Vitreous Metastasis in a Case of Metastatic Breast Cancer

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Established Facts

- Metastatic breast cancer (BC) to the vitreous is very rare, with only five prior cases confirmed by vitreous biopsy having been reported in the literature.
- Metastatic BC to the vitreous can present with clinical and imaging findings mimicking an infectious or inflammatory process.

Novel Insights

- This report is the first to document heterogenous clumpy material on the retinal surface using spectral-domain optical coherence tomography.
- This report is the first to document vasculitis-like findings with modern wide-field retinal photography and fluorescein angiography.

Keywords

Metastatic breast cancer · Vitreous metastasis · Vasculitis

Abstract

A 35-year-old female with a history of metastatic breast cancer (BC) presented with unilateral blurred vision and floaters over 6 weeks. Examination findings showed vitreous opacities and a vasculitis concerning for an infectious process. Diagnostic vitrectomy revealed no infectious cause, but rather metastatic cells in the vitreous, with no obvious retinal or choroidal metastatic focus. In this report we illustrate a case of vitreous metastasis in a patient with metastatic BC, highlighting the importance of recognizing this rare entity

which can mimic an inflammatory or infectious process. Novel to this report is the use of modern wide-field retinal imaging, spectral-domain optical coherence tomography, and a surgical video to document the findings of this disease entity.

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Introduction

Metastatic breast cancer (BC) to the vitreous is very rare [1]. To the best of our knowledge, only 5 prior cases of BC metastasis to the vitreous confirmed by vitreous biopsy have been reported in the literature [2–5]. We re-

Fig. 1. Color fundus photos OS at presentation. **a** The posterior pole showed vitreous clumpy opacities, vascular attenuation, intraretinal hemorrhages, and deposits on the macular surface and arcades. **b** The superotemporal periphery showed similar changes with denser vitreous opacities. **c** The inferior periphery showed preretinal deposits. **d** Wide-field Optos image at postoperative month 1 from vitrectomy showed significant clearing of the vitreous opacities. The superotemporal periphery showed vascular attenuation with perivascular sheathing. There was improvement of the previously seen vitreous deposits inferiorly.

port a case of a patient with metastatic BC who presented with vitreous metastasis confirmed by vitreous biopsy. We utilized modern retinal imaging with wide-field retinal photography and angiography as well as spectral-domain optical coherence tomography (SD-OCT) to document the retinal and vitreous findings. Furthermore, an intraoperative video from the diagnostic vitrectomy illustrated these findings.

Case Presentation

A 35-year-old female presented with floaters and blurry vision OS over 6 weeks. Her past medical history was significant for BC (cT2–3 N1, ER/PR-negative, HER2 positive) and BRCA2-positive. She received 4 months of chemotherapy (docetaxel, carboplatin, trastuzumab, and pertuzumab) 3 years earlier and bilateral nipple-sparing mastectomy followed by breast reconstruction. She developed metastases to bone, liver, and brain. Whole-brain eye-sparing radiotherapy was completed 3.5 months prior presentation, and additional chemotherapy (paclitaxel, trastuzumab, pertuzumab,

and denosumab) was started. New areas of disease were found and ado-trastuzumab was started 1 month prior to presentation.

On presentation, uncorrected visual acuity was 20/30⁻² OD and 20/70⁻¹ OS without pinhole improvement. Intraocular pressures were within normal limits. A 1+ relative afferent pupillary defect OS was present. Anterior segment examination was unremarkable OU, in particular there were no cell/flare or posterior synechiae. The crystalline lenses were clear. Dilated fundus examination was normal OD. There were moderate vitreous opacities OS. The optic nerve appeared within normal limits. There was attenuation of the vasculature in the fundus (Fig. 1). In the superior periphery there were vascular sheathing, ischemia, and intraretinal hemorrhages, while the inferior periphery had preretinal deposits. The retina was attached with no holes or tears.

SD-OCT showed trace cystoid macular edema with heterogeneous clumped material on the retina and no intraretinal masses. Snow-like hyperreflections were seen in the overlying vitreous (Fig. 2). Wide-field fluorescein angiography was normal OD. There were segmental filling defects in the posterior pole OS and the periphery showed phlebitis with areas of ischemia and blockage from hemorrhage (Fig. 3). There was no neovascularization of the disc or elsewhere. B-scan ultrasound OS showed moderate vitreous opacities with posterior vitreous detachment and no retinal

Fig. 2. Spectral-domain optical coherence tomographies through the foveal center OS. **a** At presentation the patient showed cystoid macular edema, a small pocket of subretinal fluid, and diffuse premacular deposits as well as vitreous opacities. **b** At postoperative month 1 after vitrectomy the patient showed resolved cystoid macular edema and subretinal fluid, while the premacular deposits and vitreous opacities had decreased. There was some ellipsoid zone disruption.

Fig. 3. Wide-field fluorescein angiography OS taken on postoperative day 9 after vitrectomy. **a** Shortly after venous filling the patient showed marked vascular attenuation, segmental filling defects of arterioles and venules, and scattered areas of blockage from intraretinal hemorrhages. **b** Late-phase frame showed continued segmental vascular filling defects and perivascular leakage. **c** The superotemporal periphery showed phlebitis with ischemic areas and blockage from intraretinal hemorrhages. **d** The inferior periphery showed vascular attenuation and phlebitis.

detachment. No choroidal lesions or extraocular extensions were evident on examination or ultrasound.

The patient reported that she had recently been treated with systemic steroids for a foot drop. With the history of immunosuppression and a catheter port present for chemotherapy, there was concern for an infectious etiology. To further evaluate an infectious, inflammatory, or metastatic etiology, she underwent diagnostic pars plana vitrectomy with intravitreal injections of vancomycin, ceftazidime, voriconazole, and foscarnet (see online suppl. video, www.karger.com/doi/10.1159/000506949). Undiluted and diluted vitreous samples as well as the cassette were sent for bacterial and fungal cultures, viral (HSV, VZV, and CMV) PCR, and cytology. Bacterial and fungal cultures and viral PCR were negative. Cytology revealed metastatic carcinoma, specifically numerous clusters of malignant epithelial cells with high nuclear cytoplasmic ratios. Immunohistochemistry showed that the cells were CK7-immunoreactive and express +1 HER2/neu membranous staining and were CK20-, TTF-1-, BRST-2-, mammaglobin-, E-cadherin-, ER-, and PR-negative.

At postoperative month 1 the patient's vision had improved to 20/50 and the vitreous opacities had markedly improved (Fig. 1). SD-OCT at that time showed decreased material overlying the retina and resolved cystoid macular edema (Fig. 2). An orbital MRI with and without contrast showed no optic nerve or orbital lesions. A brain MRI with and without contrast showed widespread metastatic disease involving multiple parenchymal intracranial lesions, calvarial lesions, but no leptomeningeal disease, and there was no enhancement of the optic nerves. The brain metastases were interpreted as slightly improved compared to the most recent study 2 months earlier. No lumbar puncture had been performed in the past or after the vitreous metastasis had been discovered. She was recommended to proceed with external beam radiation therapy to the left eye after consultation with ocular oncology (B.P.M.), but passed away at postoperative month 2 from acute hypoxemic respiratory failure.

Discussion and Conclusion

Most metastatic disease to the eye occurs in the choroid. Metastasis to the vitreous is exceptionally rare. It has been reported with metastatic skin melanoma, but less commonly with BC, despite BC being most common primary that metastasizes to the eye. Theories of the pathway responsible for vitreous metastasis include transoptic nerve spread from central nervous system disease or hematologic spread through the retina or from an existing choroidal metastasis that has invaded through the retina. Our patient showed no conclusive support for or opposition against a specific mechanism, but OCT showed no intraretinal masses or lesions in the areas imaged.

Piro et al. [2] reported the first case of vitreous involvement from metastatic BC which was confirmed by diagnostic vitrectomy. They reported that histopathologic study of the eyes obtained postmortem disclosed that

most of the tumor was located in the vitreous, and only rarely were individual tumor cells and small clusters of tumor cells observed in the retina.

Leys et al. [3] reported a case with a similar presentation to that of our patient. They observed collections of cells suspended in the vitreous in front of the retina temporal to the macula, and angiography revealed leaking retinal vessels in the affected area. Their patient underwent vitrectomy for concern of a fungal etiology, which was negative by culture. Electron microscopy of their sample confirmed malignant metastatic cells.

Zaldivar et al. [4] reported two cases of vitrectomy-confirmed BC metastatic to the vitreous. They described similar vascular sheathing as seen in our patient mimicking angiitis. Sirimaharaj et al. [5] also reported a case of vitreous metastasis, noting posterior vitreous cell clumps using time-domain OCT and sheathing of retinal vessels, with no choroidal lesions. Prior to their report, Truong et al. [6] used time-domain OCT to document features of a presumed BC metastasis to the retina without vitreous involvement.

Shields et al. [7] reported that metastatic tumors of the retina are rare and simulate retinitis. In their case series of 8 patients, 2 had primary cancer site of breast, but neither were reported to have had vitreous seeding. Interestingly, 5 of the 8 patients in their series were reported to have an initial misdiagnosis of infectious or inflammatory retinitis.

De Potter [1] hypothesized that the neoplastic cells may break through the internal limiting membrane of the retina and extend along its inner surface or invade the vitreous. Our patient presented with clinical and angiographic findings mimicking infectious or inflammatory retinitis. Vitrectomy confirmed no infectious etiology, but rather metastases to the vitreous. Wide-field fluorescein angiography highlighted the segmental vascular filling defects. Other significant clinical findings in our case and described by others included particulate clumping of material on the surface of the retina, vascular sheathing, clumpy rather than diffuse vitreous debris, and lack of a distinct choroidal or retinal metastatic source.

In summary, we report the sixth case of BC to the vitreous confirmed by vitreous biopsy. Novel to our report are: (1) documentation of the retinal and vitreous findings using modern photography and angiography, as previous reports used black and white photography and narrow-field angiography; (2) documentation of the preretinal deposits using SD-OCT, as previously reported OCT findings employed time domain; and (3) an intraoperative video from the pars plana vitrectomy showing the

vitreous and retinal findings described in this report. To the best of our knowledge, no prior reports have published an intraoperative video of this disease entity. Timely recognition and confirmation via diagnostic vitrectomy of this very rare entity are important as it can be initially misdiagnosed as an inflammatory or infectious process rather than from a malignant etiology.

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Statement of Ethics

The patient gave her written informed consent for publication of her case prior to her death.

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Disclosure Statement

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Author Contributions

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