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3. Choroidal metastasis

Choroidal metastasis likely represents the most common form of intraocular malignancy in adults.[1] These secondary malignancies most often originate from primary tumours of the breast (47%) and lung (21%), and less often originate from gastrointestinal tumours (4%) or tumours of other solid organs.[1] Nearly 20% of patients with choroidal metastases have unknown primary malignancies.[1]

Intraocular metastasis occurs when cells from a primary tumour spread hematogenously to the eye. Because the choroid is the most highly vascularized structure in the eye, it is not surprising that it is the most common site of intraocular metastasis. Indeed, in the largest study to date, Shields et al reported that by far most (88%) uveal metastases occurred in the choroid, with metastases to the iris (10%) and ciliary body (2%) occurring much less commonly.[1]

The incidence of ocular metastases in patients with breast cancer varies from 9% to 37%, occurring at a median of 3 years from the diagnosis of breast cancer and at a mean age of 56 years.[2-5] Although by far most patients with choroidal metastases from breast cancer have known systemic metastases, approximately 14% of patients present with choroidal metastases as the first manifestation of metastatic disease, and nearly 3% do not have known diagnoses of breast cancer.[2] Significant risk factors for choroidal metastasis from breast cancer include known disseminated breast cancer to more than one organ, and the presence of lung or brain metastases.[4]

Diagnosis

Assessment of a patient with suspected choroidal metastasis entails obtaining a full medical history, including a full cancer history. Patients with choroidal metastases might develop metamorphopsia, decreased visual acuity, or visual field changes from direct tumour involvement or from secondary exudative retinal detachment.[2] However, in one series, nearly 11% of patients with choroidal metastases were asymptomatic.[1]

A complete ophthalmic examination including slit lamp examination and dilated fundoscopic examination is required. On fundoscopic examination, choroidal metastases typically appear as creamy yellow-coloured subretinal lesions with a plaque or dome shape. Overlying pigment mottling is typically present.[1] These lesions can be single or multiple, and can occur in one eye or both. Secondary exudative retinal detachment at the border of these lesions can occur. Choroidal metastases are usually found at the posterior pole of the eye and generally do not have accompanying retinal exudate or retinal hemorrhage—features that can help differentiate choroidal metastases from other lesions.[2,6]

Ancillary examinations, such as fluorescein angiography, can be useful if the diagnosis is unclear and to better appreciate areas of leakage. Ultrasonography with A- and B-scans is extremely helpful in differentiating choroidal metastasis from other lesions. Optical coherence tomography can be used to assess for exudative retinal detachment within the macular region. Magnetic resonance imaging can be helpful in characterizing the morphology of choroidal lesions and determining whether orbital extension is present. If choroidal metastases are suspected in the setting of an unknown primary cancer, fine-needle aspiration biopsy with cytologic evaluation might be required.[6]

The presented case is not a choroidal melanoma because such lesions are generally solitary, elevated, dome- or mushroom-shaped, and can demonstrate an intrinsic circulation. These lesions characteristically show low to medium reflectivity on A-scan ultrasonography. Amelanotic melanomas, which represent up to 20% of primary intraocular melanomas, can be more difficult to distinguish from choroidal metastasis. Adjunctive testing, particularly ultrasonography, can be invaluable in such circumstances. Choroidal hemangiomas are typically reddish-orange and can have associated areas of fibrous metaplasia. Such lesions invariably demonstrate high internal reflectivity on A-scan ultrasound. Finally, the lesion is not a choroidal nevus because such lesions are brownish, pigmented, and flat, with feathery margins.

The overall prognosis for patients with choroidal metastases is poor. For example, patients with choroidal metastases from breast cancer generally have a median survival time of 314 days.[7] It has been reported that patients with stage 1 or 2 breast cancer with choroidal metastases have a median survival time of 29 months. Patients with stage 3 or 4 breast cancer with choroidal metastases have a median survival time of 5 months.[7]

Treatment

Inactive or asymptomatic metastatic choroidal tumours might not require specific ocular treatment. For larger lesions, symptomatic lesions, and lesions with subretinal fluid or exudative retinal detachment, treatment is generally indicated. Most metastatic choroidal tumours respond to systemic chemotherapy. External beam radiation therapy is generally effective for controlling active tumours and tumours refractory to systemic chemotherapy. This procedure can be performed in an outpatient setting over a 3- to 4-week period. Radiotherapy promotes tumour regression, prevents secondary glaucoma, and preserves the globe in almost all patients.[5] A higher dosage can lead to better tumour control, but increases the risk of radiation-induced complications such as loss of vision, dry eye syndrome, cataracts, and radiation retinopathy.[4] Focal treatment with plaque brachytherapy can also be performed, which offers the advantage of minimizing damage to other ocular structures and inducing a more rapid tumour regression.

More recently, the off-label use of an intravitreal anti-vascular endothelial growth factor agent such as bevacizumab has shown promise in treating subretinal fluid and inducing regression of metastatic choroidal lesions.[8,9] Very rarely, in severe cases, choroidal metastasis refractory to chemotherapy or radiotherapy might require enucleation or surgical excision.[7]

It is important to note that some tumours do not respond to systemic chemotherapy and that systemic treatments do not necessarily prevent the development of further choroidal metastases. Therefore, it is important for at-risk patients to undergo ophthalmic examinations.[2]

Conclusion

Patients with suspected choroidal metastases should be referred to ophthalmologists for assessment. Dilated fundoscopic examination in concert with ultrasonography generally provides sufficient diagnostic information. It is important for patients with known primary malignancy to undergo full workup to search for other areas of systemic dissemination. Patients with suspected choroidal metastases without known primary malignancy should be referred to internists for comprehensive workup. If noninvasive systemic investigations are unable to identify a primary cancer, a fine-needle aspiration biopsy might be warranted.

Because most lesions respond to systemic chemotherapy, patients with asymptomatic choroidal metastases might not require specific ophthalmic intervention. Patients with large or symptomatic metastatic choroidal lesions might benefit from radiotherapy. All patients should be monitored carefully for the development of other secondary metastases.

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Competing interests
None declared

References

1. Shields CL, Shields JA, Gross NE, Schwartz GP, Lally SE. Survey of 520 eyes with uveal metastases. *Ophthalmology* 1997;104(8):1265-76.
2. Demirci H, Shields CL, Chao A-N, Shields JA. Uveal metastasis from breast cancer in 264 patients. *Am J Ophthalmol* 2003;136(2):264-71.
3. Bloch RS, Gartner S. The incidence of ocular metastatic carcinoma. *Arch Ophthalmol* 1971;85(6):673-5.
4. Wiegel T, Bottke D, Kreusel KM, Schmidt S, Bornfeld N, Foerster MH, et al. External beam radiotherapy of choroidal metastases—final results of a prospective study of the German Cancer Society (ARO 95-08). *Radiother Oncol* 2002;64(1):13-8.
5. Mewis L, Young SE. Breast carcinoma metastatic to the choroid. Analysis of 67 patients. *Ophthalmology* 1982;89(2):147-51.
6. Shields JA, Shields CL. Metastatic tumors to the uvea and retina. In: Shields JA, Shields CL, editors. *Diagnosis and management of intraocular tumors* Philadelphia, PA: WB Saunders; 1992. p. 207-38.
7. Freedman MI, Folk JC. Metastatic tumors to the eye and orbit. Patient survival and clinical characteristics. *Arch Ophthalmol* 1987;105(9):1215-9.
8. Amselem L, Cervera E, Díaz-Llopis M, Montero J, Garcia-Pous M, Udaondo P, et al. Intravitreal bevacizumab (Avastin) for choroidal metastasis secondary to breast carcinoma: short-term follow-up. *Eye* (Lond) 2007;21(4):566-7. Epub 2006 Nov 24.
9. Yao HY, Horng CT, Chen JT, Tsai ML. Regression of choroidal metastasis secondary to breast carcinoma with adjuvant intravitreal injection of bevacizumab. *Acta Ophthalmol* 2010;88(7):e282-3. DOI:10.1111/j.1755-3768.2009.01684.x.