Intrameningioma metastasis of breast carcinoma

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Abstract

Tumor-to-tumor metastasis of breast carcinoma to meningioma is a rare phenomenon. It is likely underdiagnosed given the relatively high prevalence and comorbidity of these two primary tumor types, the lack of standardized methodologies for its diagnosis, and the tendency to obfuscate this lesion with simple meningioma or cerebral metastasis of breast carcinoma. Careful histopathologic study of the resected meningioma is the cornerstone of diagnosis of these lesions, although certain conventional radiological features along with specialized modalities may clue the diagnosis. Vigilance for this lesion is appropriate in selected patients with known breast cancer or meningioma, as the two are often coexistent in the same patient, permitting tumor-to-tumor metastasis. Detection of this rare disease process may alter the treatment plan and prognosis. Here, we report a case of breast carcinoma-to-meningioma metastasis in a patient who developed subacute neurological decline while undergoing long-term treatment of her primary, late-stage breast cancer.

Introduction

Multiple, comorbid primary tumors afflict around one in 35 patients with cancer.[1] Metastasis of one primary neoplasm to another is a highly unusual phenomenon. In a patient with a preexisting malignancy, the differential diagnosis of a dural mass includes meningioma, dural metastasis, and, infrequently, intrameningioma metastasis.[2] Central nervous system (CNS) spread of primary breast carcinoma, which is present in 8% to 10% of patients with stage IV breast cancer,[3] is relatively uncommon unless diffuse systemic metastases are also present.[4] When cerebral metastases are detected in breast cancer, radiotherapy is often commenced by default without verifying the tissue diagnosis.[5]

Breast cancer and meningioma have a strong epidemiological association, as first observed by Schoenberg et al. in 1975, and women with either meningioma or breast cancer have a higher risk of being diagnosed with the other condition.[6] Meningiomas are twice as common in women than men, and, like breast cancer, have a predilection for the fifth or sixth decades of life and similarly tend to grow during pregnancy.[7] Collectively, these features suggest a shared pathogenetic mechanism.[3]

In rare instances, the discovery of a tumor-to-meningioma metastasis may herald an occult primary malignancy, including breast carcinoma. Among all malignancies, renal cell carcinoma and lung carcinoma are the most common recipient and donor tumors, respectively.[2] Meningioma is the most common benign tumor to accept metastases, which most frequently originate from breast and lung carcinomas.[8] Furthermore, meningioma, which comprises over one-third of all CNS tumors,[9] has the highest proclivity for accepting metastases among all intracranial tumors.[2] Intrameningioma metastases documented in the literature were overwhelmingly located intracranially, except for two reported cases of spinal meningioma.[10,11]

Case Report

A 50-year-old woman presented to our service complaining of a recent episode of dizziness and syncope. The patient's medical history was notable for a diagnosis of breast carcinoma seven years earlier. She had been managed with bilateral mastectomies, adjuvant chemotherapy, and hormonal therapy with tamoxifen for two years thereafter. After bone, liver, and lung metastases were detected three years after her mastectomies, she received palliative radiotherapy to her sternum, clavicle, and spine, and salvage chemotherapy was initiated.

Although the patient's neurological examination was normal, a head CT scan demonstrated a large anterior extra-axial mass consistent with meningioma. Over the course of the four weeks preceding the procedure, the patient went on to develop complete left monocular blindness. MRI showed a 5.3×5.4×5.9 cm mass with areas of focal hypoenhancement. Axial fast spin-echo T2-weighted (Figure 1A) and axial FLAIR (Figure 1B) images demonstrated a midline heterogeneous mass in the anterior cranial fossa with surrounding edema. On unenhanced (Figure 1C) and enhanced (Figure 1D) T1-weighted images, avid and homogeneous enhancement of the lesion was evident. A color map of relative cerebral volume map (Figure 2), derived from dynamic susceptibility-weighted perfusion MRI (pMRI), showed markedly increased intratumoral blood volume on the right side of the mass. A T2* susceptibility intensity time curve (Figure 2) within two different regions of the brain demonstrated markedly disparate curve characteristics, suggesting different tumor vascular properties.

Prior to the operation, the mass was embolized. The patient underwent an extended bifrontal craniotomy, aided by previously obtained Stealth MRI scans co-registered with scalp fiducials. A curvilinear incision was made in the coronal plane over the patient's scalp, and a single myocutaneous flap was mobilized anteriorly. The Anspach drill was used to craniectomize above the sinuses, and orbital contents, including the supraorbital nerve, were separated bilaterally. The orbital bar was removed, and the dura was incised

with Lahey scissors in a curvilinear fashion, flapping towards the sagittal sinuses on either side. The anterior portion of the dura was ligated and cauterized, and the sinus was subsequently pulled posteriorly. The tumor was immediately evident upon pulling back the falx. Using bipolar cautery, suction, irrigation, and ultrasonic aspiration, the tumor was internally debulked and delivered into itself. Microscopic dissection facilitated removal of the tumor with preservation of the anterior cerebral artery, optic nerves, and optic chiasm. The tumor was completely resected, and samples were sent for pathologic analysis.

Postoperatively, the patient was clinically stable and demonstrated slow improvement of her vision. Six weeks after surgery, the patient had intact central vision in her left eye with a peripheral ring of blurriness. At this time the patient had evidence of progressive metastatic disease, including significant ascites.

Pathological findings

The surgical material consisted of multiple fragments of hemorrhagic tissue with variable texture and consistency, measuring 7×6×2.5 cm in aggregate and weighing 22 grams. On routine H&E sections, two distinct histologic patterns were identified (Figure 3). The predominant pattern (approximately two-thirds overall) consisted of a neoplasm with glandular architecture. The glands contained intraluminal mucin and were lined by moderately pleomorphic cuboidal to columnar cells with eosinophilic cytoplasm, open chromatin, and distinct nucleoli. Intracytoplasmic mucin was noted. Mitotic figures were easily identified as well as numerous foci of necrosis. These features are consistent with a metastatic adenocarcinoma. The tumor intermingled with a neoplasm composed of syncytial and whorled collections of cells with oval nuclei, powdery chromatin, and inconspicuous nucleoli. Mitotic figures were rare. Atypical features were not identified. This histologic appearance is consistent with a benign meningioma, WHO grade I. Immunohistochemical studies showed that the adenocarcinoma was diffusely and strongly positive for epithelial membrane antigen (EMA) and pancytokeratin; the estrogen receptor (ER) was only focally positive and the progesterone receptor (PR) and Her2/CB11 were negative. The meningioma showed strong and diffuse membranous staining for EMA and positivity for PR, while the ER, pancytokeratin, and Her2/CB11 were negative.

Discussion

Carcinoma metastatic to meningioma is a rare CNS lesion. The most common extracranial tumor to display this dispersive pattern is

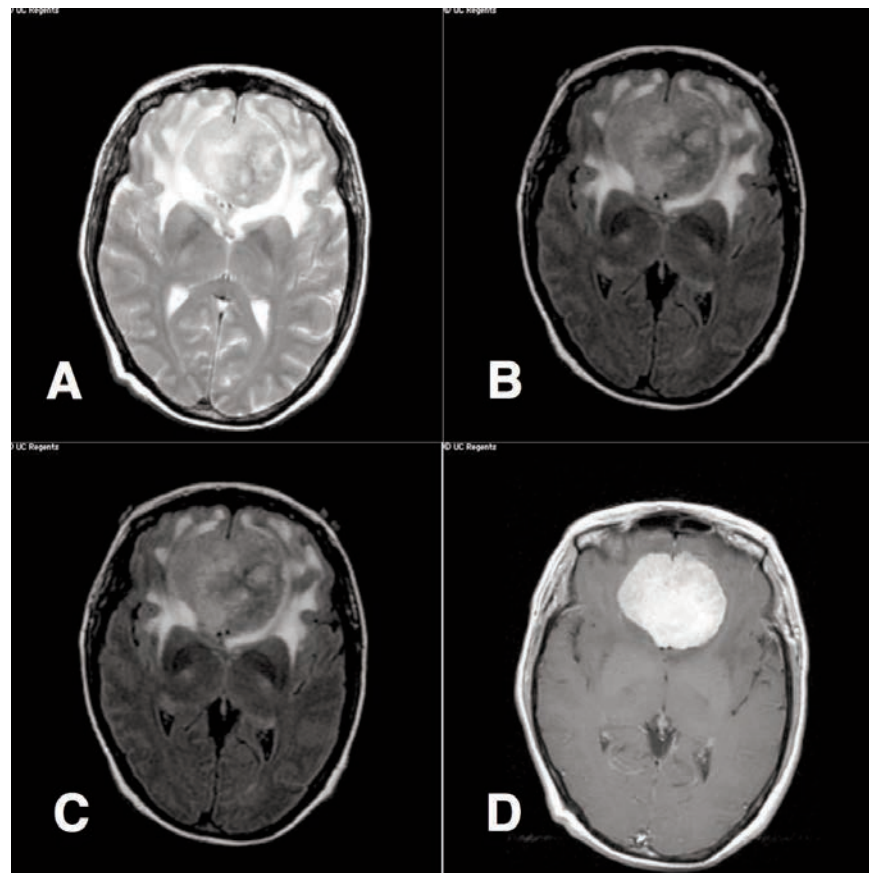
Figure 1. Axial fast spin-echo T2-weighted (A) and Axial FLAIR (B) images show a midline anterior cranial fossa heterogeneous mass with surrounding edema. Unenhanced T1-weighted (C) and enhanced T1-weighted (D) image demonstrate avid and homogeneous enhancement of the mass.
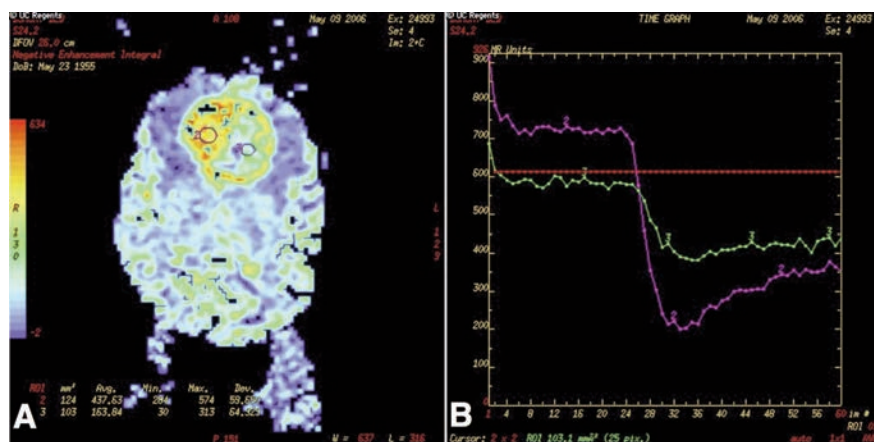

Figure 2. A) A color map of relative cerebral volume map derived from dynamic susceptibility-weighted perfusion magnetic resonance imaging shows marked increase in blood volume within tumor on the right. B) A T2* susceptibility intensity time curve within two different regions of the brain demonstrates markedly different curve characteristics suggesting different tumor vascular properties.

breast carcinoma, typically arising in women in their fifth and sixth decades of life.[8] In 1968, Campbell *et al*. proposed four criteria for the diagnosis of tumor-to-tumor metastasis: i) at least two primary tumors must exist; ii) the host tumor must be a true neoplasm; iii) the metastatic focus must show established growth inside of the host tumor, and must not be the result of contiguous growth, a collision process, or embolization; and iv) the host tumor cannot be a lymph node involved by leukemia or lymphoma.[12] According to this scheme, less than 100 cases of tumor-to-tumor metastasis have been reported in the literature,[2] and around 50 cases implicate meningioma as the recipient tumor.[4,13]

In the interest of distinguishing this phenomenon from so-called collision tumors, Pamphlett outlined two diagnostic criteria for *true* tumor-to-meningioma metastasis: i) the metastatic focus must be at least partially enclosed by a rim of histologically distinct host tumor tissue; and ii) the existence of the metastasizing primary carcinoma must be proven and compatible with the metastasis.[13] Identification of the metastatic epicenter and local leptomeningeal involvement, if present, are likewise suggestive of a true intrameningioma metastasis rather than a collision tumor.[2]

Various pathophysiological mechanisms have been proposed to explain the tumor-to-tumor metastasis of breast carcinoma to meningioma. The highly collagenous and vascular histology of meningiomas, combined with the comparatively low growth requirements of this indolent tumor, provide a rich metabolic environment for metastases.[14] Local immunosupression and the reciprocal expression of cell-cell adhesion factors may facilitate the seeding of one tumor by another.[15]

Overexpression of oncogenes, in particular c-Myc, is a typical molecular alteration in both meningioma and metastatic breast carcinoma cells,[16] along with the breast carcinoma and meningioma compartments of a reported tumor-to-tumor metastasis,[17] and could contribute to the predilection of these two disease processes to occur together.

Breast carcinoma and meningioma are each conspicuous for high rates of steroid receptor immunopositivity, likely contributing to the gender-disparate epidemiology of meningiomas. Expression of progesterone and estrogen receptors in meningiomas may be as high as 90% and 30%, respectively.[18] The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program reported that 79.6% of breast cancers display steroid receptor expression, including ER positivity in 76.3% and PR positivity in 66.8%.[19] Hormone receptor status is also a histopathologic correlate of breast cancer metastasis: ER-positive tumors preferentially spread to the bone, soft tissue, or reproductive tracts, whereas ER-negative tumors largely metastasize to the brain and liver, sites that forebode a more ominous prognosis.[20]

In this case, radiological studies were not diagnostic of the tumor-to-tumor metastasis. Although characteristic radiological features have been described, they are neither sensitive nor specific.[8,21] Consequently, intrameningioma metastasis cannot be excluded by routine neuroimaging with CT and MRI. Even with a sufficient index of suspicion, it is very difficult to diagnose this lesion before performing surgical biopsy and pathological analysis of the meningioma.[4] Specialized, physiology-based neuroimaging modalities, namely magnetic resonance spectroscopy (MRS) and pMRI, have a superior diagnostic yield for this lesion.[8] MRS achieves detailed tissue and metabolic characterization of tumors relative to MRI, while pMRI differentiates tissue types on the basis of hemodynamic patterns of tumor blood flow.[21] Adjunctive use of these imaging modalities may be warranted in selected patients with established diagnoses of such tumors and/or clinical features of an occult carcinoma. The shortcomings of radiological diagnosis of this unusual lesion underscore the importance of careful pathologic analysis. While its histopathologic features are incontrovertible, the diagnosis of breast carcinoma-to-meningioma metastasis can be missed if the entire tumor is not systematically studied. This merits careful coordination between surgeons and pathologists in cases where tumor-to-tumor metastasis is possible, given its potential implications for patient prognosis and subsequent management.

Conclusions

Clinicians caring for patients with either meningioma or breast cancer should be familiar with the possibility for intrameningioma metastasis, an uncommon pathological entity that can precipitate progressive worsening of neurological status. This phenomenon is most likely to occur in women in their fifth or sixth decades of life. Certain radiological features may suggest the diagnosis, but, as these are neither sensitive nor specific, specialized radiological modalities such as MRS and pMRI may be indicated in select cases. The only definitive method of diagnosis is thorough scrutiny of the biopsied tissue specimen. Going forward, it will be important to define the prognostic impact and optimal management approach for meningioma patients who are discovered to have this superimposed lesion.
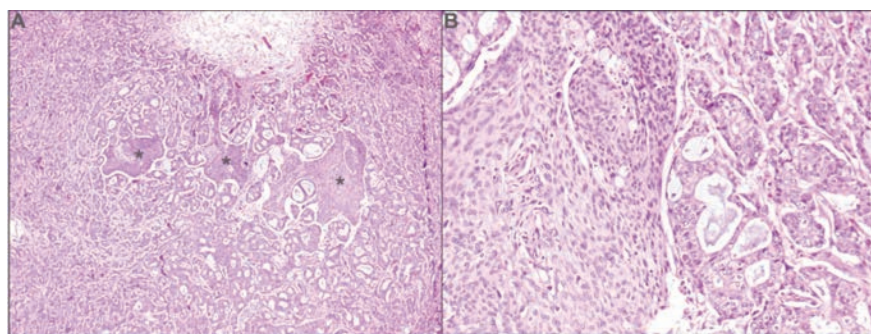

Figure 3. Representative histologic sections of the collision between metastatic adenocarcinoma and benign meningioma. A) Islands of meningioma surrounded by adenocarcinoma (*marks meningioma islands. Magnification: 40×. B) The adenocarcinoma (right half) consists of glands containing intraluminal mucin and lined by moderately pleomorphic cuboidal to columnar cells with eosinophilic cytoplasm, open chromatin, and distinct nucleoli. The meningioma (left half) consists of syncytial collections of cells with oval nuclei, powdery chromatin, and inconspicuous nucleoli. No atypical features are identified. Magnification: 100×.

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