Lung adenocarcinoma metastasizing to fibrous histiocytoma

A case report

Yang Liu, PhD, MDa,b,c, Bing Dai, PhD, MDd,*

Abstract

Rationale: Tumor-to-tumor metastasis is an uncommon phenomenon, and the tumor metastatic to mesenchymal tumor is extremely rare. To our knowledge, this is the first case of lung adenocarcinoma metastasizing to fibrous histiocytoma.

Patient concerns: A 58-year-old Chinese woman was admitted to our hospital with a complaint of progressive enlargement of a mass in the right upper arm without pain, heat (localized warmth), redness, and swelling, for a year.

Diagnoses: Ultrasound revealed a mass with relative clear boundary in the right upper arm near elbow joint. Uneven echoes, and blood flow signals were showed within the mass. The tumor was well-demarcated from the surrounding tissue a thin fibrous capsule. Scattered enlarged cells with hyperchromatic pleomorphic nuclei were dispersed in an otherwise typical cutaneous fibrous histiocytoma. These atypical cells arranged in poorly glandular structures or irregular epitheloid nest and were demonstrated as metastatic lung adenocarcinoma by immunohistochemical staining. We reviewed the biopsy section and found these 2 sites of adenocarcinoma shared similar histologic morphological features. Therefore, the final diagnosis was lung adenocarcinoma metastasizing to fibrous histiocytoma.

Interventions: The patient was diagnosed with lung adenocarcinoma by bronchoscopic biopsy 3 months ago and received 4 cycles of NP (Vinoreltayre [NVB] + cis-platinum) chemotherapy program. The patient underwent a total resection of the mass in right upper arm.

Outcomes: The patient died of multiple organ failure after 10 months since she was diagnosed as lung adenocarcinoma.

Lessons: The accumulation of lipid droplets in fibrous histiocytoma may be a potential reason for modifying pre-metastatic niche, and therefore create a tumor microenvironment suitable for metastasis.

Abbreviations: EMA = epithelial membrane antigen, NP = vinoreltayre + cis-platinum, NVB = vinoreltayre.

Keywords: fibrous histiocytoma, immunohistochemistry, lung adenocarcinoma, TTF-1, tumor-to-tumor metastasis

1. Introduction

Tumor-to-tumor metastasis is an uncommon phenomenon which was first reported by Fried in 1930.[1] Histopathologically, a definite tumor-to-tumor metastasis should meet the following 4 criteria proposed by Campbell et al[2]: >1 primary tumor; the recipient tumor is a true neoplasm (either benign or malignant), and histologically different from the primary tumor; the metastatic tumor is a true metastasis, collision tumor and embolism of neoplastic cells in the recipient tumor should be excluded; and the recipient tumor should not be lymphoreticular malignant tumors. Based on the scattered reports and autopsy series review, the most common “donor” tumors were breast cancer and lung cancer and the most common “recipient” tumors were renal cell carcinoma, thyroid carcinoma, adenocortical adenoma, and meningioma.[3-10] Tumor metastatic to mesenchymal tumor was extremely rare. Sporadic cases of tumor metastatic to renal angiomyolipoma, schwannoma,[11-16] neurofibroma, lipoma,[18] and solitary fibrous tumor[19,20] have been reported. To our knowledge, there were no reports described the fibrous histiocytoma as the “recipient” tumor of tumor-to-tumor metastasis.

Tumor microenvironment (so called seed and soil theory) was proposed to explain the reason why tumor-to-tumor metastasis favored to occur in specific tumor, such as renal cell carcinoma, thyroid carcinoma, adenocortical adenoma, and meningioma. Likewise, lipid-rich organs were favorable for implantation of metastatic cancer. In the current case, we noticed the accumulation of numerous lipid-filled foam cells within the tumor, which...
also created a lipid-rich microenvironment. This abnormal tumor lipid metabolism might be a potential reason for modifying premetastatic niche, and therefore created a tumor microenvironment suitable for metastasis.

Without a comprehensive clinical history, image examination, this case might be misdiagnosed as atypical fibroxanthoma or giant cell fibroblastoma and therefore caused inappropriate treatment or evaluation.

2. Case presentation

2.1. Ethic approval

The study was approved by the China Medical University Institutional Review Board for human studies. The ethical board approval number is LS[2018]016. Written informed consent was obtained from the patient for use of her clinical records in our study.

2.2. Clinical history

A 58-year-old Chinese woman was admitted to our hospital with a complaint of progressive enlargement of a mass in the right upper arm. She felt no pain, heat (localized warmth), redness, and swelling since the illness began. Half a year ago, the patient was short of breath and felt chest stuffiness. Pulmonary computed tomography (CT) scanning was performed and found a mass with soft tissue density (5.4 × 2.6 cm; CT value: 45HU) near the hilm of inferior lobe of left lung. Calcification was observed within the tumor. The CT value was 67HU after enhancement. Distal bronchial cut-off sign of left inferior lobe was observed (Fig. 1A–C). She was diagnosed with lung adenocarcinoma by bronchoscopy biopsy and received 4 cycles of vinorelbine + cisplatinum (NP) chemotherapy program. She found that the elbow mass grew rapidly within a week since the end of chemotherapy. Ultrasound revealed a mass (2.75 × 2.58 × 2.77 cm) with relative clear boundary in the right upper arm near elbow joint (Fig. 1D). Ultrasound showed uneven echoes, and blood flow signals within the mass and suspected for malignancy because of the lobulated structure within the mass and high internal tension. The patient underwent a total mass resection and the mass was completely excised. After complete sampling, we rendered a diagnosis of lung adenocarcinoma metastasizing to fibrous histiocytoma. The primary lung adenocarcinoma shared similar histological morphologies with those of subcutaneous metastatic sites. The patient died of multiple organ failure after 10 months since she was diagnosed as lung adenocarcinoma. The final diagnosis was pulmonary adenocarcinoma accompanied with distant metastasis (metastasizing to elbow fibrous histiocytoma), Stage IVB.

2.3. Immunohistochemical staining

The intramuscular mass in the right upper arm was completely sampled following the routine guideline of sampling 1 block/cm
of tumor. All specimens and samples of fine needle aspiration biopsy were fixed in 10% formalin and embedded in paraffin. A series of 4-μm-thick sections was cut from each paraffin-embedded block. Commercially available prediluted monoclonal antibodies directed against epithelial membrane antigen (EMA), Cytokeratin AE1/AE3 (AE1/AE3), CD68, S-100, smooth muscle actin (SMA), Desmin, cytokeratin 7 (CK7), thyroid transcription factor-1 (TTF-1), Vimentin, and Ki-67 were purchased from Mai Xin Inc., Fuzhou, China. Immunohistochemistry staining was performed using the streptavidin-peroxidase system (Ultrasensitive; Mai Xin Inc., Fuzhou, China) according to the manufacturer’s instructions. The primary antibody was replaced with phosphate-buffered saline for negative controls.

2.4. Morphological and immunohistochemical findings

At low magnification, the tumor is circumscribed with sharp demarcation from surrounding adipose tissues by a thin fibrous capsule (Fig. 2A and B). The tumor was composed of blind, spindle cells, and amount of foam cells and arranged in lobulated

---

Figure 2. Histologic features. (A) At low magnification, the tumor is circumscribed with sharp demarcation from surrounding adipose tissues (O indicated the component of fibrous histiocytoma; * indicated the necrosis area; the arrow head indicated the component of adenocarcinoma). (B) The tumor was well-demarcated from the surrounding tissue a thin fibrous capsule. (C and D) The tumor was composed of blind, spindle cells, and amount of foam cells and arranged in lobulated or nodule pattern. Necrosis were observed even under low magnification in the central of nodule (★ indicated the necrosis area). (E and F) The epithelioid atypical cells arranged in nests, cords or even formed poorly glandular or papillary structures. (G) The tumor cells showed prominent atypia at high magnification. (H) Focally, the tumor cells arranged in cords and caused the confusion with proliferative vascular endothelial cells.
or nodule pattern (Fig. 2C and D). Meanwhile, large areas of necrosis were observed even under low magnification in the central of nodule. At high magnification, some atypical cells arranged in nests, cords, or even formed poorly glandular or papillary structures. These atypical cells inserted among the spindle fibrous histocytes and foam cells (Fig. 2E and F). Atypical mitosis may be observed in this region (Fig. 2G). Focally, the tumor cells arranged in cords and caused the confusion with proliferative vascular endothelial cells (Fig. 2H). In addition, multinuclear giant cells and hemosiderin deposition were easy to observe.

The epithelioid atypical cells arranged in nest, cord or poorly glandular, or papillary structures were diffusely positive for AE1/AE3 (Fig. 3A and B), TTF-1 (Fig. 3C), Napsin-A, and CK7, but...
negative for Vimentin (Fig. 3D and E), SMA, Desmin, S-100, and CD68 (Fig. 3F). The immunostaining results supported the diagnosis of metastatic lung adenocarcinoma. On the other hand, the blind, spindle cells, foam cells, and multinuclear giant cells were diffusely positive for Vimentin (Fig. 3D and E), CD68 (Fig. 3G), and focally positive for SMA, but negative for AE1/ AE3, EMA, TTF-1, Napsin-A, CK7, and S-100, and supported the diagnosis of benign fibrous histiocytoma. The Ki-67 labeling index was approximately 60% in the adenocarcinoma component (Fig. 3H) and was <2% in the region of fibrous histiocytoma.

3. Discussion

As described in the introduction, rendering a diagnosis of tumor-to-tumor metastasis has strict criteria. In clinical practice, a definite diagnosis is hard to achieve because of the difficulty to acquire the sample of primary lesion or unnecessary to do so as the tumor has already metastasized to multiple organ and the patient cannot benefit from it. In particular, the primary tumor may be found occasionally in autopsy. Therefore, the real incidence of the tumor-to-tumor metastasis is underestimated. Although some mesenchymal tumors have been reported as recipient tumors in tumor-to-tumor metastasis, fibrous histiocytoma has never been reported to our knowledge.

As reported in the past, the most common recipient malignant tumors are renal cell and thyroid carcinoma, while the benign counterparts are adrenocortical adenoma and meningioma. These tumors are either rich in blood or rich in lipids. Hypervascularity, tumor microenvironment (so called seed and soil theory), cell–cell adhesion, and complex interactions involving hormonal factors have been used to explain this organ specificity. Abnormal lipid metabolism is a fairly new field among tumor microenvironment and has received attention recently. It has been recognized as an important metabolic rewiring phenomenon in tumor cells. The lipid accumulation not only provide energy storage for tumor cells, but also involve in metastatic cascade by modifying premetastatic niche, and therefore create a suitable microenvironment and facilitate metastasis.

It is worth noting that the accumulation of lipid-filled “foam cell” macrophages is observed within the recipient tumor (Fig. 1D). Likewise, the other common recipient tumors, such as renal cell carcinoma and adrenocortical adenoma are also characterized by the abundance of cytoplasmic lipid droplets. This leads us to speculate that the abnormal tumor lipid metabolism may be a potential reason for modifying premetastatic niche, and therefore create a tumor microenvironment suitable for metastasis.

In the current case, the differential diagnosis included “collision tumor,” atypical fibroxanthoma, and giant cell fibroblastoma. Ultrasound image and the whole picture at low magnification showed that the component of adenocarcinoma neither invaded from the extracapsular tissue, nor adjoined to the fibrous histiocytoma. Therefore, a diagnosis of “collision tumor” could be excluded. The obvious necrosis and prominent cell atypia did not support the diagnosis of atypical fibroxanthoma and giant cell fibroblastoma, although the images at low magnification may be misleading. Detailed clinical history and rational immunohistochemical pattern let us have the confidence to make a diagnosis of lung adenocarcinoma metastasizing to fibrous histiocytoma. In addition, scattered osteoclast-like giant cells is observed within the tumor. Pan-CK and CD68 staining indicate that these cells are not multicellular giant cell of adenocarcinoma. We also review the slide of the previous biopsy. These 2 sites of adenocarcinoma share similar histological features.

The patient died of multiple organ failure after 10 months since she was diagnosed as lung adenocarcinoma. This prognostic data again indicate that tumor-to-tumor metastasis has a poor prognosis than “collision tumor.” Tumor-to-tumor metastasis is probably a potent or local presentation of multiple organ metastasis and the prognosis depends on the malignancy of the primary tumor.

Here, we reported a first case of lung adenocarcinoma metastasizing to fibrous histiocytoma. Our report is a supplement for the recipient tumor type in tumor-to-tumor metastasis.

Author contributions

Conceptualization: Bing Dai.
Funding acquisition: Yang Liu.
Methodology: Yang Liu, Bing Dai.
Writing – original draft: Yang Liu, Bing Dai.
Writing – review & editing: Yang Liu, Bing Dai.
Yang Liu orcid: 0000-0002-6333-0648.

References

[1] Fried BM. Metastatic inoculation of a meningioma by cancer cells from a bronchiogenic carcinoma. Am J Pathol 1930;6:47–52.
[2] Campbell LVJr, Gilbert E, Chamberlain CCRJ, et al. Metastases of cancer to cancer. Cancer 1968;22:635–43.
[3] Acosta AM, Pims MR. Papillary thyroid carcinoma with extensive squamous differentiation metastatic to the lung: BRAF mutational analysis as a useful tool to rule out tumor to tumor metastasis. Virchows Arch 2016;468:239–42.
[4] Petraki C, Vlaslamatzis M, Argyrokos T, et al. Tumor to tumor metastasis: report of two cases and review of the literature. Int J Surg Pathol 2003;11:127–35.
[5] Mori K, Kitazawa R, Kondo T, et al. Lung adenocarcinoma with micropapillary component presenting with metastatic scrotum tumor and cancer-to-cancer metastasis: a case report. Cases J 2008;1:162.
[6] Sawada T, Takahashi H, Hasatani K, et al. Tumor-to-tumor metastasis: report of an autopsy case of lung adenocarcinoma metastasizing to renal cell carcinoma. Intern Med 2009;48:1525–9.
[7] Hashimoto K, Yamamoto H, Nakano T, et al. Tumor-to-tumor metastases: lung adenocarcinoma metastasizing to a follicular variant of papillary thyroid carcinoma. Pathol Int 2011;61:435–41.
[8] Aggarwal N, Amin RM, Chung D, et al. Tumor-to-tumor metastasis: case report of a pulmonary adenocarcinoma metastatic to a clear cell renal cell carcinoma. Pathol Res Pract 2012;208:50–2.
[9] Rickets R, Tamboli P, Czerwinski R, et al. Tumor-to-tumor metastasis: report of 2 cases of metastatic carcinoma to angiomylipoma of the kidney. Arch Pathol Lab Med 2008;132:1016–20.
[10] Martin JT, Alkhoury F, Helton S, et al. Metastatic adenocarcinoma within a functioning adrenal adenoma: a case report. Cases J 2009;2:7965.
[11] Wu PS, Pan CC. Lung adenocarcinoma metastasizing into a renal angiomylipoma. Int J Surg Pathol 2015;23:30–3.
[12] Amin M, Radkay L, Pantanowitz L, et al. Tumor-to-tumor metastasis (TTM) of breast carcinoma within a solitary renal angiomylipoma: a case report. Pathol Res Pract 2013;209:605–8.
[13] Noh MG, Moon KS, Kim JY, et al. Tumor-to-tumor metastasis of breast carcinoma to cervical spinal schwannoma: case report. Br J Neurosurg 2015;29:435–7.
[14] Hamperle M, Goehe F, Schwam S, et al. Tumor-to-tumor metastasis-bronchial carcinoma in meningioma. Clin Neuropathol 2015;34:302–6.
[15] Lua BK, Lau AS, Hwang SL. Breast carcinoma metastasized to vestibular schwannoma: a rare case of tumor-to-tumor metastasis and literature review. Kaohsiung J Med Sci 2012;28:397–9.
[16] Fukushima Y, Ota T, Mukasa A, et al. Tumor-to-tumor metastasis: lung adenocarcinoma metastasizing to vestibular schwannoma suspected on
preoperative [18F]-fluorodeoxyglucose positron emission tomography imaging. World Neurosurg 2012;78:553:e9–13.

[17] Cohn ML, Elliott DD, El-Naggar AK. Metastatic acinic cell carcinoma in a neurofibroma mistaken for carcinosarcoma. Head Neck 2005;27:76–80.

[18] Nomura S, Kurihara N, Ishikawa T, et al. Gastric cancer metastatic to neck lipoma: a case report with imaging consideration. Skeletal Radiol 2018;47:575–8.

[19] Velez-Cubian FO, Gabordi RC, Smith PV, et al. Tumor-to-tumor metastasis: an unusual case of breast cancer metastatic to a solitary fibrous tumor. J Thorac Dis 2016;8:E374–8.

[20] Kragel C, Wei S. Renal cell carcinoma metastasizing to solitary fibrous tumor of the pleura: a case report. J Med Case Rep 2011;5:248.

[21] Arnold AC, Hepler RS, Badr MA, et al. Metastasis of adenocarcinoma of the lung to optic nerve sheath meningioma. Arch Ophthalmol 1995;113:346–51.

[22] Liu N, Guli QR, Ming XC, et al. Tumor-to-tumor metastasis: lung renocarcinoma metastasizing to intracranial benign meningioma as a first clinical manifestation, with literature review. Int J Clin Exp Pathol 2018;11:2852–8.

[23] Maan M, Peters JM, Dutta M, et al. Lipid metabolism and lipophagy in cancer. Biochem Biophys Res Commun 2018;504:582–9.

[24] Syed S, Karambizi DI, Baker A, et al. Case report: a comparative report on intracranial tumor-to-tumor metastasis and collision tumors. World Neurosurg 2018;116:454.e2–63.e2.