Regression of Choroidal Metastasis of Non-small-cell Lung Cancer with Intravitreal Bevacizumab and Photodynamic Therapy

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A 56-year-old female patient presented with decreased visual acuity in her right eye lasting for one day. During the first visit, best corrected visual acuity (BCVA) was 20/80 and 20/20, in the right and left eye, respectively. Fundus examination of the right eye revealed an elevated mass in the superior area of the optic disc and exudative retinal detachment in the macula. Choroidal metastatic tumor secondary to non-small-cell lung cancer (NSCLC) was diagnosed after systemic work up. Photodynamic therapy (PDT) and the intravitreal bevacizumab injection for choroidal metastatic carcinoma were performed. After six months, the BCVA of the right eye was improved to 20/25. Complete regression of the tumor was noticed and serous detachment was resolved. There has been no recurrence for six months. We observed that combined treatment with PDT and intravitreal bevacizumab injection is effective in BCVA improvement and tumor regression, in a patient with choroidal metastasis of NSCLC.

Keywords: Bevacizumab; Choroidal metastasis; Non-small-cell lung cancer; Photodynamic therapy

INTRODUCTION

The most widely used treatments of metastatic carcinomas of the choroid are systemic chemotherapy and external beam radiotherapy. In addition, brachytherapy, photodynamic therapy (PDT), proton radiation therapy, cryotherapy, and transpupillary thermotherapy may be used [1]. Similarly, there has been a recent report of tumor regression when systemic chemotherapy was combined with intravitreal injection of bevacizumab, in patients with choroidal metastatic cancers [2]. Herein, we report a case of regression of choroidal metastasis secondary to lung cancer, which was treated with PDT and intravitreal bevacizumab combination therapy.

CASE REPORT

This study was approved by the institutional review board of Soonchunhyang University Seoul Hospital, and written informed consent was obtained from the participant.

A 56-year-old female patient presented with decreased visual acuity in her right eye lasting for one day. She did not have any medical history. Her best corrected visual acuity (BCVA) was 20/80 and 20/20, in the right and left eye, respectively. Fundus examination of the right eye revealed an elevated subretinal mass in the superior area of the optic disc and exudative retinal detachment in the macula. The mass was about 5 disc diameter in size and extended to superonasal quadrant (Fig. 1A). Fluorescein angiography (FA) showed multiple lobulated hyperfluorescent lesions, with surrounding leakage in the superior area of the optic disc (Fig. 2A). Optical coherence tomography (OCT) showed exudative detachment corresponding to fundus examination (Fig. 2B). Choroidal metastatic tumor was suspected, and systemic work up was conducted. A lobular mass in the right upper pulmonary lobe was detected on the chest computed tomography (CT), and multiple metastatic lesions were found. Lung adenocarcinoma was diagnosed after biopsy.

The patient started systemic chemotherapy with gefitinib 250 mg once daily. However, after 2 weeks, the patient refused to continue treatment due to extensive skin rashes and severe nausea. Thus, the systemic chemotherapy was completely stopped. Meanwhile, PDT and the intravitreal bevacizumab injection for choroi-
dal metastatic carcinoma were to be performed. PDT was conducted according to the TAP (treatment of age-related macular degeneration with photodynamic therapy) standards with 6 mg/m² iv. of verteporfin for 10 minutes [3]. After 5 minutes, diode laser (689 nm) was administered (600 mW, 50 J/cm², 83 seconds). This procedure was applied in overlapping manner, to cover the entire area of lesions. Four days after the treatment, new exudative detachment occurred in the inferior retina (Fig. 1B). After a month, the detachment was improved, but there was no change in the tumor size. Consequently, intravitreal bevacizumab 1.25 mg/0.05 mL injection was performed. PDT was repeated, as previously stated, after a month. Intravitreal bevacizumab injection was repeated after another month.

After six months treatment, the BCVA of the right eye was improved to 20/25. Complete regression of the tumor was noticed and serous detachment was resolved (Fig. 1C). FA demonstrated decreased leakage within both tumor mass and adjacent retina (Fig. 2C), and OCT revealed complete resolution of detachment and recovery of foveal anatomy (Fig. 2D). There has been no recurrence for six months.

**DISCUSSION**

We managed vision improvement and tumor regression, without severe complications, by alternating PDT and intravitreal bevacizumab injection in choroidal metastasis of non-small-cell lung cancer. This method can be considered for patients unable to receive radiotherapy.

In the absence of ocular symptoms, metastatic choroidal cancers are treated only for the primary cancer. However, if visual acuity deteriorates in spite of the systemic chemotherapy, local treatment should be performed [4]. In this presented case, chemotherapy with gefitinib was administered in a patient with stage IV cancer. However, chemotherapy was stopped after 2 weeks, because the patient refused the treatment due to extensive skin rashes and severe nausea. Thus, PDT and intravitreal bevacizumab injection were performed for the choroidal metastasis. In this case, temporary systemic chemotherapy may have possible additional benefit of PDT and intravitreal bevacizumab injections, but the benefits are thought to be small due to the short duration of treatment.

PDT has been used in choroidal hemangioma and choroidal melanoma because it suppresses vascularization. PDT makes use of a feature of verteporfin, which absorbs only lasers of certain fre-
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Fig. 2. (A) Fluorescein angiography (FA) showed multiple lobulated hyperfluorescent lesions, with surrounding leakage in the superior area of the optic disc. (B) Optical coherence tomography (OCT) revealed massive fluid accumulation and serous retinal detachment in the macula. (C) After two sessions of photodynamic therapy (PDT) and two intravitreal bevacizumab injections, FA demonstrated decreased leakage within both tumor mass and adjacent retina. (D) After two PDT sessions and two intravitreal bevacizumab injections, OCT revealed complete resolution of serous detachment and recovery of foveal anatomy.

quences, to destroy vascular endothelial cells selectively. The blood clot from the destroyed endothelial cells induces blood vessel blockage and can secondarily reduce the size of the tumour [5]. By using anti-vascular endothelial growth factor (VEGF), it suppresses tumour vascularization and reduces vascular permeability; hence, it suppresses cancer development. Amselem et al. [6] reported a regression of tumor using 4 mg/0.16 mL bevacizumab injections in metastasis from breast cancer. Similarly, Kuo et al. [7] used 1.25 mg/0.05 mL bevacizumab injections in metastasis from colorectal cancer. In this presented case, we found no complications when 1.25 mg/0.05 mL bevacizumab was administered twice. If PDT and intravitreal bevacizumab injection are administered alternately, bevacizumab will suppress VEGFs and, in general, neo-vascularisation. Meanwhile, locally administered verteporfin blocks the blood vessels in the tumour. It is thought that these two treatments have synergistic effect in reducing the tumour size in this case. PDT and the intravitreal bevacizumab injection are known to be a safe therapy for intraocular tumours. Intraocular complications occur only in 0.1% of the patients with diabetic retinopathy, retinal vein occlusion and age related macular degeneration [8]. A study on treating ocular capillary hemangioma with PDT reported decrease in the tumour size, without any complications, after administering 100 J/cm² of laser dose [9]. In this presented case, 50 J/cm² of laser was applied in an overlapping manner and the tumour regressed without complications. Rogers et al. [10] reported acute inflammation with increase in the subretinal fluid, which occurred in the first week after applying PDT in classic choroidal neovascularisation, and attributed this complication to acute damage of the
vascular endothelium from inflammatory cytokines. The subretinal fluid decreased and atrophy replaced inflammation, stage by stage, after two to four weeks of treatment. In the case presented here, serous detachment developed after four days of PDT, and the improvement observed after 4 weeks, without any treatment, was considered as a subsequent change. There was no other complication.

PDT and intravitreal bevacizumab injections might be a useful treatment option of metastatic choroidal tumor in some selected cases. However, further studies are mandatory to determine the safety and the efficacy of such treatment in this disease.

REFERENCES