Kapesitabin ile Tedavi Edilen Bir Hastada Bilateral Kistoid Makula Ödemi

Bilateral Cystoid Macular Edema in a Patient Treated With Capecitabine

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ÖZ

Yetmiş altı yaşındaki kadın hasta son 5-6 aydır olan bilateral ağrısız görme azalması şikayetiyle başvurdu. Düzeltilmiş en iyi görme keskinlikleri sağ gözde 20/640, solda 20/500 idi. Biyomikroskobik muayenesinde bilateral psödofak olması dışında bir özellik yoktu. Göz içi basınçları normaldi. İndirekt retina ve optik koherens tomografi (OKT) muayenesinde bilateral şiddetli kistoid maküla ödemi izlendi. Hastaya 10 ay önce kolon kanseri nedeniyle oral kapesitabin başlanmış olduğu ve 4 ay önce tedavisinin tamamlanmış olduğu öğrenildi. Kapesitabin dışında sistemik veya topikal bir ilaç kullanım öyküsü yoktu. Asetozolamid tablet, topikal stereoid ve nonstereoid anti-inflamatuar damla tedavisinden bir ay sonra düzeltilmiş en iyi görme düzeyleri sağ gözde 20/200, solda 20/63'e yükseldi. OKT'de kistoid maküla ödeminin sağ gözde azaldığı, sol gözde kaybolduğu görüldü. Olgumuz literatürde kapesitabine kullanımına bağlı bilateral kistoid maküla ödemi geliştiği raporlanan ilk olgudur.

Anahtar Kelimeler: Kolon kanseri, kapesitabin, maküla ödemi.

ABSTRACT

A 76-years old woman presented to our clinic with bilateral painless decrease in vision for 5 to 6 months. Best corrected visual acuity was 20/640 in the right and 20/500 in the left eye. Slit lamp examination was unremarkable except bilateral pseudophakia. Intraocular pressures were within normal limits. Bilateral severe cystoid macular edema was identified in indirect retina examination and optical coherence tomography (OCT). Patient was prescribed oral capecitabine therapy 10 months ago, which was completed 4 months ago. There was no history of topical or systemic medication other than capecitabine. After treatment with oral acetazolamide and topical steroid and non-steroidal eye drops, best corrected visual acuity was increased to 20/200 in right eye and 20/63 in the left eye. On OCT, it was seen that cystoid macular edema was regressed in the right eye and disappeared in the left eye. This is the first case report about bilateral cystoid macula edema related to capecitabine therapy in the literature.

Key Words: Colon cancer, capecitabine, macular edema.

GİRİŞ

Capecitabine (Xeloda-Roche-United Kingdom) is a pro-drug that is converted to 5-fluoruracile (5-FU) by thymidine phosphorylase within cancer tissue. It is an oral agent used as adjuvant therapy after resection in colon cancer. The most common adverse effect is hand-foot syndrome[1]. Ocular adverse effects are rare, including retinal vein thrombosis, superficial keratitis and subepithelial deposits, and lacrimal duct occlusion reported in case reports[2-5]. Here, we aimed to present a case developed bilateral cystoid macular edema (CME) related to oral capecitabine use.

CASE REPORT

A 76-years old woman having no systemic disorder other than sigmoid colon adenocarcinoma presented with decreased vision for 5-6 months. In the history, it was found that the patient received chemotherapy for sigmoid colon adenocarcinoma in another facility.

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From patient's file, it was found out that chemotherapy regimen was initiated with oral capecitabine at dose of 1000 mg twice daily for 2 weeks; followed by a week of drug-free period (3-weeks session) and that, on session 4 which was given 70 days after commencement of chemotherapy, capecitabine dose was escalated to 2000 mg twice daily by oncology department. The patient was consulted to ophthalmology department with progressive bilateral painless decrease in vision on month 3 after commencement of treatment (6 days after completion of session 4). In ophthalmological examination, the best corrected visual acuity was recorded as 20/640 in right eye and 20/500 in the left eye. The slit lamp examination was normal other than bilateral pseudophakia and intraocular pressures were found to be normal. Bilateral severe cystoid macular edema was detected in indirect retina examination and on OCT. Central macular thickness was found to be 613 µm in right and 578 µm in left eye on Cirrus HD spectral domain OCT (Carl Zeiss Meditec, Dublin, CA, USA) (Figure 1).

Following ophthalmology consultation, oncology department evaluated intracranial metastasis but no metastasis was detected. Capecitabine was withdrawn for 2 weeks; then, recommenced and evening dose was reduced to 1500 mg. However, the patient did not attend to control visit; thus, received no treatment for CME. The patient received additional 4 sessions of capecitabine therapy (3 months at latter dose). The patient presented to our clinic with decreased vision in both eyes 4 months after completion of treatment. In ophthalmological examination in our clinic, best corrected visual acuity was 20/500 in right eye and 20/400 in left eye. Slit lamp examination revealed bilateral pseudophakia with no other remarkable finding and IOP was normal in both eyes. Bilateral CME was observed in indirect retina examination. On fundus fluorescein angiography (FFA), petaloid hyperfluorescence caused by filling of dye within cystoid spaces was observed at late phase, which is compatible with CME. There was mild hyperfluorescence overlying right optic disc at late phase, although it was failed to distinguish clearly due to posterior capsular opacity. On spectral domain (SD)-OCT (Heidelberg Engineering, Inc., Heidelberg, Germany), bilateral CME and subfoveal serous detachment at left were observed. Central macular thickness was 475 µm at right and 437 µm at left (Figure 2).

The best corrected visual acuity was 20/200 in right and 20/63 in left eye one month after treatment including acetazolamide (250 mg, twice daily), topical prednisolone acetate (1% eye drop; four times daily) and nepafenac (0.1% eye drop; three times daily. On SD-OCT, central macular thickness was 304 µm at right and 293 µm at left (Figure 3). There was marked recovery in bilateral CME. Persisting reduction in vision in right eye was attributed to posterior capsular opacity.

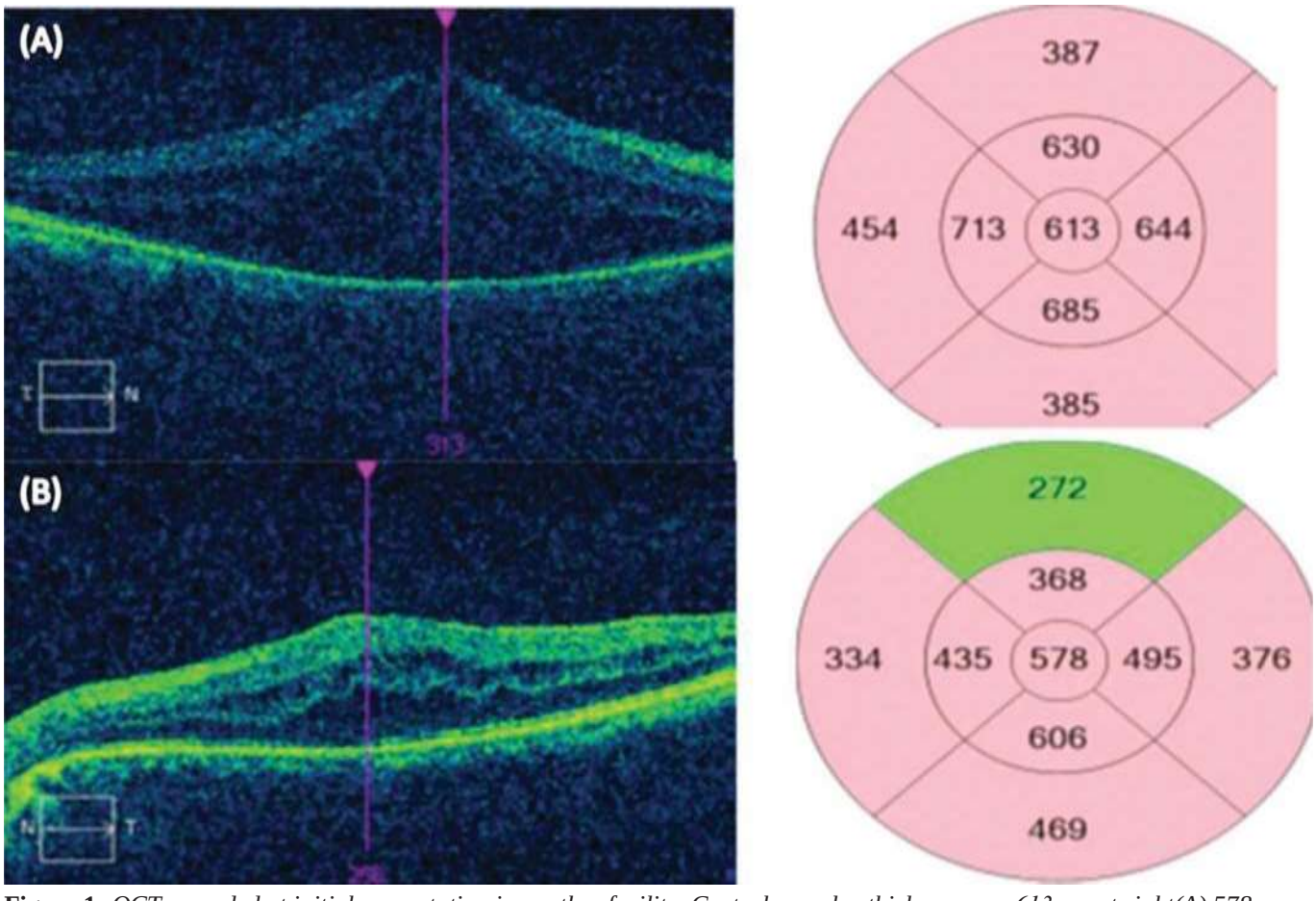

Figure 1: *OCT recorded at initial presentation in another facility. Central macular thickness was 613 µm at right(A) 578 µm at left (B).*

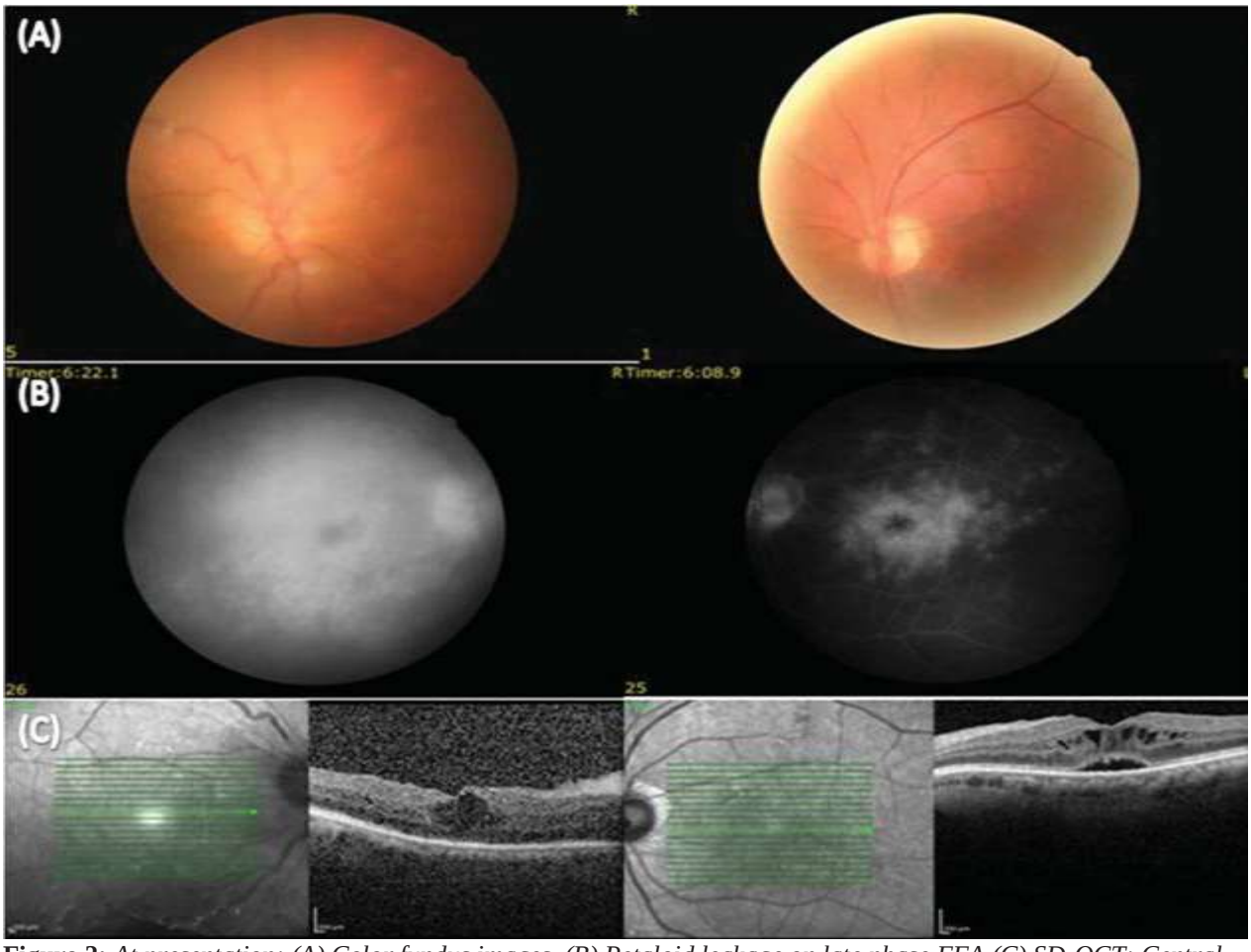

Figure 2: *At presentation: (A) Color fundus images. (B) Petaloid leakage on late phase FFA (C) SD-OCT: Central macula thickness was 475 µm at right and 437 µm left.*

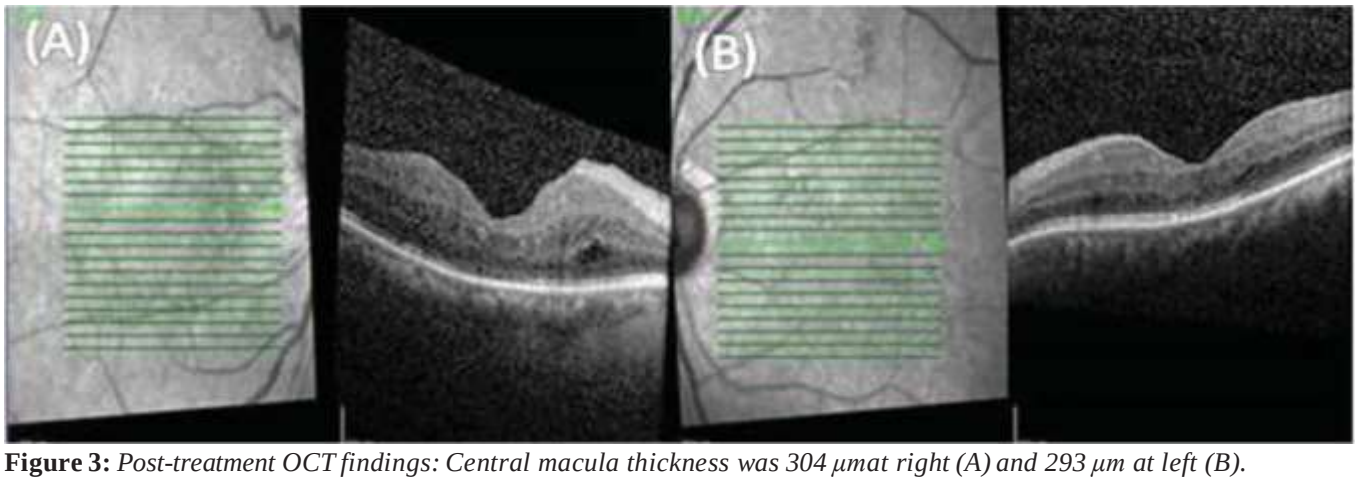

Figure 3: *Post-treatment OCT findings: Central macula thickness was 304 µmat right (A) and 293 µm at left (B).*

DISCUSSION

The cystoid macular edema (CME) is a common clinic feature of several conditions rather than being a specific entity. Ocular conditions associated to CME development include diabetic retinopathy, retinal vascular surgery, uveitis, and post-cataract surgery (Irvine Gass)[6]. Anti-diabetic agents (thiazolidinediones), chemotherapeutic agents such as taxanes (docetaxel and paclitaxel), tamoxifen, interferon, and several systemic agents such as niacin can cause CME. Topical prostaglandin analogs, epinephrine, ß-blockers and preservatives can also cause CME[7].

Capecitabine is a pro-drug that is converted to 5-fluoruracile (5-FU) by thymidine phosphorylase within cancer tissue.

It was approved for oral use in metastatic colon cancer by American Food and Drug Agency (FDA)[1]. Capecitabine-related ocular adverse events have been reported as case reports. In a case report, retinal vein thrombosis was attributed to oral capecitabine used in combination with intravenous bevacizumab[2]. In another case report including 2 patients, capecitabine-related superficial keratitis and subepithelial corneal deposits were observed[3]. In another case, bilateral lacrimal duct occlusion was developed. In this case, it was seen that epiphora was resolved after withdrawal of capecitabine[4]. In the experimental studies on dogs, superficial keratitis was developed in 2 of 6 subjects with capecitabine use following renal transplantation[5].

Considering this agent as 5-FU, retinal pathology related to systemic 5-FU use was reported in one case in the literature. However, bilateral central serous chorioretinopathy in this case was attributed to intravenous dexamethasone use for management of chemotherapy-related nausea and vomiting[8].

Post-cataract surgery CME presents with painless decrease in vision and is known as Irvine Gass syndrome. It is generally associated with clinical resolution after month 6[9]. The Irvine Gass syndrome was excluded in our patient as our patient underwent cataract surgery 15 years ago and decreased vision developed only 6 months ago. Our patient had no history of systemic vascular or ocular disorder or topical agent use. The patient reported that decreased vision occurred following chemotherapy. No additional chemotherapeutic use was reported. The CME was improved but not completely resolved after completion of capecitabine therapy despite lack of specific treatment (Figure 1 and Figure 2). Based on history and findings, macular edema was attributed to capecitabine use.

In this case, CME development may have been due to cellular dysfunction leading fluid transport in RPE and/or inflammation disrupting retina-blood barrier caused by capecitabine. Treatment response to drug used favors this assumption. Carbonic anhydrase inhibitors enhance fluid transport across retinal pigment epithelium by inhibiting carbonic anhydrase and probable RPE dysfunction might have been resolved by acetazolamide[10]. In our case, a mild hyperfluorescence was observed at right optic disk on FFA. Although clear images could not be captured in posterior capsule in right eye, no considerable cell presence or retinitis or choroiditis foci was observed in anterior chamber and vitreus; however, mild hyperfluorescence at right optic disc may indicate posterior segment inflammation. Non-steroidal anti-inflammatory drugs such nepafenac can be helpful in the treatment of macular edema by inhibiting cyclooxygenase while corticosteroids via phospholipase A2 inhibition. In our case, drug-related inflammation might have been suppressed by these treatments, aiding recovery of macular edema[11].

In conclusion, capecitabine, a chemotherapeutic agent, may cause cystoid macular edema and decreased vision, which may improve with treatment. Oncologist should refer patients suffering decreased vision during capecitabine therapy.

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