Journal of Radiotherapy in Practice

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Choroidal metastases: case report and review

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Original Article

Cite this article: Duque V, de la Pinta C, Corral C, Vallejo C, Martin M, Hernanz R, Mezherane EM, Pelari L, Hernandez A, Valero M, and Sancho S. (2022) Choroidal metastases: case report and review. *Journal of Radiotherapy in Practice* **21**: 215–221. doi: 10.1017/S1460396920001090

Received: 25 September 2020
Revised: 10 November 2020
Accepted: 16 November 2020
First published online: 29 December 2020

Key words:
choroidal metastasis; intraocular tumour; radiotherapy; radiation therapy; SBRT

Abstract

Introduction: Choroidal metastases are the most frequent intraocular secondary tumours, with a prevalence of 2–7% according to the literature. Our aim was to review a clinical case of choroidal metastasis.

We present a case of a 63-year-old male patient diagnosed in 2018 with lung adenocarcinoma cT4N0M1. The patient had three metastases in the brain, which were successfully treated with radiosurgery (RS). The patient was treated with chemotherapy with pemetrexed–cisplatin schedule. Five months after diagnosis, the patient presented with decreased vision in the right eye. After ophthalmologic evaluation, he was diagnosed with a right choroidal metastasis, which was treated with external beam radiotherapy with 20 Gy in five fractions, resulting in improved visual acuity and a complete clinical and radiological response.

The patient took part in a clinical trial that continued with systemic chemotherapy. Twenty-two months after radiotherapy to the eye, the patient has good visual acuity without any side effects.
Conclusions: Choroidal metastasis treated with radiotherapy achieves good local control, with limited side effects, allowing an improvement in visual acuity and consequently, an improvement in the patient´s quality of life.

Introduction

The incidence of choroidal metastasis is increasing according to the available literature. The increase in the incidence is due to the longer survival rates of oncology patients and the improvement in the diagnostic studies that allow the identification of these metastases. Some studies report a prevalence of choroidal metastases from 2 to 7% of all oncology patients[1–4].

The most frequent primary tumour associated with choroidal metastasis is breast cancer, 47% of cases arising from breast cancer.[5–7] The second most frequent primary tumour is lung cancer, 20–29% of cases arising from lung cancer.[7,8] Other primary tumours include prostate cancer, kidney cancer, skin cancer or gastrointestinal tumours.

The diagnosis of choroidal metastasis occurs in the progression of the primary tumour in 67% of cases. However, among the patients diagnosed with choroidal metastases from lung cancer, 44% present the choroidal metastasis as the first symptom.[2]

About 75% of choroidal metastases have other synchronous or metachronous extraocular metastases[3,9] requiring multidisciplinary assessment with local and systemic therapies.

Overall survival is poor, with 57 and 23% at 1 and 5 years, respectively. Analysing the two most frequent cancers, overall survival after diagnosis of choroidal metastasis at 5 years for breast cancer is 25% and for lung cancer is 13%, worsening the prognosis of these patients.[7,10]

In this study, we present a case of lung adenocarcinoma with choroidal metastasis.

Case

A 63-year-old male, non-smoker for a year, without comorbidities and without medical treatment.

In April 2018, the patient attends the emergency department for paresthesia in the left arm. The neurological examination showed no other findings. Chest X-ray showed a mass in the upper left lobe. A 52 × 51 mm hypodense mass in the left upper lobe with infiltration of the bronchus and the left pulmonary artery was observed on computerised tomography (CT). Brain CT showed two brain lesions, one in the right frontal lobe and the other in the left parietooccipital region. Magnetic resonance imaging (MRI) confirmed the presence of these two intraparenchymal lesions and one more in the left occipital lobe.

The diagnostic investigations were completed with a bone scan and positron emission tomography (PET) without new findings. Finally, the biopsy confirmed a non-small-cell lung

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adenocarcinoma, anaplastic lymphoma kinase (ALK) negative, Kirsten rat sarcoma 2 viral oncogene homolog (KRAS) mutated.

This case was presented to the Tumor Board and it was decided to treat the three brain lesions with radiosurgery (RS) with a single dose of 17 Gy and induction chemotherapy with cisplatino–pemetrexed to a subsequent surgical salvage of the primary tumour.

After RS, a complete response of the three brain metastases was observed. After four cycles of induction chemotherapy, a partial response of the primary tumour was observed.

In August 2018, the patient presented with a loss of vision, ptosis, pain and oedema in the right eye. The patient was evaluated by the Ophthalmology Department. The fundoscopy showed a choroidal white mass, with intraretinal and subretinal flows, without bleeding and a normal papilla (Figures 1 and 2). The left eye was normal.

An ultrasound of the right eye showed a choroidal mass of 3–4 mm and angiography revealed a choroidal block (Figures 3 and 4). These characteristics established the diagnosis of choroidal metastasis.

In August 2018, the patient received external beam radiotherapy for the choroidal metastasis. The patient was immobilised using a thermoplastic mask and underwent CT simulation, contouring and planning using 6 MV photons produced by a linear accelerator. The total prescribed dose was 20 Gy in five fractions (Figures 5 and 6).

The treatment was well tolerated, with no relevant toxicity and with improved pain and complete recovery of vision.

After treatment, the right fundus showed an area of non-elevated, mottled pigment alteration in the location of the previous lesion (Figure 7). Optical coherence tomography (OCT) showed a complete response of the choroidal metastasis (Figures 8 and 9).

The patient continued treatment with pemetrexed for 3 months. In October 2018, he presented lung and mediastinal progression, and he started on a second chemotherapy agent, Nivolumab and a month later Docetaxel was added to treatment due to a progression of locoregional disease.

In July 2019, he was referred to Radiation Oncology for treatment for the pain of the primary tumour. He was treated with a total prescription dose of 37·5 Gy in 15 fractions, which resulted in an improvement of pain.

In November 2019, he presented progression with a right adrenal metastasis so the patient took part in a clinical trial that continued with systemic chemotherapy.

In July 2020, 22 months after treatment with radiotherapy, the patient had a complete response in the brain and choroidal metastases, with good vision and no late side effects associated with the treatment.

Discussion

We present the case of a 63-year-old male with a choroidal metastasis in the right eye of lung adenocarcinoma treated with external beam radiotherapy. After 22 months of follow-up, the patient continues with a complete choroidal response and good visual acuity.

The differential diagnosis of choroidal metastasis should be made in an oncology patient presenting with a loss of vision or intraocular pain. Intraocular pain has been described as the main symptom of choroidal metastasis specifically from lung cancer according to different studies.[5,8,11] However, many of these patients are asymptomatic, which causes a delay in diagnosis. Among asymptomatic patients, the presence of choroidal metastasis in autopsy represents 12·6%.[12]

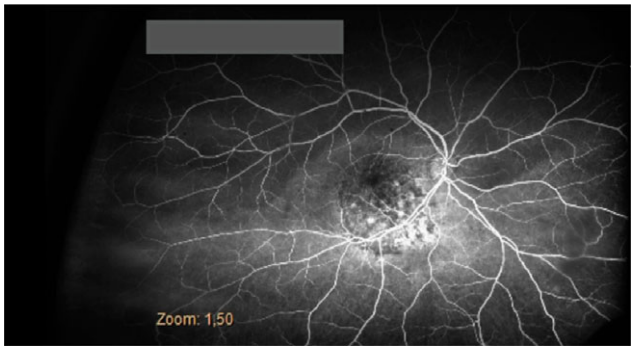


Figure 1. Right eye fundus with choroidal metastasis.

Early diagnosis is essential and includes the assessment of visual acuity by the Ophthalmology Department. In the eye fundus, choroidal metastasis appears as a flat, yellowish-whitish (86%) orange (8%) or brown (4%) lesion, associated or not with intraretinal or subretinal fluid.[7]

These characteristics are not pathognomonic and are sometimes indistinguishable from choroidal melanoma, which is the second most frequent intraocular tumour.[13]

Intraocular ultrasound shows differences between metastasis and choroidal melanoma due to reflectivity and the height/base ratio, which is the maximal prominence and the maximal base diameter of the tumour. In choroidal metastasis, there is greater reflectivity with a mean of 70% compared to 22% in melanoma. Also, the height/base ratio is lower in choroidal metastasis with a mean of 0·18 mm compared to 0·6 mm in melanoma.[14,15]

Angiography in choroidal metastasis shows global hyperfluorescence that starts in the arterial phase and increases gradually, while fluorescence at choroidal area is obstructed during the complete test. OCT allows evaluation of the density and irregularity in the anterior part of the lesion; an elevated cupula is common.[16–18] Other techniques such as OCT angiography or Enhanced Displacement Imaging (EDI-OCT) are also used in the diagnosis.

Biopsy is used in patients with unknown oncological diagnosis.[19]

A diagnosis of choroidal metastasis presents a poor prognosis for patients, the mean survival is between 4 and 12 months.[7,10,20–22]

Among the different treatment options for choroidal metastasis, radiotherapy is the most commonly used in the literature.[9,18] Radiotherapy improves visual acuity between 81 and 90% and has good results with 64–80% complete responses in several studies.[5,8,9,20,23,24]

External beam radiation therapy (EBRT) is the most commonly used technique, allowing the treatment of single and multiple lesions. Hypofractionated schemes are the most used, included 30 Gy in 10 fractions (biologically effective dose (BED) = 39 Gy) and 20 Gy in 5 fractions (BED = 28 Gy).[9,12,25] In our case, we have performed a hypofractionated treatment with 20 Gy in five fractions. Hypofractionated schemes are effective with low acute complications and they provide a good treatment option due to the reduced life expectancy of the patients.[9,12]

In selected patients, who have a longer life expectancy, treatments with conventional dose schemes, 40 Gy in 20 fractions (BED = 48 Gy) are suitable to decrease the late side effects.[20,24,26]

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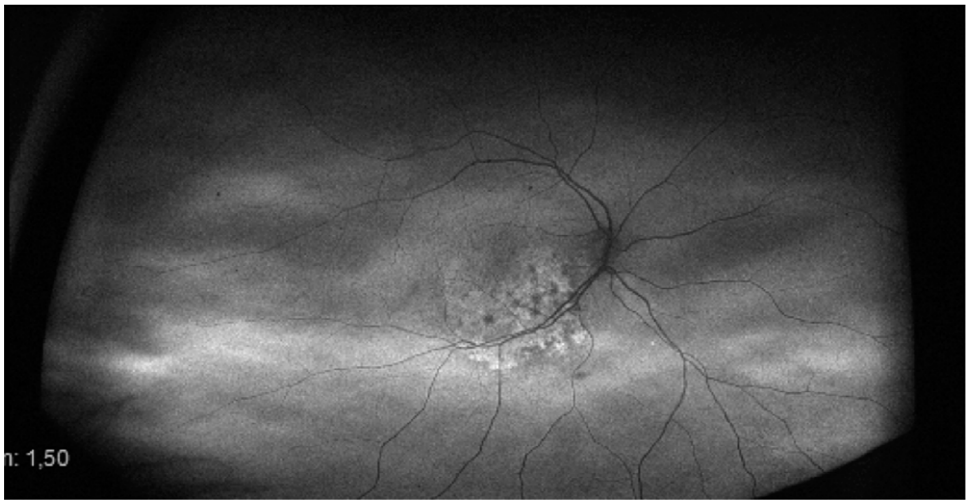


Figure 2. Pretreatment right eye fundus shows a whitish choroidal mass, with intraretinal and subretinal fluids.

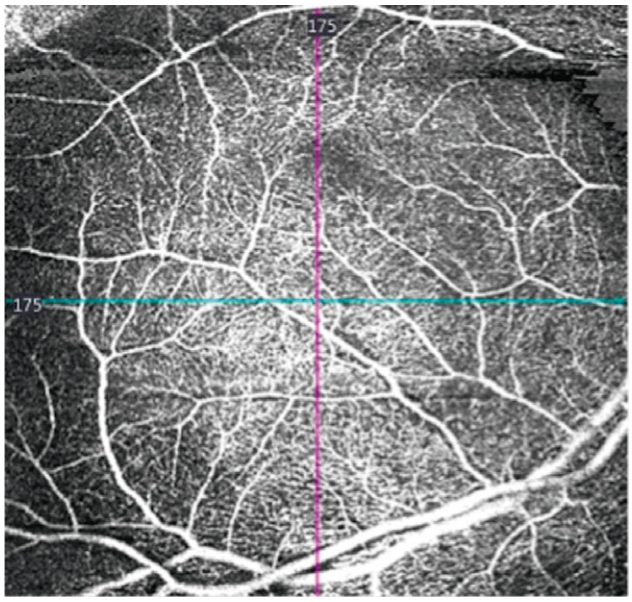


Figure 3. Superficial normal angiography.

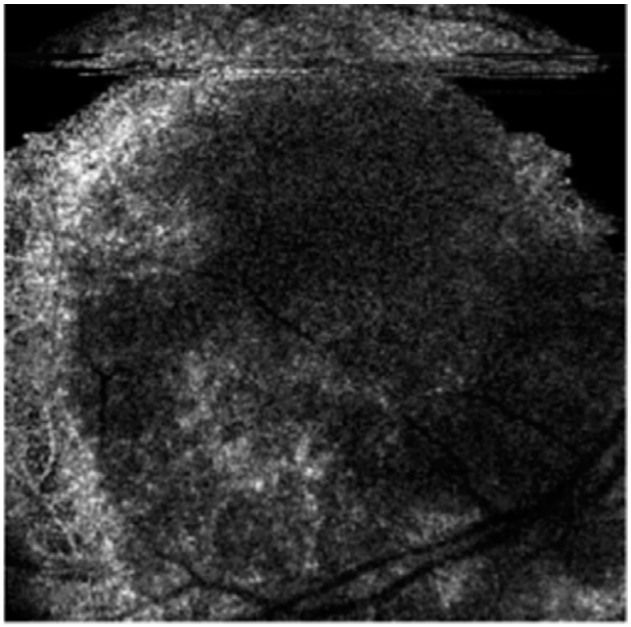


Figure 4. Choroidal block angiography.

EBRT achieves 80% complete responses and 57–89% clinical improvement.[5,8,9,20,24,27] Fifty percent of patients present with mild acute toxicities such as skin erythema and conjunctivitis. Late side effects are uncommon and include cataracts (6·5%), glaucoma (3%), neovascularisation of the iris (2%), vitreous haemorrhage (2%), retinopathy (<1%), papillopathy (<1%), macular oedema (1%), dry eye syndrome (<1%), eye pain (<1%).[8,20,24]

Some studies describe the use of lens-sparing technique with a contact lens mounted lead shield during the treatment to reduce complications.[20,24,28] Table 1 summarises the main studies of choroidal metastases treated with EBRT.

Up to 38% of patients have bilateral choroidal metastases. For these cases, some studies recommend prophylactic bilateral treatment.[23] Others use a treatment plan with two anteroposterior and lateral fields, this may eliminate the microscopic disease in the contralateral eye due to the lateral field.[9,20]

Depending on the size, proximity to the macula, number of lesions, intention to treat, histology or prognosis of the patient, other radiotherapy techniques may be used.

In the treatment of choroidal metastasis, high-dose radiotherapy techniques, such as stereotactic body radiation therapy (SBRT), may be used in one or more fractions. SBRT allows a high radiation dose to the tumour with low doses to the organs at risk, achieving better local control and lower side effects. SBRT is indicated in patients with a good performance status. The mean dose used is 20 Gy in a single fraction and local control is 80–100%.[29–31] Table 2 summarises the main studies of choroidal metastases treated with SBRT.

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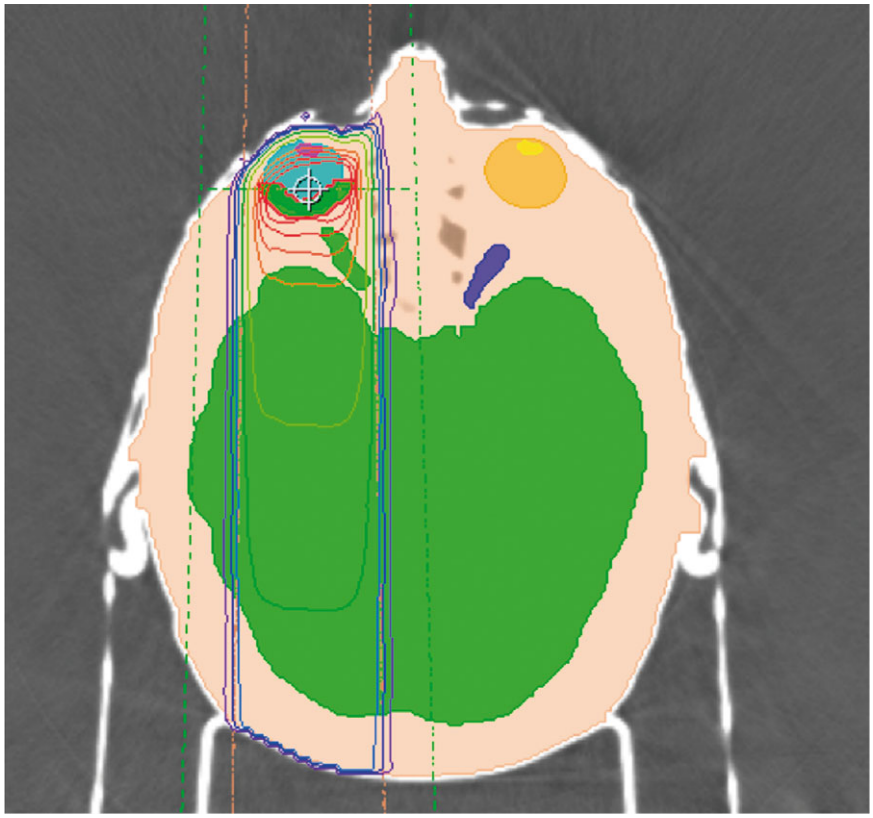


Figure 5. Radiotherapy treatment plan (axial view).

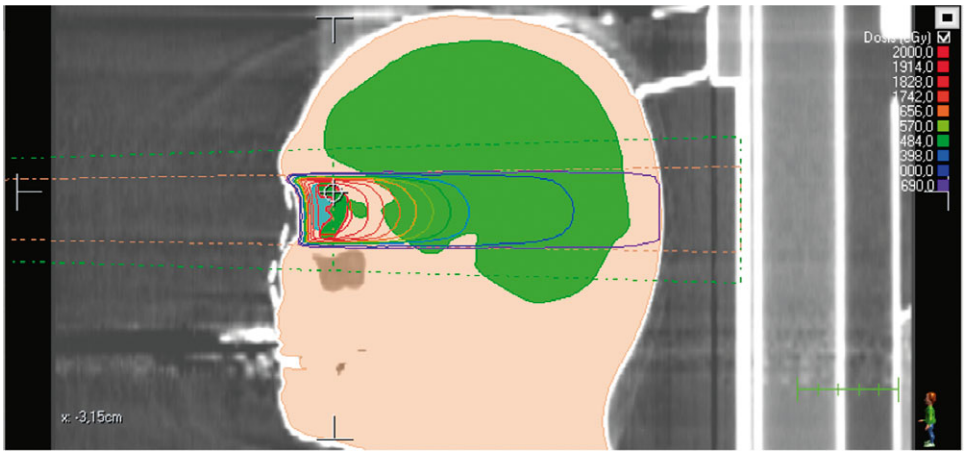


Figure 6. Radiotherapy treatment plan (sagittal view).

Brachytherapy is indicated as initial or salvage treatment. Brachytherapy is used in defined metastasis with a diameter of <18 mm. The most commonly used radioactive isotope is Iodine-125 with a mean dose of 40–70 Gy applied over 3 days. Brachytherapy has very good results with 90–100% tumour response[8,32–34] and the duration of treatment is shorter compared to EBRT. However, it is an invasive technique that is done exclusively in specialised centres. Complications such as retinopathy, cataracts and atrophy of the optic nerve similar to EBRT.[32] Table 3 summarises the main studies of choroidal metastases treated with brachytherapy.

Proton beam therapy is indicated in radio-resistant histologies, including melanoma, sarcoma or renal cell carcinoma and in long-term survival patients. The mean total dose used is

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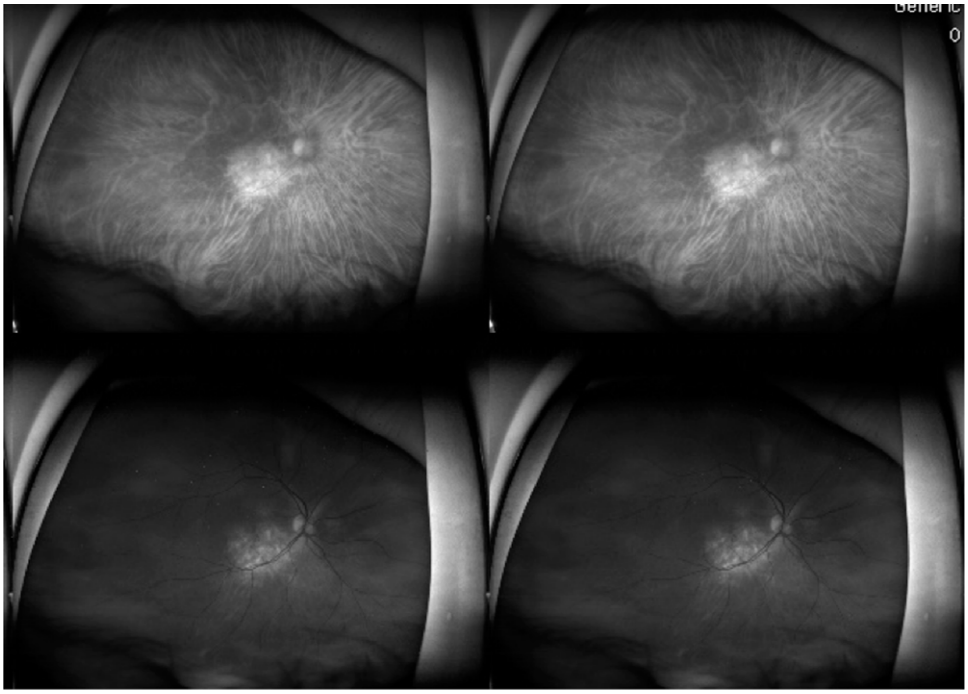


Figure 7. Post-treatment right eye fundus.

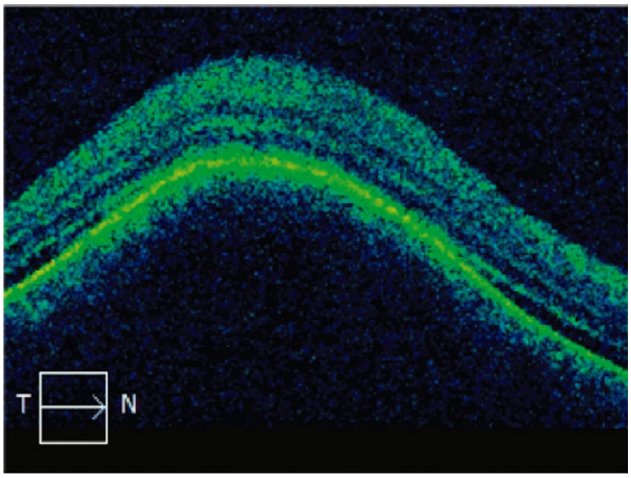


Figure 8. Pre–treatment OCT.

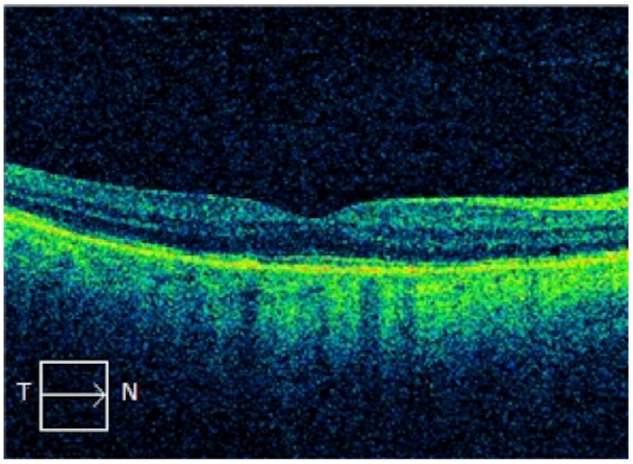


Figure 9. Post–treatment OCT.

20–28 Gy in two fractions, with local control rates between 94 and 98%.[35] The characteristics of protons and its energy liberation (Bragg peak) provide superior dose distributions and have a dosimetric advantage compared to photon beam therapy, with a better protection of the organs at risk and a shorter treatment duration. However, proton therapy is not always accessible.[34,36] Table 4 summarises the main studies of choroidal metastases treated with proton beam therapy.

Photodynamic therapy associated with intravitreal verteporfin is another local treatment option for choroidal metastases. However, its effectiveness is variable (39–81%) depending on the results from different studies.[37–41] It appears not to be useful in large tumours. Intravitreal injections of anti-vascular endothelial growth factor therapy (anti-VEGF) have also been used in combination with systemic therapies, but their benefit is not completely clear.[37] Table 5 summarises the main studies of choroidal metastases treated with photodynamic therapy.

This review has some limitations, as there are no clinical trials, most of the studies are cases with a limited number of patients. Besides these studies are heterogeneous, including different primary tumours, with different doses and fractions of radiotherapy and different endpoints. While acknowledging these limitations, radiotherapy is an effective and safe treatment option for these patients.

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Table 1. Main studies of choroidal metastases treated by external beam radiation therapy (EBRT)

Authors	*n*	Primary	Dose/fractions	Mean follow-up (months)	Response
Rudoler et al.[24]	188	Breast 53% Lung 23%	30–40 Gy/2–3	5·8	57% improvement of visual acuity
Wiegel et al.[20]	50	Breast 62% Lung 26%	40 Gy/20	5·8	86% stability or improvement of visual acuity
Demirci et al.[5]	137	Breast 100%	36 Gy/18	21	85% local control 64% improvement of visual acuity
D'abbadie et al.[27]	97	Breast 71% Lung 9%	30 Gy/10	Not reported	55% improvement of visual acuity
Shah et al.[8]	88	Lung 100%	Not reported	12	74% improvement of visual acuity

Table 2. Main studies of choroidal metastases treated by stereotactic body radiation therapy (SBRT)

Authors	*n*	Primary	Dose/fractions	Mean follow-up (months)	Response
Bellman et al.[29]	10	Breast 30% Lung 30% Colon 30% Melanoma 10%	12–20 Gy/1 30 Gy/10	6·5	100% local control 80% tumour regression
Cho et al.[30]	7	Lung 70% Gastric 15% Renal 15%	20 Gy/1	8	71% stability or improvement of visual acuity 100% tumour regression

Table 3. Main studies of choroidal metastases treated by brachytherapy

Authors	*n*	Primary	Dose	Mean follow-up (months)	Response
Shields et al.[32]	27	Breast 40% Lung 7% Others 51%	68·8 Gy Apex	11	94% tumour regression
Lim et al.[33]	5	Breast 83% Pancreas 17%	40–70 Gy Apex	Not reported	100% tumour regression
Demirci et al.[5]	15	Breast 100%	Not reported	21	86% stable or tumour regression
Shah et al.[8]	12	Lung 100%	Not reported	12	100% tumour regression

Table 4. Main studies of choroidal metastases treated by proton beam therapy

Authors	*n*	Primary	Dose	Mean follow-up (months)	Response
Tsina et al.[36]	63	Not reported	28 Gy/2	8	98% stable or tumour regression
Kamran et al.[35]	77	Breast 49%	20 Gy/2	7·7	94% local control

Table 5. Main studies of choroidal metastases treated by photodynamic therapy

Authors	*n*	Primary	Number of sessions	Mean follow-up (months)	Response
Kaliki et al.[39]	8	Breast 50% Lung 37·5% Leiomyosarcoma 12·5%	Not reported	17	Mean tumour thickness reduction of 39% Complete control 78%
Ghodasra et al. [40]	10	Breast 70% Lung 10% Thyroid 10% Pancreas 10%	1 session 38% 2 sessions 52% 3 sessions 5% 5 sessions 5 %	12	69% stable or improved visual acuity. 31% decreased visual acuity. Mean tumour Thickness reductions of 81%.
Shields et al.[38]	43	Lung 39% Breast 37% Kidney 8% Thyroid 6% Other sites 10%	1 session 71% 2 sessions 7%	20	Tumour control 78%

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Conclusions

Choroidal metastasis treated with radiotherapy achieves good local control, with limited side effects, allowing an improvement in visual acuity and consequently, an improvement in the patient´s quality of life.

Acknowledgements. None.

Financial Support. None.

Conflicts of Interest. None.

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