Carcinoma of the Breast Metastatic to the Optic Nerve Mimicking an Optic Nerve Sheath Meningioma: Case Report and Review of the Literature

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ABSTRACT

Isolated metastatic tumors to the optic nerve are extremely rare. We describe a rare and unusual case of metastatic breast carcinoma to the optic nerve that mimicked an optic nerve sheath meningioma in its presentation due to its indolent symptom progression, initial radiological appearance, and minimal growth on serial imaging. The patient, a 46-year-old woman with a history of stable metastatic breast carcinoma, presented with progressive visual loss in her right eye over a 6-month interval. Magnetic resonance imaging revealed an enhancing lesion in the optic canal with an extension to the right anterior clinoid process and planum sphenoidale and into the right orbital apex, consistent with the presumptive diagnosis of optic nerve sheath meningioma. The tumor was resected and pathologically confirmed to be metastatic carcinoma of the breast. The clinical course, radiological features, surgical approach, and treatment strategies are reviewed.

KEYWORDS: Breast carcinoma, metastatic disease, ocular metastasis, optic nerve tumor, optic nerve sheath meningioma

Carcinoma metastatic to the eye is rare.¹ The reported incidence of ocular metastasis varies from 0.07 to 12%. The most frequently involved location is the uveal tract, particularly the posterior

temporal choroid.²⁻⁷ Metastases to the optic nerve occur far less frequently than ocular metastases. In a series of 227 patients with ocular metastasis, orbital metastasis, or both, Ferry and Font³ reported that

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only 3 cases (1.3%) involved metastases limited to the optic nerve or optic nerve sheath. In another review, Arnold and colleagues⁸ reported that before 1981, only 15 cases of isolated optic nerve metastasis had been reported. Of these 15 cases, 4 were reported to be carcinoma of the breast. Only 6 additional cases have been reported since 1981 (Table 1), bringing the total number of reported cases of isolated metastases to the optic nerve from carcinoma of the breast to 10.

We describe a case of metastatic breast cancer to the optic nerve that was preliminarily diagnosed based on its radiographic characteristics and indolent presentation as an optic nerve sheath meningioma. The clinical course, radiographic features, and treatment strategies are reviewed in the context of relevant data from the few reported cases that are similar.

CASE REPORT

A 46-year-old woman sought treatment after progressive loss of vision in her right eye for 6 months. Her medical history was significant for metastatic breast carcinoma, which was originally diagnosed in her right breast in 1990 (T4/N0/M0). She had previously been treated by a modified radical mastectomy followed by six cycles of chemotherapy with Doxorubicin and cyclophosphamide, radiation, and finally tamoxifen. The patient remained asymptomatic until 2001, when she was diagnosed with systemic metastatic disease in the right kidney, gallbladder, and small asymptomatic pulmonary nodules. For her metastatic disease, she was started on anastrozole. Her disease remained stable over the next 2 years.

The patient first noticed a decrease in her vision 6 months before presentation. Three months after her initial symptoms, visual acuity in her right eye decreased to a total loss of her right temporal field. At presentation, her symptoms had progressed to loss of light perception in her right eye. Vision in her left eye was normal. Fundoscopic examination

revealed mild hyperplasia of the retinal pigment epithelium, a cup-to-disc ratio of 0.2 on the right and of 0.1 on the left, and pallor of the right optic disc. Magnetic resonance (MR) imaging showed an enhancing lesion in the optic canal with an extension to the right anterior clinoid process and planum sphenoidale and into the right orbital apex consistent with the diagnosis of optic nerve sheath meningioma (Fig. 1A). Due to the already complete visual loss on the right and the presumptive diagnosis of optic nerve sheath meningioma, it was initially decided to observe the patient with close follow-up and repeat imaging.

Approximately 6 months later, the lesion had progressed slightly toward the optic chiasm (Fig. 1B). Given this mild progression and to prevent loss of vision in her unaffected eye, it was decided that a surgical biopsy and resection were indicated to obtain a definitive tissue diagnosis. A right-sided supraorbital approach was used to access the optic nerve. Upon resection, the consistency of the tumor appeared to be characteristic of metastatic carcinoma. The tumor directly involved the optic nerve. Pathological specimens confirmed metastatic tumor. Surgery was terminated once the tumor was significantly debulked and sufficient pathological specimens were obtained.

Postoperatively, the patient received additional chemotherapy, which included courses of Faslodex and Capecitabine, as well as fractionated radiotherapy (10 cycles 3000 cGy) to treat the residual tumor. Permanent pathological specimens confirmed metastatic adenocarcinoma from the breast. Four months after surgery, the patient's systematic metastases had progressed despite chemotherapy; she is currently being treated palliatively. Vision in her left eye remains unaffected.

DISCUSSION

In a review of all patients with orbital lesions referred to a specialty center, Shields and associates¹ noted that metastatic tumors to the orbit accounted

Table 1 Review of Clinical Data from All Reported Cases of Isolated Breast Metastases to the Optic Nerve

Reference	Age	Optic Nerve Involved	Presenting Symptoms	Fundoscopic Exam	Status of Disease at Presentation	Time to Symptom Onset after Mastectomy	Survival after Initial Symptom	Initial Radiological Diagnosis
Holden ²⁷ 1902	41	L	Visual loss + pain	Normal	DM (stomach, lung, liver)	2 years	3 mos	Not stated
Norton ²⁸ 1959	31	L	Visual loss	Elevated optic disc	LRR	5 years	6 mos	Not stated
Ferry, Font ³ 1974	Not stated	Both	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated
Arnold et al ⁸ 1981	70	L	Visual loss	Visible mass	LRR	3 years	3 years	Not stated
Mansour et al ²⁹ 1993	41	L	Visual loss	Mild disc pallor	DM (L frontal mass)	7 years	Not stated	Met
Hashimoto et al ²⁴ 1995	45	R	Exophthalmos	Not stated	NED	2 years	Not stated	ONSM
Allaire et al ³⁰ 1995	39	R	Visual loss	Visible mass over nerve head	DM (lung)	21 mos	6 mos	Met
Newman et al ³¹ 1996	61	L	Visual loss	Moderate disk edema	NED	2 years	Not stated	ONSM
Backhouse et al ²³ 1998	60	L	CRVO + visual loss	Vitreous hemorrhage	Not stated	3 years	4.5 mos	ONSM
Baeesa, Benoit ³² 1999	45	Optic chiasm	Bitemporal hemianopsia	Normal	NED	6 mos	6 mos	Not stated
Present Case	47	R	Visual loss	Optic disc pallor	DM (kidney, gallbladder, lung)	13 years	Alive at 4 mos	ONSM

DM, distant metastases (locations); CRVO, central retinal vein occlusion; L, left; LRR, local-regional recurrence (location); Met, metastasis; Mos, months; NED, no evidence of disease; ONSM, optic nerve sheath meningioma; R, right.

Figure 1 Coronal, T1-weighted, gadolinium-enhanced MR images at (A) the patient's initial presentation and (B) 6-month follow-up examination show a slight but definite progression of the tumor on the right optic nerve. A "dural tail" sign (arrow) is present.

for only 91 of 1264 (7%) of the studied cases. Isolated metastases to the optic nerve are much less frequent. The most recent reviews of only patients with eye and ocular metastases reported low rates of isolated metastases to the optic nerve: only 3 of 227 cases (1.3%) in one report³ and only 12 of 300 cases (4%) in another.⁹

In decreasing order of frequency, the most common tumors that have been reported to metastasize to the orbit and associated structures are as follows: breast, lung, genitourinary, and gastrointestinal cancers.^{10,11} In 1997, in a review of the 22 known cases of isolated metastases to the optic nerve, Mack and Jakobiec¹² reported that 15 originated from primary carcinomas (5 lung, 4 breast, 4 gastrointestinal tract, 1 pancreatic, and 1 prostatic), 3 from sarcomas, 2 from primary central nervous system tumors, 1 from a melanoma, and 1 from a carcinoid tumor.

Our review of the literature, including this case report, shows a total of 11 cases of carcinoma of the breast metastatic to the optic nerve have been reported since 1902 (Table 1). Their mean age at presentation was 48.0 years old; 50% were between 40 and 49 years old. This finding correlates with a previous review by Arnold et al⁸ in 1981 in which

the mean age at the onset of ocular symptoms from all metastatic carcinomas to the optic nerve was 48.9 years. Most patients (7 of 11) with metastatic breast carcinoma to the optic nerve had left optic nerve involvement (6 of 11 involved the left optic nerve alone, 3 of 11 involved the right optic nerve alone, 1 of 11 involved both, and 1 of 11 involved only the optic chiasm).

Visual loss was the initial symptom in 80% of the patients (8 of 10, 1 report did not state the presenting complaint). Of the remaining 2 patients, 1 presented with exophthalmos and 1 with bitemporal hemianopsia. In 2 patients who presented with decreased vision, 1 had accompanying pain and 1 had central retinal vein occlusion. In a review of carcinoma metastatic to the orbit and eye, Ferry and Font³ reported that the detection of the primary neoplasm preceded eye symptoms in 50.2% of the cases, symptoms preceded detection of the primary neoplasm in 46.3% of the cases, and the symptoms and diagnoses occurred at the same time in the remaining cases. However, in the breast cancer patients, the primary tumor and other sites of systemic metastases uniformly occurred before the eye metastasis was recognized. When these tumors do metastasize to the eye, however, Freedman and

Folk⁴ reported that they are typically aggressive and often occur bilaterally (~40%) and in multiple ocular locations (~20%). The latter frequency is much higher than that associated with metastases from other primary sites such as lung carcinoma (only 7% multiple ocular locations).¹³

In most patients with breast carcinoma metastatic to the optic nerve (9 of 10, 1 case did not report), the mean time to symptomatic presentation was about 4 years after mastectomy. The remaining patient, whose metastasis was located in the optic chiasm, presented 6 months after the mastectomy. In this case, the shorter interval may partially reflect its unique location and size ($2.5 \times 2.7 \times 3.0$ cm). Stephens and Shields reported⁵ that the interval between initial diagnosis and diagnosis of uveal metastasis from breast carcinoma is longer (range, 8 to 240 months) than it is from carcinoma of the lung (range, 2 to 15 months). The interval associated with optic nerve metastases reported here (range, 0.5 to 13 years; mean, 4 years) agrees with those of Stephens and Shields.⁵ Stephens and Shields attributed the difference to the longer, more indolent natural history of breast carcinoma.⁵ Improved understanding of the natural history of breast carcinoma and recent advances in treatment strategies also contribute to longer and more effective periods of remission than in earlier studies, as shown by the 13-year interval between mastectomy and the onset of visual symptoms in our patient.

The overall prognosis and survival times of patients with isolated metastatic breast carcinoma to the optic nerve are relatively poor. Survival after initial presentation of symptoms ranged from 3 months to 3 years; most patients (83%) survived less than 6 months (5 of 6 patients, 4 reports did not mention survival time, and our patient is on palliative care at 4 months). Despite treatment advantages compared to those available in the earliest reports, our patient's clinical course is following the same trend. Four months after identification of her optic nerve metastasis, her systemic metastases are progressing.

Although most patients (6 of 9, information unavailable for 2 patients) with optic nerve meta-

stases showed evidence of systemic metastatic breast carcinoma at or before their optic nerve tumor was diagnosed, 3 of the 9 patients (33.3%) did not. Even with a significant history of breast cancer, 4 of the 6 cases listed optic nerve sheath meningioma as the original presumptive diagnosis. (Four reports antedate contemporary diagnostic imaging technology. A recent report did not mention the presumptive diagnosis.)

Isolated metastatic tumors of the optic nerve remain a diagnostic challenge because of their similarities to more common primary tumors of the optic nerve. The most common optic nerve tumors are gliomas, followed by meningiomas.^{14,15} Meningiomas account for almost a third of all primary optic nerve tumors.¹⁴ Optic nerve sheath meningiomas account for 1 to 2% of all meningiomas and for 1.7% of all orbital tumors.^{15,16} Optic nerve sheath meningiomas have a female predominance (61%) and most are unilateral.¹⁵ The incidence of meningiomas is higher in patients with breast cancer.¹⁷ According to data from the Swedish Cancer Registry and from the United States Surveillance, Epidemiology and End Results (SEER) Program, the risk of developing a meningioma after having breast cancer increases by a factor of 1.57 to 1.90.^{18,19} Primary meningiomas have also been reported in patients previously diagnosed with metastatic breast cancer.^{20,21}

Radiographic features considered characteristic of optic nerve sheath meningioma,²² such as the "tram track sign" or central optic nerve lucency seen on contrast-enhanced computed tomography (CT), have also been found in metastases to the optic nerve.^{23,24} Although typically more specific and sensitive than CT, MR imaging can still be inconclusive because the appearances of these two pathologies on imaging overlap considerably. Optic nerve sheath meningiomas can be isointense (60 to 90%) or hypointense (10 to 30%) on T1-weighted imaging. On T2-weighted imaging, 30 to 45% of meningiomas are hyperintense, while 50% are isointense.²⁵ Metastatic carcinomas are characteristically isointense or slightly hyperintense on T1-weighted images and hypointense on T2-weighted

images.⁹ Therefore, MR and CT may help localize the lesion and offer some useful information to help narrow the differential diagnosis, but it cannot offer a conclusive diagnosis.

The classic presentation of an optic nerve sheath meningioma is that of a slowly progressive, painless loss of vision,²⁶ identical to the presenting symptom in our patient. Fundoscopic examinations can reveal similarities between the two disorders such as pallor of the optic disc, elevation of the optic disc, and the appearance of shunt vessels caused by central retinal vein occlusion.²³ Although the rate of tumor progression identified by serial MR imaging is typically rapid in carcinomas, it may mimic the indolent nature of optic nerve sheath meningiomas. Not surprisingly, optic nerve metastases have often initially been misdiagnosed as optic nerve sheath meningiomas.^{23,24}

Typically, optic nerve sheath meningioma in a patient with a blind eye and lack of encroachment on the opposite eye has been managed with serial clinical and radiographic follow-up. Progression of the tumor would then trigger treatment, either surgical or more commonly radiotherapeutic. However, in patients with optic nerve lesions and a known history of metastatic breast cancer, surgical biopsy should be obtained.

CONCLUSION

In contrast to the typical observational or radiotherapeutic management of optic nerve sheath meningioma, in patients with a history of breast cancer, the presumptive diagnosis of optic nerve sheath meningioma should be confirmed by surgical biopsy and pathological analysis.

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Commentary

The authors present an interesting case and an important reminder that while imaging studies have substantially improved our ability to make a diagnosis, they are no substitute for pathological analysis. As CT and MRI have improved, neurosurgeons have been more reluctant to obtain tissue material surgically in lesions considered better treated by other modalities. This reluctance is true for the treatment of optic nerve sheath meningiomas, for which recent studies have indicated that the results associated with fractionated radiation therapy are far better than those associated with observation, surgery, or surgery combined with radiation therapy.¹ Thus, it is often advocated that

patients with lesions that look like optic nerve sheath meningiomas be treated without pathologic confirmation.

It is well recognized that other pathologic processes can produce a radiographic appearance similar to that of an optic nerve sheath meningioma. These entities most importantly include sarcoid lesions and infiltration related to lymphoproliferative disorders, such as lymphoma or leukemia. In addition, idiopathic orbital inflammatory disease may affect primarily the optic nerve sheath. There are often specific clues to exclude these unusual lesions, including the almost universal presence of pain in patients with orbital inflammatory disease. Another clue is evidence of additional systemic involvement, as often found in sarcoid or lymphoproliferative disorders. Radiographically, breast carcinoma also may be indistinguishable from meningioma.²

It is important to recognize that this patient did not have a typical optic nerve sheath meningioma.³ Although the optic nerve sheath may be involved secondarily from meningiomas originating in the anterior clinoid or tuberculum sella regions, primary optic nerve sheath meningiomas arise within the orbit itself. The conclusions of Turbin and coworkers¹ were based on a limited series of patients that excluded all with primary involvement of the clinoid or tuberculum. In this patient's case, the lesion had several atypical features. The lesion not only involved the superior portion of the canal and the intercanalicular optic nerve, but the patient had a clinical history of rapidly deteriorating vision. Although meningiomas can worsen suddenly, most have an exceptionally slow course. In particular, primary optic nerve sheath meningiomas can be unrecognized for years or thought to represent such chronic diseases as optic neuritis.

The final key piece of atypical information in this case was the patient's history of breast carcinoma. Breast carcinoma metastatic to the area of the optic canal is unusual but occurs. This patient's history is similar to that of patients with known prostrate carcinoma⁴ and remains a red flag for additional evaluation.

In the discussion, the authors note an additional problem: identifying different locations for involvement of the visual system. Metastatic lesions to the optic nerve head, optic nerve sheath, and intracranial portion of the optic nerve all decrease visual acuity, but their incidence is definitely different. The authors quote Ferry and Font,⁵ who studied metastatic tumors to the globe. None of their patients had tumors that were metastatic to the optic nerve. However, Ferry and Font's series was generated from an ophthalmic pathology study that only considered the globes and anterior orbit. Therefore, although we have good data on metastatic tumors to the choroid and proximal nerve, good data regarding metastasis to the optic canal are lacking.

The authors correctly note that involvement of the optic nerve within the globe by metastatic tumor is unusual.⁶⁻⁸ However, choroidal involvement of metastatic breast carcinoma and other metastatic disease is not all that rare. Pathologically, metastatic disease is the most common neoplastic process found in the eye. Its incidence is slightly higher than that of the most common primary tumor of the choroid, melanoma. Many of these tumors, however, are asymptomatic and found only at autopsy. Breast carcinoma can metastasize to the optic nerve sheath but not involve the canal or tuberculum sellae. A patient with a tumor involving the optic nerve sheath was reported from Emory in 1996⁹ and a second patient was seen in Australia in 1998.¹⁰ These patients showed characteristics similar to the patient in this study, rapidly developing complete loss of vision as opposed to the course expected for an optic nerve sheath meningioma.

I agree with the authors' contention that a metastatic lesion must be considered in a patient with a previous history of breast carcinoma and a lesion of the orbital apex involving the area of tuberculum sellae and anterior clinoid. This case also points out the importance of not relying strictly on imaging studies. The patient's clinical history, medical history, and atypical findings may provide clues that suggest the need for additional diagnostic tests.

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Commentary

Fox and colleagues present a 46-year-old woman with stable metastatic breast carcinoma who developed progressive unilateral vision loss. MRI suggested an optic nerve sheath meningioma. After surgical resection through a supraorbital approach, however, pathological analysis identified metastatic breast carcinoma. The case demonstrates that breast carcinoma can, on rare occasion, metastasize to the optic nerve and mimic an optic nerve sheath meningioma. Ten other cases reported in the literature are summarized. This diagnosis should be remembered in patients with breast

cancer in their medical history, even when mastectomy was remote, as in this case, and when the patient is thought to be in remission. The poor prognosis associated with metastatic breast carci-

noma to the optic nerve indicates a conservative surgical approach.

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