Intravitreal Bevacizumab for Radiation-Induced Cystoid Macular Oedema in Patients with Nasopharyngeal Carcinoma: A Clinical Series

Visvaraja Subrayan  Keat Ween Khaw  Mohammadreza Peyman
Adrian Choon Aun Koay  Iqbal Tajunisah

Department of Ophthalmology, University of Malaya, Kuala Lumpur, Malaysia

Key Words
Anti-vascular endothelial growth factor · Radiation maculopathy · Cystoid macular oedema · Nasopharyngeal carcinoma

Abstract
Aims: To evaluate the outcome of intravitreal bevacizumab in the treatment of radiation-induced cystoid macular oedema among patients who underwent external beam radiotherapy for nasopharyngeal carcinoma. Methods: Five patients were recruited. The length of time from the last external beam radiation therapy to presentation ranged from 12 months to 15 years. Intravitreal bevacizumab (1.25 mg/0.05 ml) was given and repeated monthly injections were administered until best corrected visual acuity (BCVA) improved to 6/9 or until 3 further injections did not show further improvement in BCVA. BCVA was measured and fundus photography, optical coherence tomography (OCT) and fluorescein angiography were performed at baseline. BCVA and OCT were recorded at each monthly visit. The duration of follow-up ranged from 6 months to 2 years. Results: Five patients (7 eyes) were recruited. At the final visit, 3 eyes (71.4%) showed reduction in the central subfield thickness (CST; mean reduction of 17.6%, range 9–149 μm) with improvement in BCVA, whilst 2 eyes worsened in terms of CST and final BCVA. Another 2 eyes remained altered in BCVA despite slight improvement in CST. Conclusion: The use of intravitreal bevacizumab in this group of patients showed variable response in terms of CST and BCVA outcome but remains a viable option to treat this challenging condition.

Introduction
Radiation-induced cystoid macular oedema (CMO) is a known complication of radiotherapy. Various treatments exist for this maculopathy [1]. Previous reports on the use of intravitreal bevacizumab have been mainly on patients who received plaque brachytherapy for choroidal melanoma [2–6]. Finger and Mukkamala [7] reported intravitreal bevacizumab treatment for external beam radiation therapy (EBRT)-related radiation maculopathy but the doses of external beam radiation used were variable and for a variety of malignancies. To our knowledge, there are no reports on its use with external beam radiation-induced CMO in nasopharyngeal carcinoma (NPC) patients. In this case series, we aim to measure changes in central subfield thickness (CST) and best corrected visual acuity (BCVA) following its use.
Materials and Methods

This interventional case series was conducted in the University of Malaya Medical Centre between January 2010 and December 2011. NPC patients previously treated with EBRT doses of 66 Gy (2.0 Gy/fraction; daily from Monday to Friday for 7 weeks) who developed radiation-induced CMO were identified. Patients with other causes of visual loss were excluded. None of the patients had diabetes mellitus or any other disease that could affect the retinal thickness and vision including cataract, radiation-induced optic neuropathy, vitreous haemorrhage as well as macular ischaemia detected on fluorescein angiography (FA). At baseline, Snellen BCVA was measured and fundus photography, spectral-domain optical coherence tomography (OCT) and FA were performed on all patients. All cases of CMO were confirmed by OCT and FA findings. An intravitreal injection of bevacizumab (1.25 mg/0.05 ml) was then given promptly after diagnosis. Patients were followed up monthly with fundus examination, BCVA and OCT. Repeated treatments, 1 month apart, were given until vision improved to 6/9. If vision did not improve, further injections were abandoned after another 2 attempts. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Results

A total of 5 patients (7 eyes) were recruited. All were males and their age ranged from 54 to 67 years. The length of time from last EBRT to presentation ranged from 12 months to 15 years. Three patients were diagnosed with stage II NPC and 2 patients with stage III NPC.

The number of injections received per eye ranged from 1 to 4. No complications occurred following injections. The duration of follow-up ranged from 6 months to 2 years. Table 1 summarizes patients’ treatment, their pre-treatment and final-treatment BCVA and CST.

Discussion

In our series, we found good improvement in patient’s CST after intravitreal injection of bevacizumab, although their corresponding BCVAs were variable and unpredictable.

At this point, it is important to know that systemic bevacizumab has also been used successfully to control radiation-induced cerebral necrosis [8].

EBRT remains the main modality of treatment for NPC. Due to the close proximity of the tumour to radiosensitive structures like the eye, radiotherapy can result in complications like radiation maculopathy. Various therapies described for the treatment of radiation-induced macular oedema include argon laser photocoagulation and triamcinolone acetonide [1].

Since 2007, there have been several small series that looked at the use of anti-vascular endothelial growth factor (anti-VEGF) in treating radiation maculopathy. Intravitreal bevacizumab was used in 1 patient by Ziemssen et al. [2], 6 patients by Finger and Chin [3], 10 patients by

<table>
<thead>
<tr>
<th>Patient</th>
<th>Eye</th>
<th>Number of treatments received</th>
<th>Pretreatment CST, μm</th>
<th>Final CST, μm</th>
<th>Pretreatment BCVA</th>
<th>Final BCVA</th>
<th>Duration of follow-up months</th>
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<tbody>
<tr>
<td>Case 1</td>
<td>OS</td>
<td>3</td>
<td>411</td>
<td>552</td>
<td>6/18</td>
<td>6/60</td>
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</tr>
<tr>
<td>Case 2</td>
<td>OD</td>
<td>3</td>
<td>350</td>
<td>524</td>
<td>6/36</td>
<td>6/120</td>
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<td>Case 3</td>
<td>OD</td>
<td>1</td>
<td>445</td>
<td>355</td>
<td>6/18</td>
<td>6/9</td>
<td>12</td>
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<tr>
<td></td>
<td>OS</td>
<td>1</td>
<td>386</td>
<td>324</td>
<td>6/12</td>
<td>6/9</td>
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<tr>
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<td>OD</td>
<td>4</td>
<td>494</td>
<td>345</td>
<td>6/24</td>
<td>6/18</td>
<td>6</td>
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<td>3</td>
<td>278</td>
<td>269</td>
<td>6/12</td>
<td>6/12</td>
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Fig. 1. Case 1: fundus photograph (a) and final OCT (b). Case 2: fundus photograph (c) and final OCT (d). Case 3: pretreatment OCT right eye (e) and left eye (f), posttreatment OCT right eye (g) and left eye (h). Case 4: pretreatment OCT (i), posttreatment OCT (j).
Mason et al. [4] and 5 patients by Gupta and Muecke [5]. There was improvement in BCVA in 1 out of 1, 2 out of 6, 5 out of 10 and 2 out of 5 patients, respectively. Mason’s study demonstrated OCT change in mean foveal thickness of 482 μm before injection, 284 μm at 6 weeks and 449 μm at 4 months after injection. Recently, Finger and Chin [6] described the use of ranibizumab in 5 patients with radiation maculopathy. There was an average of 6-letter improvement in visual acuity and 35% mean reduction in CST. Also in another study, Finger and Mukkamala [7] reported reductions of EBRT-related retinopathy after using intravitreal anti-VEGF therapy in 4 eyes of 3 patients.

In our study, repeated injections were often necessary to reduce and maintain macular thickness. One reason for this difference could be due to the underlying pathophysiology and the secretion of vascular endothelial factor may not be the only mechanism. Previous reports on the use of anti-VEGF have been on patients who received plaque brachytherapy for choroidal melanoma or EBRT with variable doses for different types of malignancies, whereas our patients received EBRT for NPC with the same dosage of radiation. Also in our series, we looked specifically into radiation-induced CMO. To our knowledge, this is the first report on the use of intravitreal anti-VEGF in this group of patients. However, radiation retinopathy is a progressive disease and thus continued periodic treatment is inevitable.

A larger sample size with longer follow-up is needed to confirm its efficacy and safety. Given the limited treatment options available, intravitreal anti-VEGF remains a viable therapy for this visually threatening condition.

Acknowledgments

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Disclosure Statement

None.

References