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Posterior Segment Toxicity Following Gemcitabine and Docetaxel Chemotherapy

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Abstract

Purpose—To report outer retinal disruption and uveal effusion following gemcitabine and docetaxel combination therapy.

Case Report—A 78-year-old woman presented with blurry vision following two cycles of gemcitabine and docetaxel combination chemotherapy for stage IV sarcoma. At presentation, visual acuity (VA) was finger counting and 20/25 in the right and left eyes, respectively. Slit lamp examination and B scan ultrasonography revealed severe uveal effusion in the right eye and choroidal folds in the left eye. Spectral domain optical coherence tomography showed disruption of photoreceptor inner segment ellipsoid band in the right eye. The patient was monitored weekly with ophthalmic examination and B scan ultrasonography, while continuing with gemcitabine monotherapy. At 8 weeks follow up, uveal effusion improved considerably and VA was 20/40 and 20/20 in the right and left eyes, respectively.

Conclusions—Uveal effusion and outer retinal disruption were reported following gemcitabine and docetaxel chemotherapy. Early detection and close ophthalmic monitoring may allow concurrent cancer treatment and prevention of possible chemotherapy-induced ocular side effects.

Keywords

retina; uveal effusion; gemcitabine; docetaxel; chemotherapy

Ocular adverse effects of anti-cancer chemotherapy are not uncommon, but are often underestimated as compared to more serious adverse effects in other organ systems.^{1, 2} The development of new agents and combination chemotherapies with more aggressive regimens have resulted in an increase in the number of cases with chemotherapy-induced ophthalmic side effects.¹ Although there is a wide spectrum of ocular toxicities induced by cancer therapy,^{1–3} to our knowledge there are no reports of outer retinal disruption and uveal effusion due to gemcitabine or docetaxel chemotherapy. We present a subject with sarcoma of unknown origin who developed outer retinal disruption and uveal effusions after chemotherapy with combination regimen of gemcitabine and docetaxel.

CASE REPORT

A 78-year-old woman with stage IV sarcoma presented to the emergency department (ED) with the complaint of vision loss in the right eye following two cycles of gemcitabine and docetaxel combination chemotherapy. The last combination chemotherapy was one week before the presentation. The ophthalmic history included an ophthalmological examination forty days before these symptoms which showed visual acuity (VA) of 20/20 in both eyes. At that time, the patient had a history of glaucoma treated with topical timolol and latanoprost, but without any sign of choroidal detachment or foveal striae. Her past medical history included diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease, aortic and mitral valve insufficiency, and glaucoma. Her medications were insulin, amlodipine, lisinopril, aspirin, and subcutaneous heparin. There was no recent change in her medications intake.

At ED, brain and orbit magnetic resonance imaging scan was performed to assess the extent of cancer metastasis which showed detachment of the medial and lateral retinal walls of the right eye and anterior and lateral retinal walls of the left eye. An ophthalmology consult was ordered which revealed VA of finger counting and 20/25 in the right and left eye, respectively. Extraocular muscle movements were within normal range. IOP was 19 mm Hg in both eyes, likely due to non-compliance with glaucoma treatment. Dilated fundus examination showed an inferior retinal versus choroidal detachment in the right eye with multiple domes of smooth choroidal effusions which were most prominent in the inferonasal retina. There was a positive shifting fluid on retinal exam without signs of bleeding, tear or break. B-scan ultrasonography of the right eye revealed a large inferior choroidal detachment with multiple domes of smooth choroidal effusions. Laboratory tests showed an increase in the creatinine level from 0.98 mg/dL before chemotherapy to 1.34 mg/dL after chemotherapy. Patient's symptoms were mostly related to the history of metastatic sarcoma. Topical atropine was prescribed, and a follow up visit in the retina clinic was set up.

In the follow up visit seven days later at the outpatient Retina Clinic, VA in the right eye improved to 20/300 and IOP decreased to 14 mm Hg bilaterally. Slit-lamp biomicroscopy disclosed a shallow anterior chamber in the right eye, and no cell and keratic precipitates in both eyes. Dilated fundus examination confirmed foveal striae and choroidal detachments nasally and inferiorly with overlying subretinal fluid inferiorly in the right eye and choroidal folds in the left eye. Scanning laser ophthalmoscope (SLO) imaging and B-scan ultrasonography revealed severe choroidal detachments which were greater in the right eye than the left eye supporting the diagnosis of uveal effusion (Figures 1 and 2). Spectral domain optical coherence tomography (SD-OCT) was performed which showed disruption of the photoreceptor inner segment ellipsoid band in the right eye in comparison to the previous SD-OCT images before initiating the chemotherapy (Figure 3). After consultation with the referring oncologist, since chemotherapy was critical for patient's health, the decision was made to discontinue docetaxel due to reported ocular manifestations and continue the gemcitabine for the next cycles, as there have been no reported ocular adverse effects of gemcitabine. The patient was instructed to return to clinic one week later for follow up or sooner if urgent symptoms including further vision loss and eye pain occurred. Patient was followed weekly for the next two weeks.

On the following visits, the patient reported improvement in her blurred vision. Ophthalmic examination and B-scan ultrasonography were unchanged. During the second cycle of chemotherapy, the patient developed a pericardial effusion due to disease progression, and thus gemcitabine was discontinued for one week and then resumed. Eight weeks after presentation to ED and while patient was on gemcitabine therapy only, the uveal effusions and ellipsoid layer disruption in the right eye improved as displayed in Figures 2 and 3. Laboratory tests at last follow up showed a creatinine level of 1.08 mg/dL. The patient achieved a final VA of 20/40 and 20/20 in the right and left eyes, respectively.

DISCUSSION

Uveal effusions due to cancer chemotherapy are uncommon, but have been reported with other medications, particularly sulfa-based medications,⁴ and anti-depressants.⁵ The SD-OCT findings in this case appear to suggest a drug effect on the neurosensory retina, most likely involving the photoreceptors with disruption of photoreceptor inner segment ellipsoid band. There has been one reported case of unilateral uveal effusion after intracarotid etoposide phosphate and carboplatin therapy;⁶ however there are no reports about outer retina disruption and uveal effusion following chemotherapy.

Docetaxel is a member of taxanes which inhibit mitosis in cancer cells. The most common reported ophthalmic side effects of docetaxel include canalicular and nasolacrimal duct obstruction,⁷ erosive conjunctivitis,⁸ and cystoid macular edema.³ Gemcitabine is an antimetabolite agent which prevents deoxyribonucleic acid (DNA) replication and arrests tumor growth. To our knowledge, there have been no reported ocular adverse effects of gemcitabine, but other antimetabolites with similar mechanism including 5-fluorouracil and cytosine arabinoside can induce ophthalmic side effects such as ocular pain,⁹ blurry vision,^{9, 10} photophobia,^{9, 10} tearing,^{9, 10} macular edema,¹¹ conjunctivitis,¹² and also bilateral vision loss.¹³

The exact cause of outer retinal disruption and uveal effusions in this patient is unclear. However, since the ocular symptoms improved while the patient was on gemcitabine only, it is likely that either docetaxel monotherapy or the combination therapy of gemcitabine and docetaxel caused visual manifestations. Docetaxel through a capillary leak syndrome-like mechanism has been shown to cause peripheral edema and pleural effusion, which is generally reversed with cessation of treatment or pretreatment with steroids.^{14–16} It is possible that docetaxel monotherapy may have been the cause of uveal effusion and outer retinal disruption in this patient through a similar mechanism. In addition, combination therapy may increase the risk and systemic conditions, including, diabetes, chronic kidney disease and hypertension, may accelerate development of ocular toxicities.² Subjects with elevated creatinine levels may have significant toxicity even at reduced doses of gemcitabine.¹⁷ The simultaneous occurrence of increased creatinine level and ocular symptoms may suggest probable increased toxicity of chemotherapy agents.

In summary, uveal effusion and outer retinal disruption were reported following gemcitabine and docetaxel chemotherapy. Early detection, and close ophthalmic monitoring may allow concurrent cancer treatment and prevention of chemotherapy-induced ocular side effects.

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Figure 1.
B Scan ultrasonography of the right eye at first visit in the Retina Clinic (while on combination therapy).

Figure 2. Scanning laser ophthalmoscope images of the right and left eye at first visit in the Retina Clinic (while on combination therapy), (**A, B**); and at 8 weeks follow up (while on gemcitabine only), (**C, D**). White arrows denote severe uveal effusions in the right eye (**A**) and black arrow denotes choroidal folds in the left eye (**B**). Improvement of uveal effusions and choroidal folds in the right (**C**) and left (**D**) eye at 8 weeks follow up.

Figure 3. Spectral domain optical coherence tomography (SD-OCT) image of the right eye 40 days before ocular symptoms (while not on chemotherapy), (A); at first visit in the Retina Clinic (while on combination therapy), (B); and at 8 weeks follow up (while on gemcitabine only), (C). White arrow denotes the disruption of photoreceptor inner segment ellipsoid band after combination chemotherapy (B).