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Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Pulmonary metastasis of matrix-producing carcinoma mimicking small cell lung cancer

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ARTICLE INFO

Keywords:

Breast cancer
Matrix-producing carcinoma
Pulmonary metastasis
Small cell lung cancer

ABSTRACT

Matrix-producing carcinoma (MPC) of the breast is an extremely rare subtype of invasive breast cancer. MPC is characterized by the production of a cartilaginous or osseous matrix without spindle cells. It is an aggressive carcinoma, often presenting as triple-negative breast cancer. MPC frequently metastasizes to the lungs; however, it rarely reoccurs as a solitary pulmonary metastasis. We report a case of a 77-year-old non-smoking woman with a solitary pulmonary metastasis of MPC, which mimicked small cell lung cancer (SCLC). Initially, the pulmonary metastasis was misdiagnosed as SCLC based on its morphological and immunochemical features, including focal positivity for CD56 and thyroid transcription factor-1. Although the portion of the chondromyxoid matrix of the primary site was not small, that of the metastatic site was small. A focal cartilaginous matrix deposition of pulmonary metastasis from MPC could make it difficult to differentiate from SCLC. We should acknowledge that the portion of chondromyxoid matrix may differ between primary and distant metastatic sites in MPC.

1. Introduction

Matrix-producing carcinoma (MPC) of the breast is an extremely rare subtype of carcinoma, accounting for 0.05–0.2% of all invasive breast cancers [1,2]. MPC is defined as an invasive breast carcinoma that directly transitions from carcinoma to a cartilaginous or osseous matrix that lacks intervening spindle cells [1]. MPC is an aggressive entity that frequently metastasizes to the lungs; however, it rarely reoccurs as a solitary pulmonary metastasis [1,3]. We present a case of a solitary pulmonary metastasis of MPC, which mimicked small cell lung cancer (SCLC).

2. Case presentation

A 77-year-old non-smoking woman underwent mastectomy for stage II cancer of the right breast at a previous hospital. Follow-up computed tomography (CT) scan one year after mastectomy revealed no pulmonary lesion. However, during her follow-up two years after mastectomy, the CT scan at our hospital revealed a solitary 1.8 cm solid pulmonary nodule in the upper left lobe (Fig. 1A).

Abbreviations: CT, computed tomography; MPC, matrix-producing carcinoma; SCLC, small cell lung cancer; TTF-1, thyroid transcription factor-1.

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<https://doi.org/10.1016/j.rmcr.2022.101699>

Received 11 April 2022; Received in revised form 14 June 2022; Accepted 1 July 2022

Available online 8 July 2022

2213-0071/© 2022 Published by Elsevier Ltd.

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Positron emission tomography-CT showed increased fluorodeoxyglucose uptake with a maximum standardized uptake value of 11.5 (Fig. 1B). No other fluorodeoxyglucose uptake was present. Pulmonary metastasis from the breast was suspected, and thoracoscopic wedge resection was performed. The frozen section examination revealed that the tumor consisted of sheets of small cells with prominent nuclear chromatin and scant cytoplasm. These findings suggested poorly differentiated carcinoma (Fig. 2A and B). The patient was clinically diagnosed with pulmonary metastasis secondary to breast cancer. Immunohistochemically, the tumor cells were focally positive for CD56 and thyroid transcription factor-1 (TTF-1), and negative for both synaptophysin and chromogranin A. However, the morphology of the viable cells and the immunohistochemical findings supported the diagnosis of SCLC (Fig. 2A and B). Surgical specimen of the primary breast carcinoma was collected and reviewed. Microscopically, the breast cancer consisted of sheets of small round cells with a high nuclear/cytoplasmic ratio and a focal chondromyxoid matrix in the central necrotic area, indicating MPC (Fig. 2C–E). The pathologic features resembled those of the pulmonary nodules. Moreover, small chondromyxoid-like matrix structures were detected in the necrotic area of the pulmonary nodule. Focally positive GATA3 immunohistological staining also supported the diagnosis of pulmonary metastasis from breast cancer. Hence, we arrived at the diagnosis of pulmonary metastasis of MPC (Fig. 2F). The patient had an unremarkable postoperative course without tumor recurrence for 24 months.

3. Discussion

MPC is a more aggressive subtype than the typical invasive ductal carcinoma of the breast [3]. MPC typically presents as triple-negative breast cancer [2], as in our case. In the present case, the breast cancer subtype was not initially recognized. Although the lung is the most common site of organ metastasis in MPC, a solitary pulmonary nodule rarely manifests as an initial recurrence [1, 3]. Furthermore, synaptophysin, chromogranin A, and CD56 were used as reliable immunohistochemical markers to detect neuroendocrine differentiation in SCLC. CD56 showed a strong diffuse positive [4,5], but up to two-thirds of synaptophysin and chromogranin A could be negative. CD56 is not a specific marker, thereby appropriate morphological context is available for pathological diagnosis of SCLC [4]. In our case, the pulmonary lesion was misdiagnosed as SCLC based on its morphological and immunochemical features. Only focally positive immunoreactivity for CD56 was atypical of SCLC. In addition, in 70–90% of SCLC cases, TTF-1 expression is positive [4]. TTF-1 is known as a tissue-specific transcription factor in the thyroid, lungs, and brain. However, TTF-1 is not always useful for differentiating between the primary sites [6]. The patient's non-smoker status was also atypical of SCLC [4]; hence, clinical interpretation was obviously important, given the medical history of malignant neoplasms. Moreover, GATA3 was previously utilized in the diagnosis of metastases from triple-negative breast cancer [7]. Here, focally positive GATA3 also supported the diagnosis of pulmonary metastasis from breast cancer.

In the present case, the minimal chondromyxoid matrix deposition in the pulmonary metastasis made pathological differentiation difficult. The proportion of cartilaginous or osseous matrix in the MPCs ranged from 2 to 98% [3]. Previously, most diagnoses of distant metastasis of MPC were based on clinicoradiological findings with few reports comparing pathological findings between the primary and metastatic site [3,8]. A previous report revealed the histological findings of a soft tissue metastasis of MPC, and no morphological differences were detected between the primary and metastatic sites [8]. However, in this case, the portion of chondromyxoid matrix deposition at the primary site was moderate, but that at the site of pulmonary metastasis was small. In another report, the metastatic site was histologically diagnosed with poorly differentiated carcinoma, not MPC, due to the lack of a matrix component, similar to the present case [1]. We should be aware that the portion of chondromyxoid matrix could differ between primary and distant metastatic sites in MPC. The median disease-free interval for MPC was 28 months [3], which was consistent with our case. The five-year overall survival rates were reported to be 38–65%, and 85% of patients with recurrent died within four years [9]. Since MPC is an aggressive malignancy, an extensive follow-up is required.

4. Conclusion

- We reported a rare case of a solitary pulmonary metastasis of MPC from the breast, which mimicked SCLC.

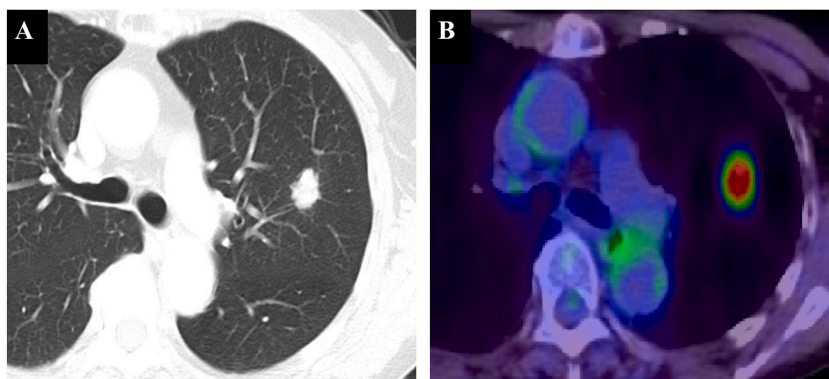


Fig. 1. Preoperative imaging findings. (A) Computed tomography scan showing a 1.8 cm solitary solid pulmonary nodule in the left upper lobe of the lung. (B) Positron emission tomography-computed tomography. A high fluorodeoxyglucose uptake with a maximum standardized uptake value of 11.5 was revealed.

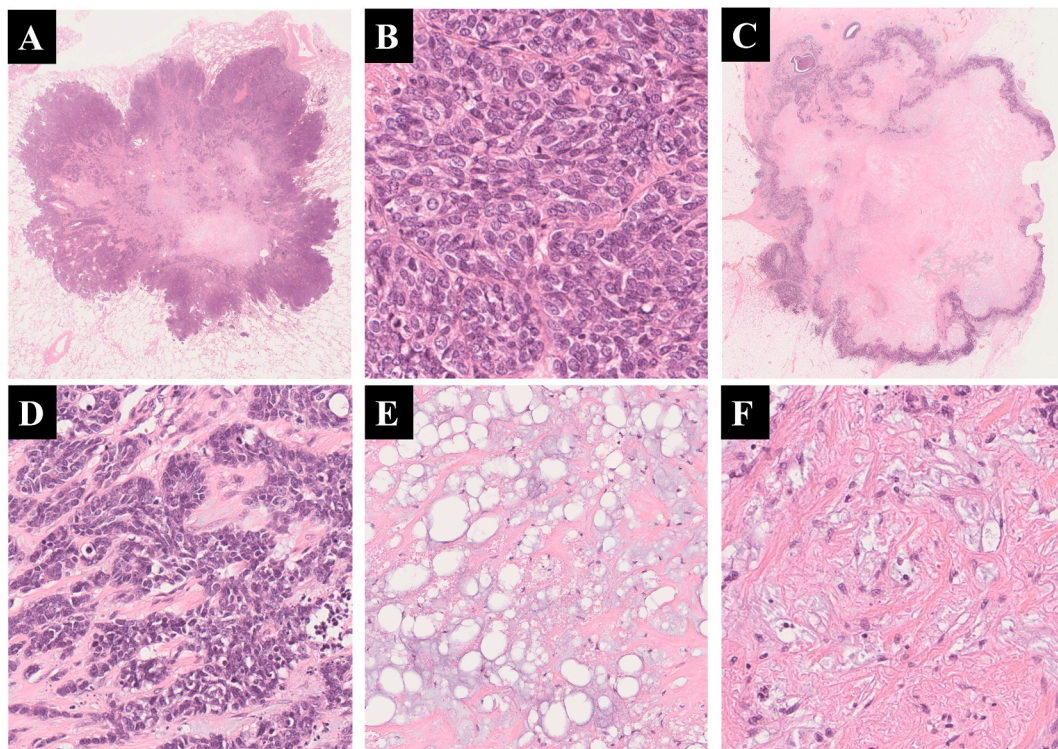


Fig. 2. Pathological findings. (A) The low-power view of the pulmonary nodule shows that the tumor comprised a necrotic center (hematoxylin-eosin staining). (B) The high-power view of the pulmonary nodule. Sheets of small round cells had prominent nuclear chromatin with molding and palisading formation (hematoxylin-eosin staining). (C) The low-power view of the initial breast cancer. Prominent central necrosis adjacent to the periphery of viable tumor, resembling a pulmonary nodule (hematoxylin-eosin staining). (D) The high-power view of the initial breast cancer. Sheets of small round cells were present with chondromyxoid matrix in the central necrotic area (E), indicating MPC of the breast (hematoxylin-eosin staining). (F) The high-power view of the pulmonary nodule. Focal chondromyxoid-like matrix is seen, indicating metastasis from MPC (hematoxylin-eosin staining). MPC: matrix-producing carcinoma.

- Pulmonary metastasis from MPC with minimal cartilaginous or osseous matrix deposition should be differentiated from SCLC.

Declaration of competing interest

The authors have no conflicts of interest.

Patient consent for publication

Informed consent was obtained from the patient for this publication.

Formatting of funding sources

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Author statement

Azusa Nakamura: Conceptualization, Data curation, Visualization, Writing - original draft. **Mikito Suzuki:** Conceptualization, Project administration, Visualization, Writing - original draft, Writing - review & editing. **Reiko Shimizu:** Data curation, Writing - review & editing. **Toshiyuki Shima:** Data curation, Writing - review & editing. **Masahiko Harada:** Writing - review & editing. **Tsunekazu Hishima:** Data curation, Writing - review & editing. **Hirotoishi Horio:** Supervision, Writing - review & editing.

Acknowledgement

None.

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