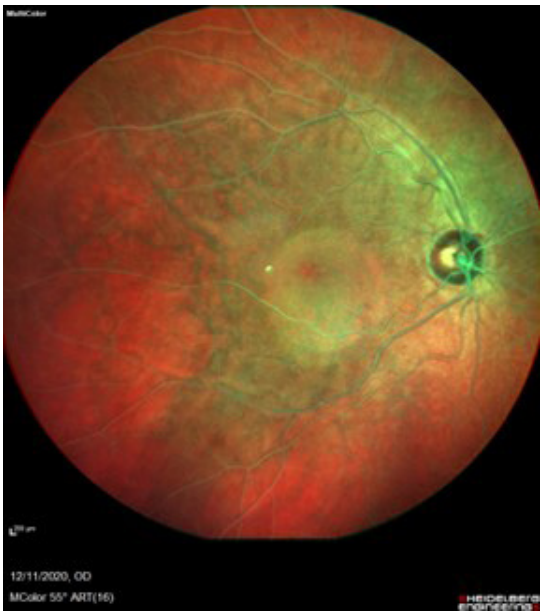
Symptoms of CME can manifest as visual disturbances, decreases in visual acuity, metamorphopsia, photosensitivity and altered colour perception.[8] These symptoms typically resolve spontaneously after stopping the chemotherapy treatment.[9,10] The prevalence of CME related to docetaxel is unknown, and only a few cases have been published. It looks reasonable that patients experiencing visual changes during chemotherapy undergo an evaluation by an ophthalmologist. Here, we present a case of bilateral CME secondary to docetaxel treatment.

Case description

A 67-year-old male was referred to the ophthalmology department following a bilateral visual loss. The patient had metastatic prostate cancer with lymph nodes metastasising (adenocarcinoma of the prostate stage T4 N0 M1). Over 3 years, he underwent multiple treatments, including androgen deprivation therapy (ADT), zoladex 3-monthly for 6 months, a radical dose of radiotherapy of 75 Gy delivered over 37 fractions, and a combination of abiraterone and prednisone. Finally, the patient received docetaxel as a palliative treatment. He experienced decreased vision following the first cycle and was then in the third cycle. The initial visual acuity was 6/12 (0.3 LogMAR) in both eyes, with an intra-ocular pressure of 16mmHg. The ophthalmological examination presented a clear cornea with mild cataracts. The posterior segments revealed a normal optic nerve along a significant bilateral CME (Figure 1). OCT confirmed the presence of CME with fovea involvement (Figure 2). The fluorescein angiography revealed CME with no leakage or increasing hyperfluorescence in the late phase (Figure 3). After excluding all the other probable causes of CME, it was considered secondary to docetaxel. The patient finished the third cycle of docetaxel, but due to an insufficient response and considering the eye side effects, the treatment was discontinued. Upon a follow-up examination at 6 weeks, symptomatology improved with a vision of 6/7 (0.1 LogMAR) bilaterally and a resolution of the CME. Unfortunately, the tumour progressed, leading the patient to opt for palliative care until his passing a few months later.

Figure 1: Colour fundus photography of the right (a) and left eye (b) showing CME.

a.



b.

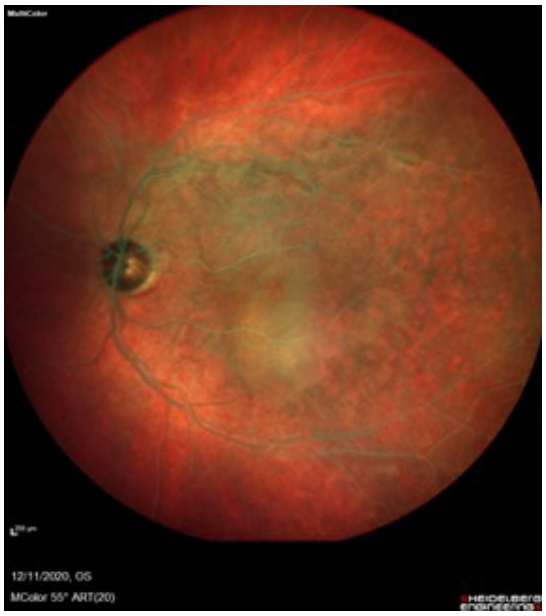
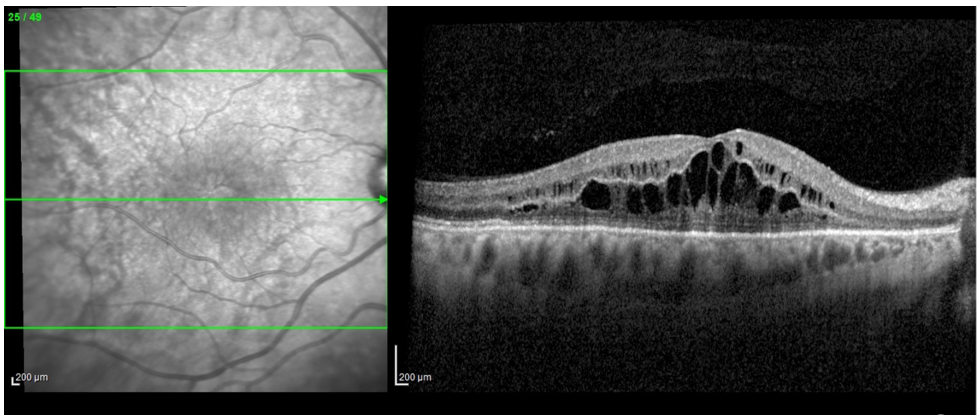


Figure 2: Spectral-domain optical coherence tomography of the right (a) and left eye (b) showing CME with intra-retinal fluid in the outer plexiform layer and cystoid changes in the inner retinal layer.

a.



b.

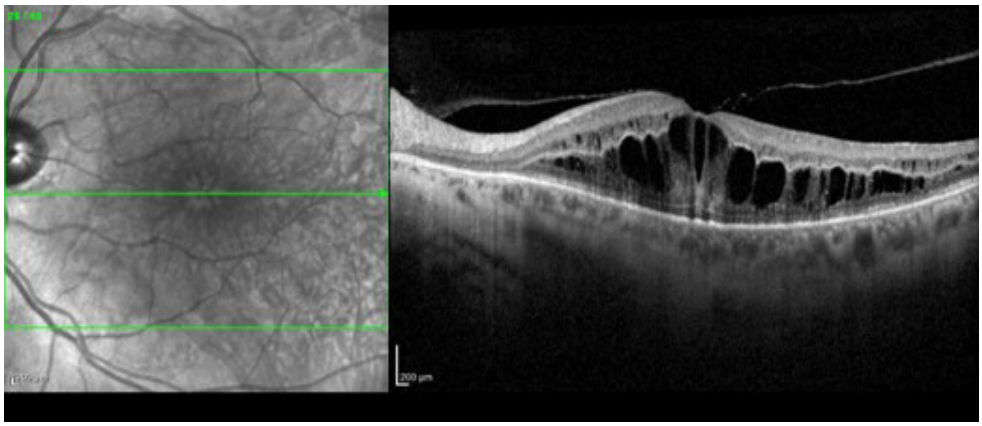
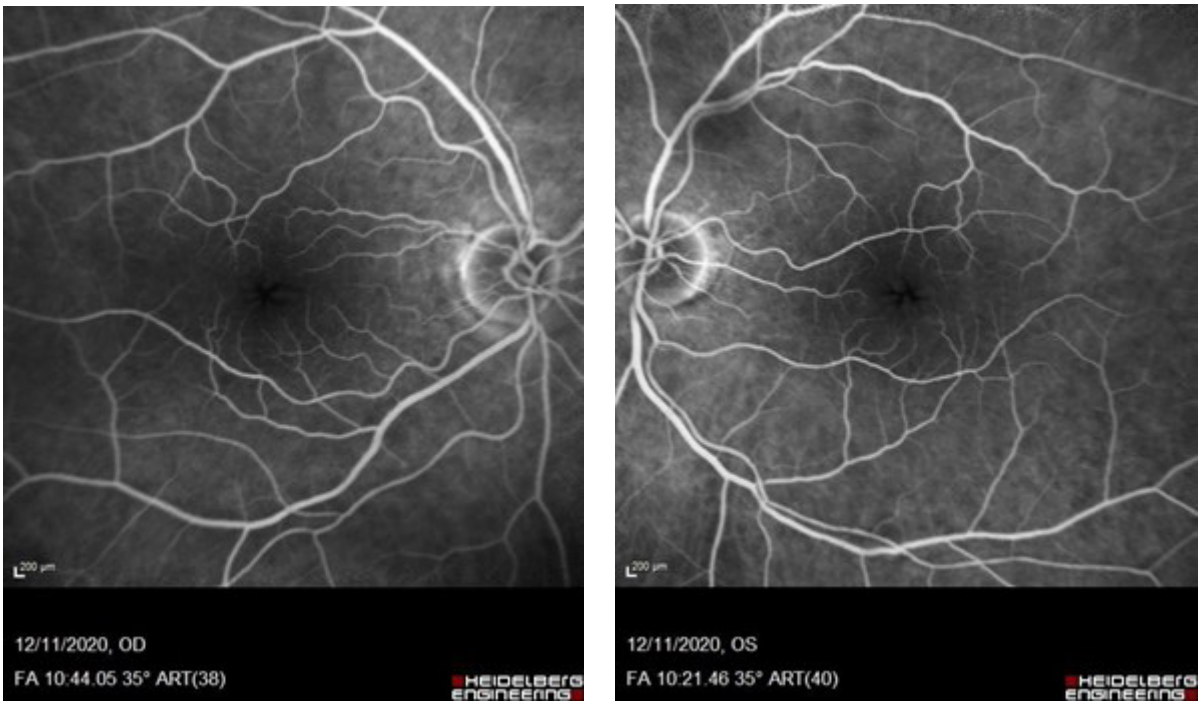


Figure 3: Fluorescein angiography showed bilateral CME with no leakage or increasing hyperfluorescence in the late phase.



Discussion

Docetaxel is a second-generation chemotherapeutic agent in the taxane drug family. Docetaxel prevents mitosis by interfering with microtubule growth and inhibiting microtubule network reorganisations. It is widely used as a chemotherapeutic agent in many types of cancers like breast cancer, certain stomach cancers, head and neck cancer, lung cancer and prostate cancer.[11,12]

Treatment with docetaxel has been exceptionally linked to CME, often appearing bilaterally with normal vascularity.[13] Published case reports commonly depict a pattern of bilateral vision loss secondary to the usage of docetaxel followed by improvement of CME after discontinuation of the treatment. The timeline for CME resolution post-treatment cessation varies from 2 weeks to 24 weeks depending on the severity of the CME itself.[14] Additionally, some cases report an association with fluid retention syndrome and retinitis pigmentosa.[3,15–18]

The pathophysiology underlying docetaxel-induced CME, as well as that of other taxane agents, remains unclear. Several theories have been proposed, including the dysfunction of RPE with intact choroid pigment epithelium border, Müller's cell toxicity and toxicity on microtubules leading to a decrease in fluid absorption across the RPE.[15,19]

Managing docetaxel-induced CME can pose challenges. Ceasing docetaxel may improve visual symptoms but could limit treatment options. However, oral carbonic anhydrase inhibitors (CAIs) have been described as helpful in paclitaxel- and docetaxel-induced CME.[20,21] CAIs function by altering the polarity of the ionic transport systems in the RPE, redirecting fluid away from the intra-cellular spaces. Topical CAIs have also been described to be effective, with fewer systemic side effects compared to their oral counterpart.[22,23]

Clinicians should remain vigilant about potential vision changes in patients undergoing docetaxel or other taxane therapies because the incidence is unknown. Management has to be individualised after discussing the benefits and risks of cessation of the treatment or other treatments with a multi-disciplinary approach.

COMPETING INTERESTS
The authors declare that they have no financial or non-financial competing interest.

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