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Case Report

A Case Report of Triple Tumors Including Intratumoral Metastasis

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Abstract

Tumor-to-tumor metastasis is a rare phenomenon that is most likely under - recognized. Lung, breast carcinomas, and meningiomas have a high prevalence in their primary state. Additionally, both lung and breast carcinomas have a propensity to metastasize, in particular to bone, brain, and liver. Despite the tumor's predisposition to metastasize to the brain, radio logically and clinically, it is difficult to recognize this phenomenon, and likely to be misdiagnosed as solely primary meningioma or cerebral metastasis. We describe a unique case of a 74-year-old female with history of breast carcinoma and lung carcinoma, who presented with a brain mass demonstrating radiological features of a meningioma. More interestingly, a separate nasal mass was incidentally found intraoperatively. The complicated clinical history and radiological differential diagnosis made intraoperative frozen section consultation extremely difficult. The final diagnosis also required the aid of immunohistochemical studies. Pathologists should be mindful of the phenomenon of intratumoral metastasis and concurrent neoplasms. Sampling should also be adequate, and meticulous histopathologic examination of the suspected meningioma is of utmost importance. Detection of this rare event can provide more precise treatment options and prognosis. More importantly, it raises the question if genetic counseling is warranted in such a patient with multiple concurrent neoplasms.

ABBREVIATIONS

HPC: Hemangiopericytoma; SMA: Smooth Muscle Actin; EMA: Epithelial Membrane Antigen; PR: Progesterone Receptor

INTRODUCTION

Approximately one in 35 cancer patients harbors multiple, coexistent primary tumors and rarely are those two primary tumors anatomically contiguous [1]. Intracranial tumor-to-tumor (intratumoral) metastases are rare but well -recognized events with less than 100 cases described in literature [2-5]. By definition, a tumor-to-tumor phenomenon signifies that a primary tumor contains a metastatic focus of another primary tumor. Meningiomas tend to be one of the most common primary tumors to receive seed metastases. The most frequent metastases are originally from breast or lung [3,6-11]. Other sites that have been found to metastasize to meningioma are renal, genitourinary, gastrointestinal, prostate, parotid, and lymphoma [3,6,10].

The differential diagnosis for infiltrative intracranial lesions may include a primary central nervous system malignancy or a metastatic tumor [6,7]. Metastasis within a primary meningioma can provide a unique differential diagnostic dilemma as the tumor can simulate either the primary or the metastatic disease clinically [8]. Thus the pathologic index of suspicion must remain high.

Sino nasal - type hemangiopericytoma, also known as glomangiopericytoma, is a distinct variant of classical hemangiopericytoma. This variant is a rare tumor, accounting for < 0.5% of all sinonasal tract neoplasms [12-14]. Patients are usually between 60 and 70 years old, with a slight female predominance, and clinically present with unilateral nasal obstruction and/or epistaxis [12]. Sinonasal - type hemangiopericytomastypically arise in the nasal cavity or paranasal sinuses as a small (3 cm average) polypoid mass and exhibit more indolent clinical course than other sites of hemangiopericytomas [15]. Prognosis is excellent (> 90% 5 - year survival) with complete surgical excision [15]. The differential diagnosis for sinonasal lesions is slightly broader and includes: glomangiopericytoma, sinonasal tract polyps (antrochoanal polyp), juvenile nasopharyngeal

angiofibroma, meningioma, solitary fibrous tumor, and lobular capillary hemangioma, among others [15].

Herein, we describe a unique case of a 74-year-old female with history of breast carcinoma and lung carcinoma presented with a brain mass demonstrating radiological features of a meningioma. More interestingly, a separate nasal mass was incidentally found intra operatively. We will describe the histomorphology and immunohistochemical studies aiding in the diagnosis and discuss the hypotheses for the tumor-to-tumor metastasis.

CASE PRESENTATION

A 74-year-old female presented with vision loss and daily headaches to our neurosurgery outpatient clinic. The three - month history of decreased vision included an inability to make out shapes and loss of peripheral vision in the right eye. The intermittent, dull headaches developed one week prior to presentation and were located in the posterior aspect of her head. She denied other symptoms. Other than an inability to perform tandem walk without difficulty, the neurological and physical examination was normal. Her past medical history was significant for lung cancer treated by chemotherapy and breast cancer treated by a mastectomy. MRI showed an enhancing extra - axial, suprasellar mass (3.0 cm antero - posterior x 2.3 cm transverse x 1.4 cm cranio - caudal). The mass abutted the anterior margin of the optic chiasm, the medial margins of the bilateral internal carotid arteries at the supraclinoid segments, and surrounded the cisternal segments of the bilateral optic nerves. Imaging was suggestive of a meningioma (Figure 1A). The mass had grown since the prior MRI conducted one-month before at an outside hospital.

She presented to the hospital for elective expanded endonasal approach to what was suspected to be a meningioma. Perioperatively, the surgeons found a left nasal mass, which was not recognized on radiological studies. The lesion was excised and submitted it for intraoperative consultation. On frozen section examination, the lesion was composed of relatively bland spindle cells forming short fascicles with rare whorling pattern. Some gate - open vessels were identified. With the clinical impression of meningioma, the case was signed out as “meningioma versus glomangiopericytoma, defer to permanent section.”

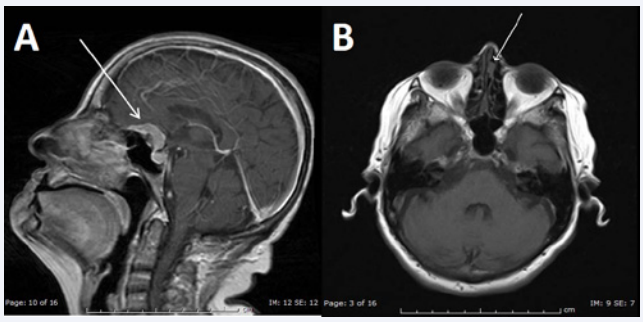

Figure 1 MRI Brain without contrast. (A) The arrow points to the suprasellar mass, measuring 3.0x2.3x1.4cm. (B) The arrow points to the left nasal mass, measuring about 1.1x1.1x0.5cm, which is initially missed by radiologists.

The suprasellar mass was also submitted for intraoperative frozen section evaluation. The tissue was divided and one - half was submitted for frozen section evaluation and other half kept for later processing. The tumor was composed of sheets of epithelioid or spindle syncytial cells in a whorling pattern. Numerous psammoma bodies were present. The intraoperative diagnosis was “consistent with meningioma.” Additional tissue was submitted by the surgeon directly in 10% formaldehyde for further processing.

Postoperatively, she did well for the first 48 hours while being maintained on antibiotics. However, shortly thereafter, she developed respiratory failure and was found to have some non occlusive pulmonary emboli secondary to deep vein thrombosis. She required aggressive respiratory and cardiac support. However, she continued to decline with multi organ failure until the family decided to withdraw care and subsequently passed away.

Retrospectively on the MRI, the incidental left nasal mass was separated by 3.5 cm from the suprasellar tumor, and measured 11 x 5 x 11 mm (Figure 1B). On permanent H&E sections, under the intact respiratory epithelial mucosa, the tumor mass comprised of closely packed spindle cells, forming short fascicles with rare whorled pattern. Hyalinized vessels with staghorn pattern were present. Rare mitoses (1/10 high power fields) were identified. The tumor cells were positive for smooth muscle actin (SMA) and Factor XIIIa, and negative for EMA, PR, and S100. The morphology and immune - profile was most consistent with hemangiopericytoma, sinonasal - type (glomangiopericytoma) (Figure 2).

The suprasellar tumor was composed of sheets of epithelioid or spindle syncytial cells with intranuclear inclusions in a whorling pattern. There were no mitotic figures or necrosis identified. Tumor cells were strongly positive for epithelial membrane antigen (EMA) and progesterone receptor (PR) with a Ki-67 labeling index of 1%. The morphology and immunohistochemical profile was consistent with meningioma, WHO grade 1. However, intermixed with the meningioma cells, were rare relative bland glandular structures, which were not present on the frozen sections. The gland lining cells were positive for GATA3 and mammaglobin and negative for TTF-1 and Napsin-A with a Ki-67 of approximately 90%. These morphological and immunohistochemical profiles were most consistent with metastatic breast adenocarcinoma to a meningioma (Figure 3).

DISCUSSION

Breast metastasis to meningioma is a rare event. In 1968, Campbell et al. outlined four criteria for the diagnosis of tumor-to-tumor phenomenon: (I) at least two primary tumors must exist; (II) the host tumor must be a true neoplasm; (III) the metastatic tumor must show growth inside of the host tumor, and must not be the result of contiguous growth, a collision process, or embolization; and (IV) the tumor cannot have metastasized to the lymphatic system that is already involved by leukemia or lymphoma [16]. Our patient qualifies for all these criteria.

The exact mechanism of this phenomenon is unclear. However, there have been two major theories put forward. The first, by Ewing et al., suggests that the more afferent blood vessels

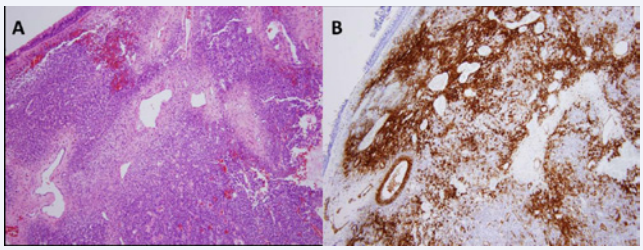

Figure 2 (A) Tumor is composed of spindle cells forming short fascicles with rare whorling. Hyalinized vessels with staghorn pattern are seen throughout the tumor (H&E, 20x). (B) Tumor cells are positive for SMA (IHC, 20x).

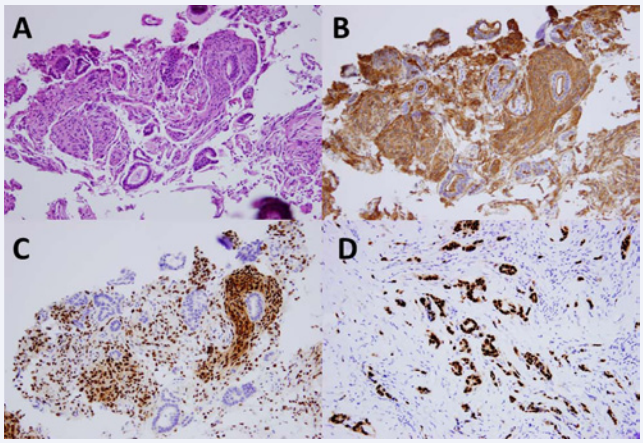

Figure 3 (A) Rare bland glands intermixed with syncytial epithelioid tumor cells in a whorling pattern (H&E, 20x). The syncytial tumor cells are positive for EMA (B) and PR (C), whereas the glandular cells are negative for both (IHC, 20x). (D) The gland lining cells are positive for GATA3 (IHC, 20x). The overall morphology and immune profile is consistent with breast duct carcinoma metastasis into meningioma (tumor-to-tumor metastasis).

provided to the tumor, the greater the number of tumor cells delivered to the site [17]. This would explain why meningiomas, with their highly vascular nature, are predisposed to receiving metastases. The second theory proposes that a higher lipid and glycogen content in the recipient tumor creates an advantageous biochemistry for the growth of metastases [18].

Tumor-to-tumor metastases remain an important clinical consideration and have become more frequent with the advances in cancer management and subsequent improvement of patient prognosis and survival. Pathologists should be aware of this phenomenon and should have a high index of suspicion when patients have a history of a prior malignancy. The diagnosis of donor and recipient tumors could drastically change management and thus meningiomas, among other tumors, should be highly scrutinized for abrupt transition in morphology.

The sinonasal variant of hemangiopericytoma is a distinct entity. Morphologically they are comprised of syncytial cells arranged in various patterns: short fascicles, storiform, whorled, "meningothelial," reticular, or short palisades of closely packed cells [15]. There are staghorn vessels with peritheliomatous hyalinization as well as mast cells, eosinophils and extravasated erythrocytes in the background [15]. Coupled with its unique histologic features and myoid phenotype (expresses smooth muscle markers), sinonasal-type hemangiopericytomas are thought to be part of the myopericytic tumor family [19-22].

Although rare in the sinonasal tract, sinonasal meningiomas account for about 2% of all meningiomas and < 0.1% of all non epithelial sinonasal tract neoplasms [23-25]. Meningiomas can either be primary or have direct extension spread into the sinonasal tract [24-26]. Histologically, meningiomas are composed of bland, syncytial cells arranged in lobules [25,27]. The cells typically demonstrate meningothelial whorling with isolated psammomatous calcifications [15]. The differential diagnosis between sinonasal - type of hemangiopericytoma and meningioma can be difficult when relying only on morphology. Immunohistochemical studies usually help in reaching the right diagnosis, as sinonasal - type hemangiopericytoma is reactive to actin and nuclear staining by beta - catenin while meningioma is usually reactive to EMA, CK18, and vimentin [15].

This interesting case presents the unique opportunity to evaluate the rare phenomenon of tumor-to-tumor metastasis and synchronous tumorigenesis. The intraoperative consultation is difficult due to the complicated clinical history and the radiological findings. Pathologists need to be aware of these phenomena and keep an open mind to make the correct diagnosis. Sampling should also be adequate and meticulous histopathologic examination of the suspected lesions is of utmost importance. Detection of this rare event can provide more precise treatment options and prognosis. More importantly, it raises the question if genetic counseling is warranted in such patients with multiple concurrent neoplasms.

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