Tumor-to-Tumor Metastasis: Mucinous Non-Small Cell Lung Carcinoma to Sphenoid Wing Meningioma

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Abstract
Tumor-to-tumor metastasis is a rare pathologic occurrence. Meningiomas are the most common intracranial host for tumor metastases, and lung adenocarcinoma primaries are the most common donor tumors. We present a patient with a moderately differentiated mucinous adenocarcinoma to an intracranial meningothelial hyperplastic bone lesion. A 76-year-old-female presented with vision loss and proptosis in the left eye, along with facial swelling. She had a previous diagnosis of stage IB left lower lobe lung adenocarcinoma that was resected without adjuvant chemotherapy. Brain MRI revealed a mildly expansive heterogenous lesion of the greater wing of the left sphenoid bone with mottled enhancement. In addition, a mild mass effect on the left orbit with possible compression of the optic nerve. Pathological examination of the resected specimen revealed nests of metastatic tumor intermingled in dura-associated and intraosseous hyperplastic meningothelial tissue. The presence of the mucinous adenocarcinoma deposits within the meningothelial tissue may represent preexisting or concomitant sphenoid wing meningioma en plaque. While tumor-to-tumor metastasis of lung carcinoma to meningioma has been reported, there have been no previous reports of metastatic lung adenocarcinoma either as a tumor-to-tumor metastasis to a sphenoid wing meningioma en plaque, or in the context of a spread to foci of reactive meningothelial hyperplasia.

Keywords
Hyperplastic meningothelial tissue; Lung adenocarcinoma; Meningioma; Metastasis

Abbreviations
TTF-1: Thyroid Transcription Factor-1
CK-7: Cytokeratin 7
MRI: brain magnetic resonance imaging
EMA: epithelial membrane antigen vimentin
PR: progesterone receptor

Introduction
The pathogenesis of tumor metastasis is a complex multistep process under genetic control, in which several genes are involved [1]. Many factors are needed for the neoplasm to metastasize to another location. This includes production of enzymes such as collagenases, the loss of expression of certain adhesion molecules such as cadherins, the secretion by the tumor cells of free soluble adhesion molecules, and the production of peptides inducing angiogenesis [2]. In addition, many properties are needed by the host, such as its anatomical place, its vascularity, and the local potential for immune reaction to the metastasizing cells [3].

Tumor-to-tumor metastasis is an infrequent occurrence [3]. Instances have been described where the most common donor primary tumors are lung cancer, followed by breast, prostate, and thyroid carcinomas [3]. While the most frequent recipient tumor is renal cell carcinoma, followed by sarcomas, meningiomas, thyroid neoplasms, and pituitary adenomas [3]. Lung cancer is the primary tumor most frequently metastasize to other neoplasms [40-50% of reported cases] and RCC is the most frequent recipient (40-70%) [4].

Meningioma is the most common intracranial tumor to host metastases, with most donor tumors being breast and lung cancers primaries [5]. Haemangioblastomas, astrocytomas, pituitary adenomas, schwannomas, oligodendrogliomas, and ependymomas have also been reported to metastasize to meningiomas [6]. Other tumors, such as genitourinary, renal,
prostate, gall bladder, parotid tumors, lymphoma and melanoma have been exceptionally reported to metastasize into meningiomas [5]. The first carcinoma metastasizing to a meningioma was reported by Fried et al. In 1930. Criteria to assess a tumor-to-tumor metastasis developed by Campbell et al. In 1968 include: 1. The metastatic focus must be at least partially enclosed by a rim of histologically distinct host tumor tissue to exclude a collision process; 2. The existence of more than one primary tumor must be documented; 3. the recipient tumor must be a true neoplasm; and 4. Metastasis to the lymphatic system has to be excluded [4].

Meningiomas are thought to be a fertile soil for metastases due to a rich vascular network that provides a medium to receive cells that have broken off from a primary tumor [7]. They are also slow growing with low metabolic rates that act as a non-competitive environment that is high in collagen and lipid content for implantation [8]. Literature suggests that cell adhesion molecules play a role in why meningioma host metastases, those molecules are the key factors into the cell-to-cell communication and include cadherins, integrins, selectins and members of the immunoglobulin superfamily of adhesion molecules such as E-cadherin [5]. The aim of this report is to highlight the importance of an in-depth histological examination of metastatic tumors of the brain in order to identify the presence of pre-existing meningioma.

Case Report

A 76-year-old woman with history of hypertension, smoking, and a resected T2N0M0, stage IB left lower lobe lung moderately differentiated adenocarcinoma carcinoma, mucinous type presented with visual loss and proptosis in the left eye along with facial swelling. Brain MRI showed mildly expansive heterogeneous lesion of the greater wing of the left sphenoid bone with mottled enhancement. Follow-up MRI showed similar findings, with an irregular heterogenously enhancing expansile mass in the greater wing of the sphenoid bone and the lateral orbital wall with mild mass effect on the left orbit and compression of the optic nerve. Associated nodular thickening and enhancement of the adjacent left frontotemporal dura was seen, as well as an extra-axial enhancing mass. A left pterional craniotomy, resection of the lateral wall of the orbit, decompensation of the optic nerve, removal of the anterior clinoid, and placement of a lumbar drain was performed. The specimen was submitted for intra-operative frozen section evaluation and permanent histological examination.

Results

Nests of metastatic tumor were identified histologically within the specimen and identified as a mucin-producing adenocarcinoma. (Figure 1-6). Additionally, abundant extracellular pool of mucin was present with free-floating cancer cells within bone and the fibrocollagenous tissue of the dura mater. Tumor cells were both microscopically columnar and cuboid epithelial cells exhibiting variably hyperchromatic nuclei, with the majority having conspicuous nucleoli. Micropapillary fronds and invasive acinar structures were also present. There were several foci of metastatic epithelial tumor cells showing moderate to pronounced nuclear and cellular pleomorphism. Focal areas of dense fibrous desmoplastic reaction and mononuclear lymphoid infiltrates accompanied the metastatic foci. Tumor cells were highlighted with thyroid transcription factor-1 [TTF-1] and cytokeratin 7 [CK-7], supporting the diagnosis of metastasis from the patient’s known primary lung adenocarcinoma.

Moreover, nests of dura-associated and intraosseous hyperplastic meningotheial tissue were present in the same specimen. Microscopically, these areas were comprised of psychological banal of syncytilialmeningotheial cells with indistinct borders with occasional optically clear nuclei. Psammoma bodies and secretory eosinophilic concretions resembling psammoma bodies were also identified. These hyperplastic meningeal nests exhibited a positive immune stain for the following: epithelial membrane antigen (EMA), vimentin, and progesterone receptor (PR). In portions of the specimen, there is

Figure 1: Metastatic mucinous lung adenocarcinoma to a suspected sphenoid wing meningioma en plaque

Figure 2: Mucinous lung adenocarcinoma, 40X

Figure 3: TTF1+, Mucinous lung adenocarcinoma

Figure 4: Meningothelial tissue
brain Autonomic Nervous System (ANS) and ii) from brain to heart using EMF communication.

Other interactions modalities between heart and brain like energy fluctuation as dynamic energy could be discussed in depth [1] [Figure 1]. These kind of interactions could be used in zoonotherapy. The logic gates and interaction between Animal and Human use the second way [2] and probably use Animal learning. The incomplete opening of the Door 2 modulate positively or negatively logic. The present investigation show that Animal brain efficacy is linked to the harmony of the first doors (Door 1).

We conclude by using the present model and theory to give more light on the unanswered questions related to the doors roles and their implication in emotion and logic.

References

an intermingling of dura-associated and intraosseous hyperplastic meningothelial tissue with metastatic adenocarcinoma.

Conclusion
The noncompetitive nature of meningiomas, along with the rich vascular network and abundant cell adhesion molecules are thought to be the leading factors in what makes meningiomas an inviting intracranial host [5,7,8]. Tumor-to-tumor metastasis were confirmed by the presence of nests of both dura-associated and intraosseous meningothelial tissue intermingled with areas of metastatic adenocarcinoma. Metastatic adenocarcinoma deposits are demonstrated within these nests of meningothelial tissue. Whether these represent foci of tumor-to-tumor metastasis adenocarcinoma to meningioma or alternatively, tumor spread into contiguous foci of reactive meningothelial hyperplasia is conjectural [9]. The non-detection of a full-blown mass of meningioma notwithstanding, the aforementioned nests of meningothelial tissue may nonetheless represent elements of a preexisting or concomitant sphenoid wing meningioma en plaque. The latter is frequently associated with hyperostosis of the sphenoid ridge and may invade the dura of the frontal, temporal, orbital, and sphenoidal regions, as well as bony structures, although osseous invasion per se does not constitute evidence malignancy [10].

Although there is a plethora of published reports of tumor-to-tumor metastasis of lung carcinoma to a meningioma [11-13], the present case has certain unique features. The isolated presentation of metastatic disease to the sphenoid wing or the orbital roof. Moreover, there are no previous reports of metastatic lung adenocarcinoma either as a tumor-to-tumor metastasis to a hyperostosing sphenoid wing meningioma en plaque, or in the context of a spread to foci of reactive meningothelial hyperplasia [9]. great role in our emotions [12]. Interactions between heart and brain could be described by two modalities i) from heart to