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Clinical Characteristics of Choroidal Metastases

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Summary: The most common intraocular tumors in adults are metastases from primary tumors: breast cancer, lung cancer, and other organ neoplasms. They are most typically located in the choroid, in the posterior pole of the eye. This article outlines the characteristic clinical features along with ultrasound and optical coherence tomography findings that aid in differential diagnosis. It also illustrates the growth pattern of metastatic nodules from their formation to their eventual fusion into a diffuse tumor conglomerate with an irregularly shaped surface and internal structure.

Key words: ocular metastases, intraocular tumor, ophthalmic ultrasound.

As the life expectancy of cancer patients continues to rise, ophthalmologists are likely to encounter intraocular metastases more and more frequently. Metastases are the most common malignant intraocular tumors. Their incidence in the United States is estimated to be 30.000 cases annually (compared to approximately 2.500 cases of primary ocular cancers). However, many ocular metastases remain undiagnosed.

While tumors can spread to the eyelids, conjunctiva, or orbit, the choroid is by far the most common site for metastases within the eye. Choroidal metastases can originate from cancers of the breast, lung, kidney, gastrointestinal tract, skin melanoma, and other types. The overall prognosis is poor, with a 5-year survival rate of 23%. However, the survival rates vary, with metastatic pancreatic cancer characterized by the worst and metastatic carcinoid tumors having the best prognosis. Choroidal metastases are typically located in the posterior pole, close to the central retina and/ or the optic nerve disc. Rarely, the iris, ciliary body or retina and optic nerve disc may be affected [1, 2].

Because the eye lacks a lymphatic system, it is an uncommon site for disseminated malignancy. Metastases to the ocular structures occur through the spread of cancer cells via the bloodstream. Arterial blood supply to the eye plays a key role in determining where cancer cells are most likely to spread. The posterior choroid, with its rich vascularization, is the most favored site for intraocular metastases. Breast cancer metastases to the eye are usually bilateral and multiple, and can occur alongside brain metastases [1]. Approximately 85% of patients with intraocular metastases of breast cancer present with a known history of breast cancer, often several or more years after previous treatment (mastectomy, chemotherapy, hormone therapy). However, in metastatic lung cancer, approximately two-thirds of patients remain unaware of their diagnosis due to the cancer's tendency to spread early [1, 2].

Despite the fact that ocular metastases are the most common type of intraocular tumor, they are rarely detected during the patients' lifetime. This is because much of the data on the incidence of ocular metastases come from autopsy reports, which reflect the rate of microscopic detection.

As Eliassi-Rad B et al. report, the incidence of microscopic metastases remains consistent, while the rate of clinically detectable intraocular metastases has decreased from 4.7% to 1% due to advancements in anticancer therapy [3]. The most common primary cancers that metastasize to the eye are breast cancer (47%), lung cancer (21%), and gastrointestinal cancers (4%) [4].

Pathogenesis

Intraocular metastases occur through the hematogenous spread of tumor cells. Metastatic choroidal tumors can persist and grow in a favorable microenvironment with rich blood perfusion.

Arterial blood supply to the eye determines the primary intraocular locations where cancer cells deposit. The posterior choroid, with its profuse vascularization, is the most favored site for the development and growth of intraocular metastases.

The primary pathway involves the short posterior ciliary arteries (*arteriae ciliares posteriores breves*), which are branches of the ocular artery that supply blood to the choroid. These arteries split from the ocular artery into two main trunks, further dividing into 10 to 20 branches. They penetrate the sclera near the posterior pole of the eye and link up with the anterior ciliary arteries. This mechanism of metastasis is supported by the presence of numerous small metastatic foci in the posterior pole of the eye. As they expand, they coalesce into a large, often irregular, thin tumor, typically accompanied by subretinal fluid, having an uneven 'lumpy bumpy' surface (Fig. 1A, 2A).

The anterior segment (the iris and the ciliary body) receives metastatic cells via the long posterior ciliary arteries (*arteriae ciliares posteriores longae*). These arteries, branches of the ophthalmic artery (typically two: lateral/ temporal and medial/ nasal), supply blood to the anterior portion of the choroid. In this area, metastases occur far less frequently.

Subjective symptoms

Patients typically present with visual disturbances, such as metamorphopsias or visual field defects. Even more common are non-specific symptoms including increased floaters or photopsias. Nevertheless, many choroidal metastases are asymptomatic. Visual disturbances tend to occur when metastatic lesions are located near the macula. Most typically, patients with metastases in vario-

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us locations are not examined by an ophthalmologist – either because they do not experience visual disturbances or do not report them due to more severe systemic health issues. The majority of patients diagnosed with ocular metastases have a prior history of treated primary cancer.

Clinical presentation

Choroidal metastases typically manifest with several distinct features. They are often located in the posterior pole of the eye, have a large base with relatively small thickness, and exhibit subretinal fluid on the tumor surface. Patients may present with total retinal detachment, with the tumor being clearly detectable only through ultrasound imaging. This contrasts with melanoma, where exudative retinal detachment is typically only observed when the tumor has reached a significant size. Metastatic lesions usually appear pale and often exhibit a distinctive mottled or 'leopard skin' pigmentation pattern caused by alterations in the retinal pigment epithelium. Lipofuscin, originating from poorly functioning retinal pigment epithelium, can be observed on the surface of both metastatic tumors and ocular melanoma.

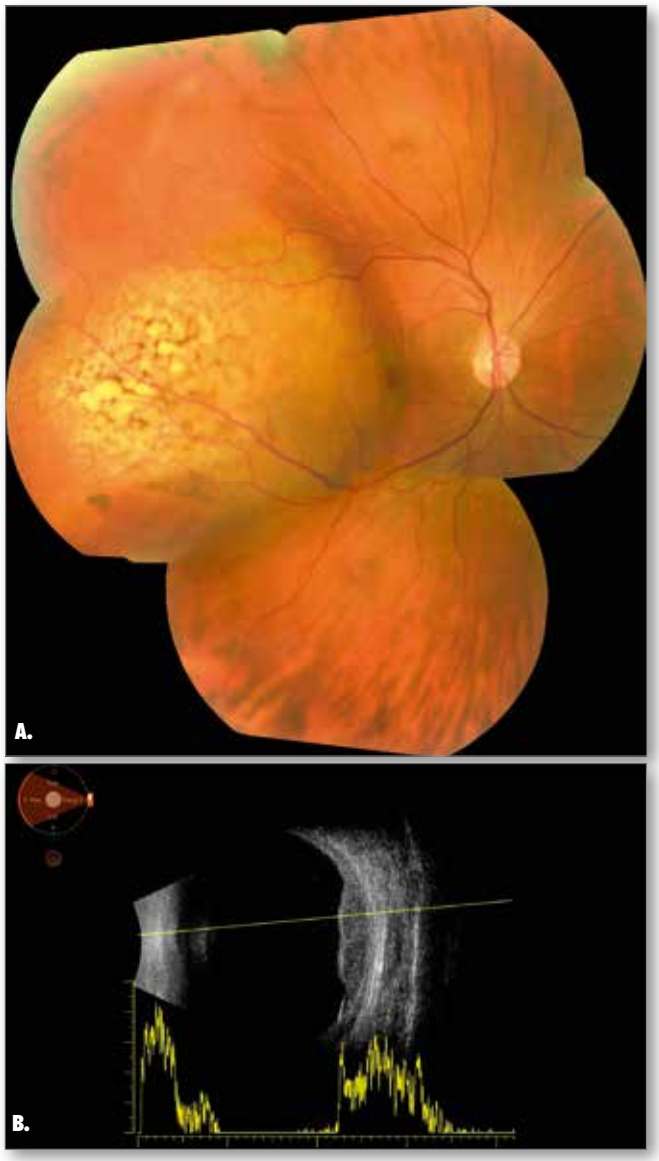

Fig. 1. Color fundus photograph of the right eye showing a metastatic choroidal lesion in a 45-year-old woman diagnosed with breast cancer (A). Ultrasound examination reveals a double-domed lesion with medium internal reflectivity and minor retinal detachment (B).

Choroidal carcinoid metastases appear orange in color, similarly to metastases from thyroid cancer. Metastases from kidney cancer are more prone to causing intraocular hemorrhage. Solitary choroidal metastases from cutaneous melanoma are pigmented and can be difficult to differentiate from primary choroidal melanoma. In such cases, the presence of pigmented infiltration in the retina and vitreous body serves as an important indicator that a pigmented choroidal tumor might be secondary.

Fluorescein angiography (FA) of metastatic lesions shows hypofluorescence during the arterial phase, followed by late hy-

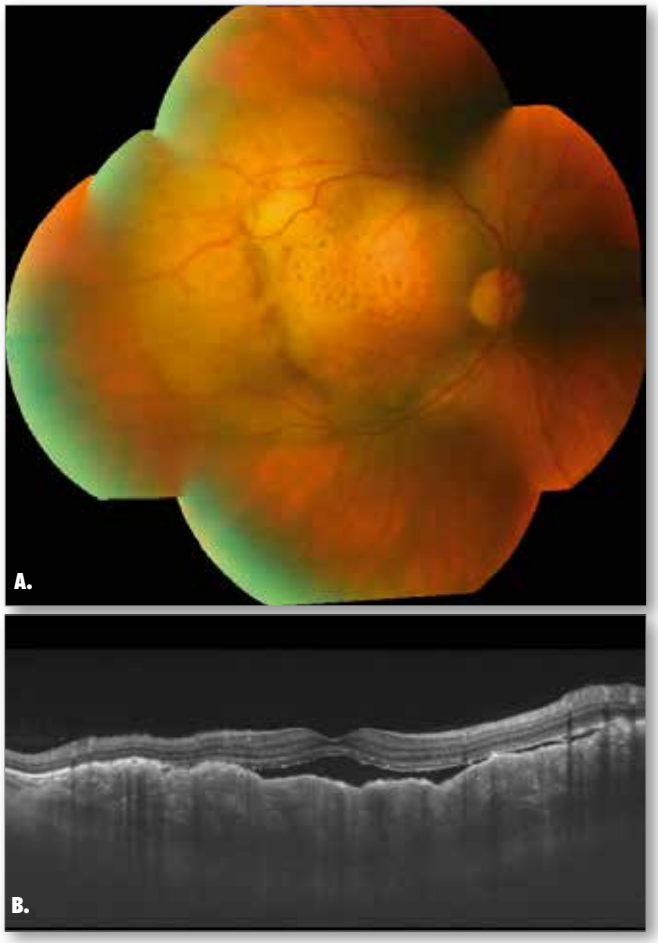

Fig. 2. Choroidal metastasis of breast cancer in a 70-year-old woman: color fundus photography (A) and OCT (B) demonstrating an irregular ('lumpy bumpy') anterior tumor surface, subretinal fluid, and retinal pigment epithelial abnormalities.

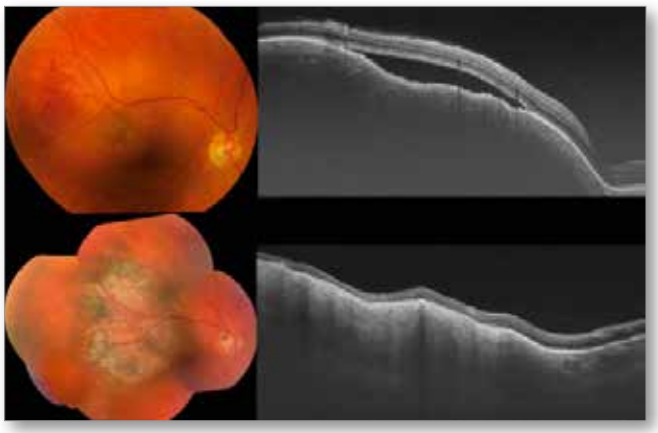

Fig. 3. Color fundus photographs and OCT scans at different periods of metastatic tumor growth in two patients. The fusion of individual foci into an irregular mass with a 'lumpy bumpy' surface is evident.

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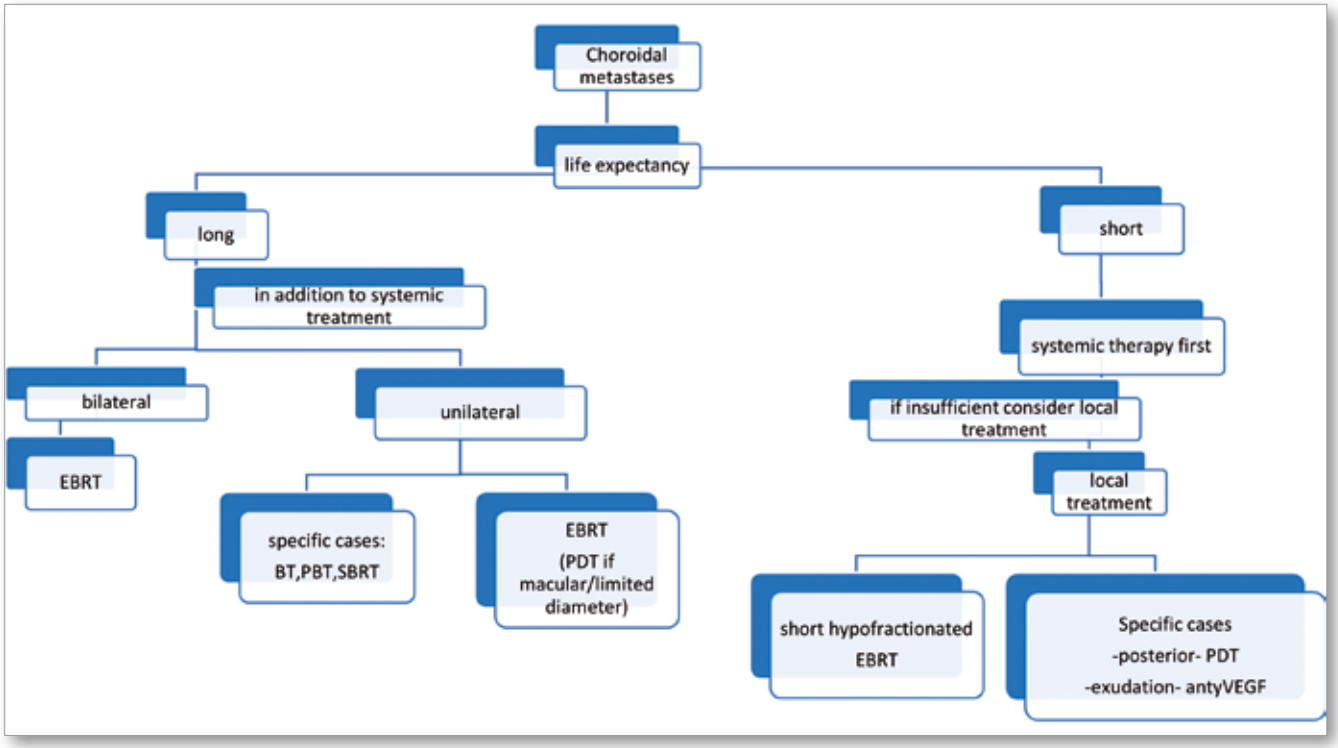

Fig. 4. Treatment algorithm for choroidal metastases (based on Thariat et al.): BT – brachytherapy, EBRT – external beam radiation therapy, PBT – proton beam therapy, PDT – photodynamic therapy, SBRT – stereotactic body radiotherapy.

perfluorescence without dye retention. Indocyanine green angiography (ICGA) is a useful modality for differentiating choroidal hemangioma from metastatic tumors. The most useful diagnostic method is A- and B-scan ultrasonography. In diagnosing and differentiating small metastatic foci, optical coherence tomography (OCT) plays an important role as well.

Ultrasound features of choroidal metastases

Ultrasound imaging may be crucial in the diagnosis of large choroidal metastases because their internal reflectivity coefficient (tumor reflectivity) varies between high and intermediate levels, whereas melanoma typically shows low internal reflectivity. This occurs because multiple small metastatic foci merge together, forming a single, irregularly structured mass with nodules separated by septa. The structure observed in the ultrasound image appears similar to that of fiberboard (Fig. 1B).

Characteristic features of metastases on optical coherence tomography (OCT)

Optical coherence tomography can show a pattern of hyperreflective, irregular patches in the photoreceptor layer and in the retinal pigment epithelium, along with subretinal fluid and evident irregularity in the retinal pigment epithelium, along with thickening and prominent undulation [5]. On OCT examination, a metastatic lesion typically presents as a nodular formation with a 'lumpy bumpy' surface and accompanying subretinal fluid (Fig. 2B) [6].

In addition, optical coherence tomography shows anterior displacement of the photoreceptor layer by subretinal fluid (a hyporeflective area), a hyperreflective and thickened retinal pigment epithelium complex, hyperreflective subretinal deposits, and a loss of the normal retinal architecture. Following effective systemic chemotherapy, OCT reveals a reduction in serous retinal detachment, a decrease in lesion size, and the restoration of normal retinal architecture [2]. Figure 3 shows color photographs and OCT images that illustrate the progression of the metastatic tumor over different periods. The merging of individual foci into a solitary irregular mass with a bumpy surface is seen.

Differential diagnosis

The differential diagnosis should include the following conditions: amelanotic choroidal melanoma, amelanotic choroidal nevus, posterior scleritis, choroidal hemangioma, choroidal granuloma, choroidal osteoma, posterior choroidal detachment, central serous chorioretinopathy, infectious lesions, organized subretinal hemorrhage, and idiopathic choroiditis [2].

Therapeutic management

Before proceeding with local treatment for choroidal metastases, it is crucial to evaluate the patient's systemic condition. This involves conducting a detailed medical history review, performing a physical examination, and analyzing laboratory tests and imaging findings.

It is also important to assess the condition of the other eye and check for the presence of multifocal metastatic intraocular tumors. A schematic representation of the procedure, based on the 2022 analysis [7], is shown in figure 4.

The treatment of choroidal metastases involves systemic chemotherapy and/or hormonal therapy, as well as local options including transpupillary thermotherapy [8, 9], radiation therapy with applicators (brachytherapy), external beam radiation therapy (EBRT), proton therapy, teleradiotherapy, and/ or photodynamic therapy [1, 2].

Treating these cases involves a collaborative effort between an ophthalmic oncologist, a radiation oncologist, and a general oncologist. If a patient has no other diagnosed metastatic sites, a PET-CT scan is recommended to check for metastases elsewhere in the body. If no other lesions are detected, a biopsy may be considered. If other metastases are found, in some cases systemic chemotherapy may lead to a substantial reduction or even complete regression of choroidal metastases [2, 9].

Brachytherapy (radiation plaque therapy) is typically reserved for larger, solitary metastases. The method ensures precise and controlled delivery of radiation to the eye. Furthermore, it is a faster treatment option, requiring only 3–4 days compared to EBRT, which can take 3–4 weeks. The duration of treatment plays an important role in managing choroidal metastases and should be carefully considered in relation to the patient's life expectancy [2].

The complications associated with brachytherapy are comparable to those seen with external beam radiotherapy and other forms of radiation treatment. These include retinopathy, radiation neuropathy, and cataract. These adverse effects are uncommon, develop late, and thus do not significantly threaten vision, considering the limited life expectancy of many patients.

External beam irradiation is indicated in cases of bilateral multifocal metastases and may reduce not only the tumor mass but also the frequently present exudative retinal detachment, potentially leading to improved vision.

Photodynamic therapy (PDT) can also be used to treat small metastases in the posterior choroid.

All photographs featured in this article are courtesy of the Department of Ophthalmology and Ocular Oncology in Krakow, and were taken by photographer Piotr Bujak.

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