CASE REPORT

Effect of treatment of rectal cancer metastasis with intravitreal bevacizumab (Avastin) in patient with subretinal fluid and macular oedema: short-term follow-up

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SUMMARY

We describe the management of subretinal fluid and macular oedema due to colorectal cancer metastasis to the choroid using intravitreal bevacizumab. A patient with grade VI KRAS mutation rectal cancer with metastasis to the lung and cerebellum presented with left eye choroidal metastasis 1 week after being started on the experimental medication KTN3379. After intravitreal bevacizumab administration, the patient had improvement in macular subretinal fluid, but eventually progressed to severe cystoid macular oedema despite monthly intravitreal bevacizumab treatment.

BACKGROUND

As one of the most common causes of cancer-associated deaths, colorectal cancer becomes metastatic in roughly 55% of cases.^{1–4} However, ocular metastasis from colorectal cancer is rare, occurring in roughly 3–4% of those with metastasis, with the uveal tract being the most common location affected.^{5–6} Presenting symptoms of colorectal choroidal metastasis include vision loss, myodesopsia and photopsia.⁷ Reported treatment includes systemic chemotherapy, radiotherapy and combination chemoradiotherapy. Additionally, treatment with bevacizumab (Avastin, Genentech, South San Francisco, California, USA) intravitreally and systemically has been reported. Two cases of intravitreal bevacizumab with mixed success have been reported, neither of which had macular oedema.^{8–9} We report a case of intravitreal bevacizumab used for treatment of subretinal fluid and macular oedema due to vision-threatening choroidal colorectal cancer. The patient was treated with monthly injections of intravitreal 1.25 mg bevacizumab for three consecutive months, showing initial improvement in tumour size and macular oedema, but with eventual progression.

CASE PRESENTATION

A 68-year-old woman was diagnosed with KRAS mutation low-grade pT1 N0 MX adenocarcinoma rectal cancer in 2006 after 2–3 months of haematochezia, treated soon after chemoradiation with 5-fluorouracil and pelvic radiation. In 2008, she developed disease progression and a large rectocele with sacral adherence, and subsequently underwent an abdominal and perineal resection of the sigmoid, rectum and anus. At this time, surgical specimen

pathology now graded her T3 NO MX, or grade IIIB. She then received 12 rounds of FOLFOX therapy. In 2012, after a PET scan found a 2.5 cm lung nodule, she was found to have needle biopsy-proven pulmonary metastasis and underwent a middle lung lobectomy. She then completed 12 rounds of FOLFIRI and systemic bevacizumab, completing therapy in 2013. One year later, in 2014, she was found to have lung and cerebellar metastasis and was started on the experimental medication KTN3379 (Koltan Pharmaceuticals, New Haven, Connecticut, USA), protocol 2013-141, a phase I trial for metastatic colon cancer, which is now discontinued. KTN3379 used human immunoglobulin, G1 λ mAb, that specifically binds with ErbB3, thereby inhibiting tumour growth at HER-2 and possibly the epidermal growth factor receptor (EGFR). One week after her first dose of KTN3379, she presented to our ophthalmology clinic with a new onset of myodesopsia and photopsia of a several-day duration. Her presenting vision was 20/20 OD and 20/70 OS. An elevated choroidal mass was seen on fundoscopic examination along the superotemporal arcade of the left eye, associated with macular subretinal fluid. She underwent fundus photography, spectral-domain OCT (Carl Zeiss SD-OCT V7.5.0.56, Meditec, Dublin, California, USA), fluorescein angiography, as well as A-scan and B-scan ultrasonography, the results of which were consistent with a non-vascular solid choroidal mass (figure 1). The lesion appeared consistent with a choroidal colorectal metastasis. After the establishment of ocular metastasis, KTN3379 treatment was discontinued. She was treated with monthly injections of intravitreal 1.25 mg bevacizumab for three consecutive months into her left eye. One month after the initial injection, she showed signs of improvement in tumour size and the amount of macular subretinal fluid. After her third intravitreal injection, however, the mass enlarged and the subretinal fluid expanded, resulting in severe cystoid macular oedema despite three consecutive doses of bevacizumab (figure 2).

DISCUSSION

Ocular metastasis occurs in 12% of patients with metastatic cancer; however, the frequency of ocular metastasis varies significantly with regard to the primary site and type of cancer.^{5–6} Although colorectal cancer is the third most common cause of

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Figure 1 Funduscopy at baseline (A) showing a yellowish subretinal mass under the superior arcade. Baseline red-free fundus photograph (B) showing the tumour (asterisk) with adjacent macular subretinal fluid (arrow). B-scan ultrasonography at baseline (C) with the choroidal mass highlighted by the yellow markers.

Figure 2 Baseline SD-OCT showing subretinal fluid (asterisk) (A). Two-month follow-up after two monthly injections of bevacizumab, showing severe progression of subretinal fluid and macular oedema (B).

cancer-related deaths in the USA, only 15 cases have been reported in our search of the literature.^{7–10} Since choroidal colorectal metastasis is uncommon, knowledge of the most appropriate treatment approach is limited to non-comparative case reports confounded by multiple concurrent treatment approaches. Bevacizumab is a humanised monoclonal antibody to vascular endothelial growth factor, which is approved by the Federal Drug Administration for systemic use in the treatment of metastatic colorectal cancer. Intravenous bevacizumab was additionally used off-label for the treatment of exudative age-related macular degeneration, after which systemic adverse effects were shown to be reduced with intravitreal administration. Since then, intraocular bevacizumab has been used in many ocular conditions, including in the treatment of various aetiologies of choroidal neovascularisation as well as macular oedema. Bevacizumab treatment of colorectal choroidal metastatic lesions has been reported with intravenous use and intravitreal administration. The only report of systemic bevacizumab administered intravenously for the treatment of ocular colorectal metastasis was confounded by the concurrent use of systemic chemotherapy and ocular radiation.¹⁰ The two cases of patients with colorectal choroidal metastasis treated with intravitreal bevacizumab only showed mixed results, and neither case had macular oedema. One patient with bilateral choroidal metastasis positively responded to intravitreal bevacizumab in one eye, but had tumour progression in the contralateral eye. The second report of intravitreal bevacizumab therapy for choroidal colorectal metastasis was confounded by concurrent radiation therapy.^{8–9}

In our patient, intravitreal bevacizumab was found initially helpful in reducing macular oedema; however, disease progression rapidly worsened as the subretinal fluid and macular oedema expanded despite local bevacizumab injections. No ocular or systemic side effects were observed. Since the initial response to 1.25 mg bevacizumab showed improvement in macular oedema, the treatment may have been underdosed in subsequent treatments. A dose of 2.5 mg bevacizumab has been shown to be

helpful in choroidal metastasis of lung carcinoma, while a 1.25 mg dose has been shown to be ineffective in choroidal metastasis secondary to ovarian serous cystadenocarcinoma.^{11–12}

Learning points

- ▶ Metastatic choroidal colorectal cancer is a systemic disease process and requires systemic therapy.
- ▶ Intravitreal bevacizumab may be useful as a treatment of macular oedema from choroidal metastasis of colorectal cancer.
- ▶ The ultimate goal of therapy is patient morbidity and mortality support through systemic care directed at the primary cancer source.

Competing interests None declared.

Patient consent Not obtained.

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REFERENCES

- 1 Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63:11–30.
- 2 SEER Cancer Statistics Review, 1975–2011, based on November 2013 SEER data submission Internet. National Cancer Institute, 2014. http://seer.cancer.gov/csr/1975_2011/ (accessed 30 Nov 2015).
- 3 August DA, Ottow RT, Sugarbaker PH. Clinical perspective of human colorectal cancer metastasis. *Cancer Metastasis Rev* 1984;3:303–24.
- 4 Van Cutsem E, Nordlinger B, Adam R, et al. Towards a pan-European consensus on the treatment of patients with colorectal liver metastases. *Eur J Cancer* 2006;42:2212–21.
- 5 Bloch RS, Gartner S. The incidence of ocular metastatic carcinoma. *Arch Ophthalmol* 1971;85:673–5.
- 6 Nelson CC, Hertzberg BS, Klintworth GK. A histopathologic study of 716 unselected eyes in patients with cancer at the time of death. *Am J Ophthalmol* 1983;95:788–93.

- 7 Tei M, Wakasugi M, Akamatsu H. Choroidal metastasis from early rectal cancer: case report and literature review. *Int J Surg Case Rep* 2014;5:1278–81.
- 8 Kuo IC, Haller JA, Maffrand R, *et al.* Regression of a subfoveal choroidal metastasis of colorectal carcinoma after intravitreal bevacizumab treatment. *Arch Ophthalmol* 2008;126:1311–13.
- 9 Lin CJ, Li KH, Hwang JF, *et al.* The effect of intravitreal bevacizumab treatment on choroidal metastasis of colon adenocarcinoma—case report. *Eye (Lond)* 2010;24:1102–3.
- 10 Khawaja MR, Minturn JT, Spittler AJ, *et al.* Ocular metastasis of colorectal cancer: an uncommon presentation of a common malignancy. *Hematol Oncol Stem Cell Ther* 2015;8:176–80.
- 11 de la Barquera Cordero AS, Hidalgo RA. Intravitreal bevacizumab for choroidal metastasis of lung carcinoma; a case report. *J Ophthalmic Vis Res* 2010;5:265–8.
- 12 Kuo IC, Sambuelli RH, Bono J, *et al.* Progression of choroidal metastasis of ovarian serous cystadenocarcinoma after intravitreal bevacizumab treatment. *Rare Tumors* 2013;5:e5.

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