Site-Specific Therapy of Metastatic Breast Cancer

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Thorax is a common site for metastasis

- ✓local or regional recurrence
- ✓bone metastases
- ✓spinal cord compression
- ✓solitary or multiple pulmonary nodules with or without cavitation, an airspace pattern (lepidic)
- ✓ endobronchial metastasis
- ✓lymph node metastasis
- ✓pleural or pericardial involvement complicated by their effusions

Pulmonary metastases

- Single or multiple pulmonary metastasis
- Malignant pleural effusion
- Lymphangitic carcinomatosis

Management of Discrete Pulmonary Nodules symptom

- most lung metastases are asymptomatic and are found incidentally
- Symptoms occur in 15–20% of patients and usually reflect proximity to the central airways; these symptoms include cough, hemoptysis, or dyspnea
- A chest CT is the recommended diagnostic tool to evaluate a pulmonary nodule
- PET Scan

Management

- Metastatic lesions (34.2–75%)
- Primary lung cancer (11.5–48%)
- Benign lesions(13.5– 17.7%)

Comparative Study > Am J Surg. 2006 May;191(5):641-5. doi: 10.1016/j.amjsurg.2006.01.036.

The evaluation and treatment implications of isolated pulmonary nodules in patients with a recent history of breast cancer

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Abstract

Background: Breast cancer patients with pulmonary lesions are often assumed to ha
disease and treated palliatively. We evaluated the proportion of these patients who a
primary lung tumor (PLT) and assessed their outcome.

Methods: We performed a 10-year retrospective review of the cancer registry in a co
hospital system.

Results: Among 54 breast cancer patients with pulmonary nodules, biopsy was pursued in 30. Although metastatic breast cancer (MBC) was presumed in 24, biopsy showed MBC in 9 patients and PLT in 21. The two groups differed in age, stage, breast tumor size, nodal involvement, and estrogen receptor (ER) positivity. However, no variable excluded the possibility of PLT. Of those with PLT, 11 had early-stage lung disease; 9 underwent curative resection.

Conclusions: Women with breast cancer and 1 or more pulmonary lesions without evidence of other metastatic disease require work-up of pulmonary lesions. Aggressive evaluation can afford treatment of lung cancer and impact survival.

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Mol Clin Oncol. 2018 Feb;8(2):250-256. doi: 10.3892/mco.2017.1511. Epub 2017 Nov 24.

Significance of lung biopsy for the definitive diagnosis of lung nodules in breast cancer patients

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Free PMC article

Abstract

The aim of the present study was to evaluate the significance of lung biopsy for the modification of the treatment strategy in breast cancer patients who develop lung nodules during follow-up after breast surgery. Of 53 consecutive patients who underwent lung biopsies in two institutions (Hiroshima University Hospital and Hiroshima Prefectural Hospital, Hiroshima, Japan) between 1997 and 2014, 45 underwent lung surgery and 8 underwent percutaneous or transbronchial tumor biopsy for lung nodules developing after curative surgery for breast cancer. The indications for lung biopsy included lung nodules for which a definitive diagnosis was difficult to achieve, and those for which the treatment strategy depended on the pathological diagnosis. The lung nodules were pathologically diagnosed as primary breast cancer metastases to the lungs in 25 (47%), primary malignant lung tumors in 21 (40%) and benign disease in 7 (13%) patients. Among the 25 metastatic patients confirmed by lung biopsy, phenotype discordance was observed in 6 patients (24%). A total of 3 patients with lung metastasis proven to have estrogen or progesterone receptor upregulation by lung biopsy received endocrine therapy. Univariate analysis revealed that patients with metastatic breast cancer confirmed by lung biopsy were significantly younger and had more locally advanced primary cancers diagnosed via clinical and pathological assessment compared with patients with other diseases. Therefore, mastectomy and axillary lymph node dissection were performed more frequently in the metastasis group compared with the others group. Multivariate analysis revealed that mastectomy ($P<0.001$) and axillary dissection ($P<0.001$) were independent factors predicting that the lung nodules would be metastases from breast cancer. Lung biopsy in breast cancer patients who developed lung nodules during the follow-up period after breast cancer surgery was crucial for making a definitive diagnosis and modifying the treatment strategy, which may improve the prognosis of breast cancer patients.

Keywords: breast cancer; lung metastases; lung nodule.

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Management of Discrete Pulmonary Nodules

Tissue diagnosis

- Transthoracic Fine needle aspiration biopsy
- Pulmonary wedge resection

Management of Discrete Pulmonary Nodules Treatment

- Resection
- 1- There are no other distant metastases
- 2- The primary tumor is under control
- 3- Complete resection can be performed
- 4- The disease-free interval is longer than 36 months

J Thorac Dis. 2015 Aug;7(8):1441-51. doi: 10.3978/j.issn.2072-1439.2015.08.10.

Prognostic factors for resection of isolated pulmonary metastases in breast cancer patients: a systematic review and meta-analysis

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Free PMC article

Results: Sixteen studies with a total of 1937 patients were included in this meta-analysis. The pooled 5-year survival rates after pulmonary metastasectomy was 46% [95% confidence interval (95% CI): 43-49%]. The poor prognostic factors were disease-free interval (DFI) (<3 years) with HR =1.70 (95% CI: 1.37-2.10), resection of metastases (incomplete) with HR =2.06 (95% CI: 1.63-2.62), No. of pulmonary metastases (>1) with HR =1.31 (95% CI: 1.13-1.50) and the hormone receptor status of metastases (negative) with HR =2.30 (95% CI: 1.43-3.70).

Ann Surg Oncol. 2017 Nov;24(12):3748-3753. doi: 10.1245/s10434-017-6067-0. Epub 2017 Aug 28.

Surgical Outcomes of Isolated Malignant Pulmonary Nodules in Patients with a History of Breast Cancer

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Results: Patients with PLC receiving surgery had better survival outcomes, including OS and PFS, than patients with lung metastases who received surgical resection. Breast cancer patients with solitary lung metastasis who received metastasectomy had a significantly better PFS than those who did not; however, no statistically significant difference in OS was observed between the two groups. A multivariate analysis conducted in patients with isolated metastatic breast cancer showed that surgery was an independent factor for better PFS.

Approach to a discrete pulmonary nodule in a breast cancer patient.

Breast cancer patient with pulmonary nodule in chest X-ray (CT or PET-CT?)

Extrapulmonary metastatic site?

If yes, go on with medical oncology and follow the nodule after chemotherapeutic response.

If no, define the lesion.

1. One nodule with FDG(+), SUVmax >5 without mediastinal FDG uptake: perform sublobar resection (lobectomy, if primary).
2. One nodule with low FDG (SUVmax <5) without mediastinal FDG uptake: consider Noguchi classification [32]; follow or perform resection.
3. At least two nodules: diagnose with bronchoscopy/transthoracic biopsy/wedge resection.
4. Single nodule with mediastinal enlarged lymph nodes (FDG+): perform endobronchial ultrasonography (EBUS) or mediastinoscopy.
5. Cavitary nodule in a smoker: perform sublobar resection (lobectomy, if primary).
6. Calcified, popcorn-shaped single lesion: radiologic follow-up.
7. Nodule increasing in size during chemotherapy: perform sublobar resection (lobectomy, if primary).
8. Nodule with pleural effusion: perform VATS-wedge resection/biopsy with/without talc pleurodesis.

Management of Malignant Pleural Effusions in Breast Cancer

- Breast carcinoma is one of the most common neoplasms and causes approximately one third of all MPEs
- The majority of patients with recurrent MPE die within 6 months
- Patients with pleural effusion due to breast carcinoma have a longer median survival time ranging from 6 to 36 months
- Survival was especially shortened in patients with triple negative breast carcinoma and in those who tested positive for malignant cells in the pleural fluid

- Immunophenotype of breast cancer metastases and/or pleural and peritoneal effusions may be different from that of the primary tumor ("receptor conversion")
- Determination of receptor status in malignant effusion specimens may help optimize patient-tailored hormonal treatment(AR-targeted therapies).

Treatment of MPE

- The ideal treatment is to remove the fluid and prevent reaccumulation
- Thoracentesis,
- Chest tube drainage,
- Permanent catheter placement
- Video-assisted thoracoscopic surgery (VATS), have been used to create pleural symphysis
- Whole-chest radiotherapy
- Decortication
- Pleurectomy
- Pleurodesis with talc or other sclerosing agent

Chemical Pleurodesis

- Strongly recommended in patients with an expected median survival greater than 6 months
- Asbestos-free talc
- Tetracycline
- Doxycycline
- Silver nitrate
- Iodopovidone
- Bleomycin

Management of Isolated Liver Metastasis

- A solitary first metastasis of the liver in breast cancer is an uncommon presentation.
- Nearly half of all patients with metastatic breast cancer develop liver metastases .
- Minority of patients present with metastatic breast cancer limited to the liver (5–12%) .
- Among patients who have died of breast. cancer, hepatic metastases are found in 55–75% of autopsies.
- Overall, the 5-year survival of patients with stage IV breast cancer is currently 23% and drops to 8.5% for those patients with liver metastases .

Management of Isolated Liver Metastasis

- Hepatic metastases generally occur at later stages of disseminated disease and carry a very poor prognosis, with a median survival of 6 months
- Median survival of patients with isolated liver metastases is approximately 1 year, if untreated .
- Even with systemic chemotherapy, the median survival time is approximately 19 months for patients with metastatic breast cancer to the liver only or with limited disease elsewhere.
- Solitary liver metastases in breast cancer patients are rare, occurring in only approximately 5% of all cases

Management of Isolated Liver Metastasis

- Hepatic resection
- Radiofrequency ablation (RFA)
- Trans arterial chemoembolization (TACE) or intra-arterial chemotherapy
- Stereotactic body radiation therapy (SBRT)
- Interstitial laser therapy (ILT)

Management of Isolated Liver Metastasis Candidates should have

- limited metastatic disease in the liver
- controlled primary disease
- younger age
- longer disease-free intervals
- and higher performance status
- The presence of extrahepatic metastatic or residual primary breast cancer is commonly but not always considered a contraindication to liver directed therapy

Candidates for Surgical Treatment

- Patients have fewer than four hepatic metastases
- No extrahepatic disease
- Disease regression or stability with systemic therapy before resection
- Patient should have a normal performance status and normal hepatic function tests

Radiofrequency Ablation Therapy

- High-frequency electrical current (375–480 kHz) that is applied through one or more needle electrodes .
- Radiofrequency current produces ionic agitation that leads to heat production
- Heating results in cellular destruction and protein denaturation at temperatures above 50 °C when applied for 4–6 min and within a few seconds at temperatures above 75 °C. Temperatures higher than 100 °C may result in tissue water boiling and gas formation within the target
- Due to the poor local effectiveness of RFA in treating metastases larger than 3 cm in diameter, surgery remains better for larger lesions