Cancer Treatment Communications 7 (2016) 4–7

Contents lists available at ScienceDirect

Cancer Treatment Communications

journal homepage: www.elsevier.com/locate/ctrc

Docetaxel maculopathy ☆

Imran Haq [a,*], Sachin Salvi [a], Lawrence Brown [b], Ian Rennie [a], Paul Rundle [a]

[a] Department of Ophthalmology, The Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JP, United Kingdom
[b] Medical Physics (Electronics), Department of Ophthalmology, The Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JP, United Kingdom

ARTICLE INFO

Article history:
Received 16 April 2015
Received in revised form
26 August 2015
Accepted 8 September 2015

Keywords:
Taxotere
Docetaxel
Breast cancer
Maculopathy

ABSTRACT

A 56 year old retired theatre nurse who has metastatic breast carcinoma complains of reduced vision in the left eye since being started on Docetaxel (Taxotere), an oral anti-mitotic chemotherapeutic agent. Best corrected visual acuity was 6/18 in the left eye, and 6/9-1 in the right. Clinical examination and subsequent examination with optical coherence tomography and Intravenous Fluorescein angiography revealed evidence suggestive of drug related maculopathy. No abnormal findings were present in the right eye. As far as we are aware, this is the first reported case of maculopathy following commencement of Docetaxel with the absence of macular oedema.

1. Clinical practice points

- Docetaxel is of the chemotherapy drug class taxane.
- Mainstay of use is for breast cancer, prostate cancer, and non-small cell lung cancer.
- Main dose-limiting adverse effect of this agent is toxicity to bone marrow, though also associated with fluid retention syndrome consisting of peripheral oedema and/or pleural effusion.
- First documented case of non-oedematous maculopathy.
- Patients started on Docetaxel therapy should be counselled for possible drug associated toxic maculopathy, and that this should be considered in all patients complaining of visual disturbance.

2. Case report

A 56 year old retired theatre nurse under the care of the oncologist for the treatment of advanced breast cancer is referred to our ophthalmology department after complaining of deteriorating vision particularly effecting the left eye. The patient has extensive lymph node and liver metastases for which she is on palliative oral chemotherapy in the form of the anti-mitotic Docetaxel (Taxotere), mainly used in the treatment of breast, ovarian, prostate, and non-small cell lung cancer.

The patient was initially diagnosed with breast cancer in December 2009, and underwent a mastectomy soon afterwards. Metastatic spread was discovered in July 2012, and chemotherapy was subsequently initiated in August 2012, on a combination of Docetaxel and steroid. Soon after commencement, the patient began to notice that her vision was starting to deteriorate, with a distinct lack of clarity. The patient initially ignored the symptoms, but in early 2013 visited her opticians felt some changes at the macula were present. It was at this stage that the Oncologists referred the patient for an Ophthalmology opinion, mainly to rule out the presence of choroidal metastases.

The patient's chemotherapeutic treatment plan consisted of monthly intravenous infusions of 100 mg/m^2 of docetaxel. The patient was on no other concurrent medication, and there was no history of tamoxifen use during the period of chemotherapy.

On presentation to the Ophthalmology department, her initial visual acuity was recorded at 6/9-1 in the right eye, and 6/24 in the left (improvement to 6/18 pin-hole). Intraocular pressures were within normal limits. Anterior segment examination was unremarkable, and dilated fundal examination revealed no evidence of vitritis. Dry macular changes were noted in the left eye indicative of toxicity (Fig. 1). This was confirmed on optical coherence tomography (Stratus OCT; Carl Zeiss Meditec, Dublin, CA, USA). Fluorescein angiography exhibited normal filling of the choroidal and retinal vessels and an intact parafoveal capillary net, and no evidence of leakage on late frames (Fig. 2). Electrodiagnostic testing was carried out to confirm macular dysfunction (Fig. 3).

The patient denies any past ocular history of note, and has never undergone any intraocular surgery, or ever taken prostaglandin eye drops. Of note in her medical history, the patient is Factor XI deficient. She does not suffer from diabetes. There is no familial ocular history of note.

☆ The Royal Hallamshire Hospital.

* Corresponding author.
E-mail address: i.haq@me.com (I. Haq).

http://dx.doi.org/10.1016/j.ctrc.2015.09.004

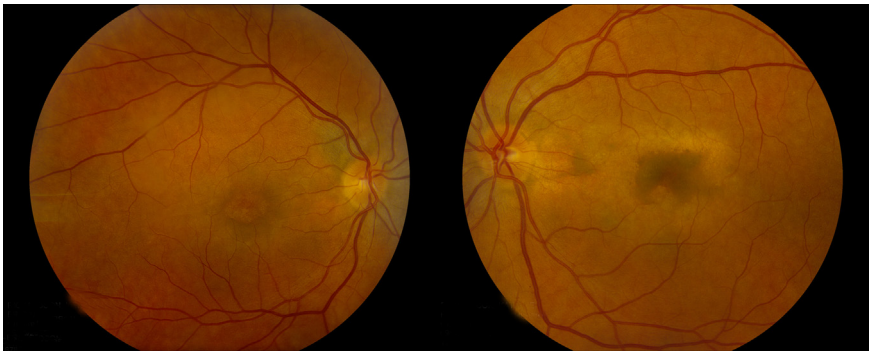

Fig. 1. Fundal photographs displaying Retinal Pigment Epithelium atrophy and hyperpigmentation in an almost "bullseye" pattern in both maculae.

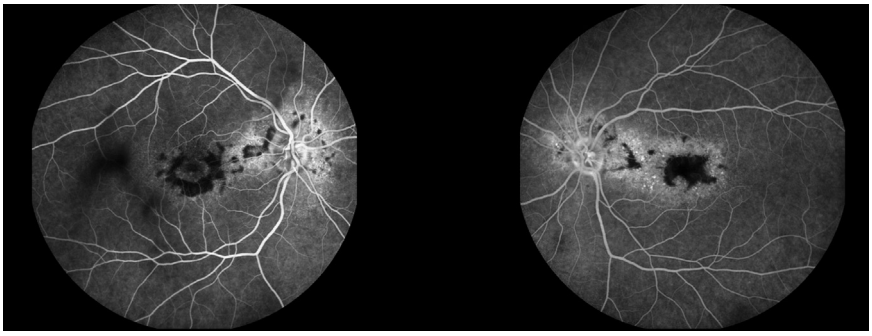

Fig. 2. Intravenous Fluorescein angiography exhibited normal filling of the choroidal and retinal vessels and an intact parafoveal capillary net, with no evidence of leakage on late frames.

Niacin maculopathy, Goldmann-Favre syndrome, and congenital X-linked retinoschisis were unlikely other differential diagnosis, given the history of onset and findings on clinical examination.

3. Discussion

Docetaxel is of the chemotherapy drug class taxane, and is a semi-synthetic analogue of paclitaxel (Taxol), an extract from the bark of the rare Pacific yew tree Taxus brevifolia, and acts by inducing microtubular stability and disrupting the dynamics of the microtubular network [1]. The mainstay of use is for breast cancer, prostate cancer, and non-small cell lung cancer. Dosage varies from 60 to 100 mg/m^2 administered as an infusion every 3–4 weeks [2]. The main dose-limiting adverse effect of this agent is toxicity to bone marrow. Docetaxel has also been associated with fluid retention syndrome consisting of peripheral oedema and/or pleural effusion. Ophthalmic adverse effects include decreased vision, scintillating scotomas, and abnormal visual evoked potentials [3].

There are five documented cases of maculopathy secondary to paclitaxel in the literature, some of which were treated successfully with acetazolamide administration [4–7]. This would only be effective however if there was the presence of fluid in the macular; i.e. the presence of a cystoid macular oedema. In our case however, acetazolamide would have no effect given the absence of any macular oedema, and to our knowledge, the only other reported case of maculopathy secondary to Docetaxel alone was cystoid in appearance (there is one report of simultaneous docetaxel-induced cystoid macular oedema in both eyes, but this was in the presence of systemic fluid retention syndrome secondary to docetaxel, and is therefore the result of a systemic mechanism) [2,8].

The authors in the prior literature have hypothesised that the occurrences may have been either as a result of intracellular fluid accumulation and the slight leakage of extracellular fluid caused by toxicity to Muller cells [4], or due to the fact that that the passage of fluid increases in the capillary due to fluid retention syndrome, which causes oedema and protein leakage of the capillary [8]. This results in cystoid macular oedema occurs due to selective damage of the blood ocular barrier from molecules with a weight less than that of fluorescein or to slow fluid movement that cannot be detected on fluorescein angiography [8].

With our patient, there was no evidence of any retinal traction, or any underlying diseases that may cause a maculopathy. Given the fact that, unlike in the other reported cases, there was no evidence of a systemic fluid retention syndrome, the observed maculopathy is probably a result of cellular toxicity derived from the suppression of intracellular microtubule reorganisation [5]. The patient was on no other medication known to cause macular disease, bar steroid treatment-this however would not result in the dry macular changes that were found, and therefore not responsible [9]. On the Naranjo adverse drug reaction probability (ADR) scale, we would grade this ADR as "probable", based on a score of 6 (on the basis of previous conclusive reports, the fact that the ADR occurred after commencement of the drug, the absence of alternative causes, and the confirmation of the ADR with objective evidence).

Although the maculopathy is currently limited to one eye, with longer term administration, it is likely that the other eye will probably become involved. This has already been shown to be the case with paclitaxel, with subsequent contralateral eye involvement in due course with continuing treatment. In the above-mentioned literature, chemotherapy stopped at the advent of cystoid macular oedema; our patient however, opted to persevere with chemotherapy. Unfortunately the patient succumbed to the breast cancer very soon after being seen by the Ophthalmology team; we are therefore unable to comment on the progression or otherwise of the maculopathy under continuous Docetaxel treatment.