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- Case Report -

## Lung metastasis from breast cancer combined with primary lung cancer: Report of a case

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**Abstract** We herein report a case of lung metastasis from breast cancer combined with primary lung cancer. A 59-year-old female had received mastectomy 5 years ago, and underwent adjuvant chemotherapy with trastuzumab and anastrozole. Chest computed tomography revealed nodules in right lobe of lung. She underwent partial resection through video-assisted thoracoscopic surgery, and metastatic breast cancer and primary lung cancer were recognized on pathological diagnosis. Two years later after chemotherapy and exemestane with trastuzumab, she was pointed out lung cancer recurrence and has been receiving chemotherapy. When nodules are removed and diagnosed as lung metastasis combined with primary lung cancer, additional treatment should be considered depending on the prognosis of each disease.

**Keyword** breast cancer, lung metastasis, lung cancer, VATS

### Introduction

Pulmonary nodules that appear in a patient with prior malignancy may be a metastasis or a second primary lung cancer [1]. Advances in computed tomography (CT) have made it possible to detect small tumors of the lung [2], however, the differential diagnosis of metastasis or primary lung cancer is usually difficult for such small nodules. The lung is a common site of metastasis in patients with breast cancer, with 12 % of breast cancer patients found to have metastatic lesions in the lung [3]. Treatment strategies for the pulmonary nodules vary depending on their diagnosis. Differential diagnosis of metastasis and primary lung cancer is therefore crucial for the planning of optimal treatment of patient with a history of breast cancer. We report a case of lung metastasis of breast cancer combined

with primary lung cancer.

### Case report

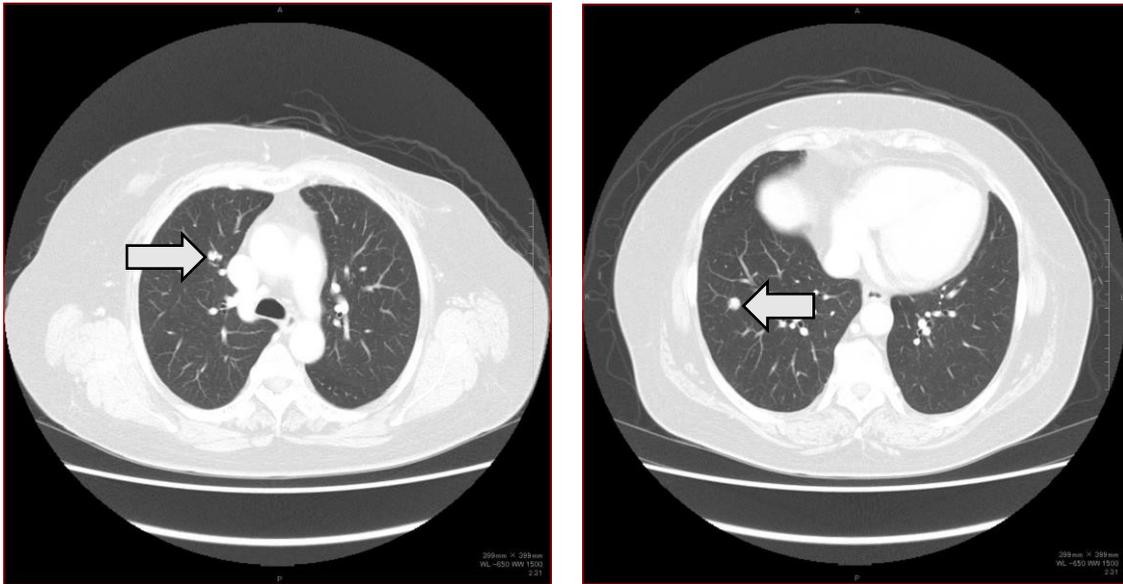
A 59-year-old non-smoking Japanese woman had received modified radical mastectomy for her left breast carcinoma 5 years ago. No sentinel nodal metastasis (0/1) was noted. The estrogen receptor (ER) and progesterone receptor (PgR) are positive, and human epidermal growth factor receptor type 2 (HER2) shows over-expression (3+) on the resected specimen. She underwent adjuvant chemotherapy with 3 courses of intravenous epirubicin, cyclophosphamide and fluorouracil followed by 3 courses of docetaxel with trastuzumab and anastrozole, an aromatase inhibitor. No local irradiation was administered before. The clinical course was smooth postoperatively, until pulmonary

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**Fig. 1 Computed tomography of the chest showed tumors**

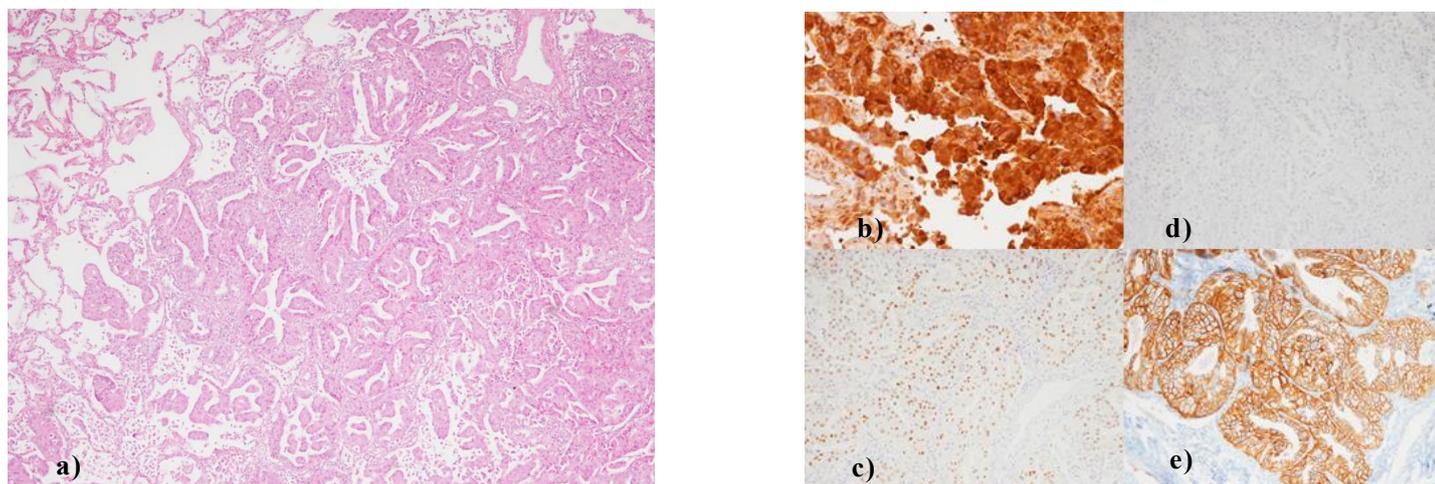
There in the right lobe measuring 0.7 cm and 0.8 cm, respectively (left; S3, right; S8)

nodules were accidentally found on the chest CT. Chest CT revealed 0.8 cm nodule with smooth margin in anterior segment of right lower lobe of lung (S8) and 0.7 cm nodule in the anterior segment of right upper lobe (S3) (Fig.1). The carcino-embryonic antigen (CEA) and neuron specific enolase (NSE) levels were within normal range. Pulmonary primary carcinoma or metastasis is highly suspected and thus she underwent partial resection through video-assisted thoracoscopic surgery (VATS) and open. Metastatic breast cancer on S8 and primary lung cancer (small cell carcinoma) on S3 were recognized on intraoperative pathological diagnosis, and she underwent right S3 segmentectomy and mediastinal lymph nodes dissection. The immunohistological staining showed that the tumor of S8 was positive gross cystic disease fluid protein-15 (GCFD-15) positive, ER positive, PgR negative and HER2 positive (Fig.2), the tumor of S3 was thyroid transcription factor-1 (TTF-1) and neural cell adhesion molecule (NCAM) positive (Fig.3). She underwent postoperatively chemotherapy with 4 courses of cisplatin and etoposide, and received exemestane and trastuzumab treatment. Two years later of re-operation, she was pointed out lung cancer recurrence and has been receiving chemotherapy of cisplatin and irinotecan, and she was transferred to palliative care due to the disease progression after 2 years later of lung cancer recurrence.

## Discussion

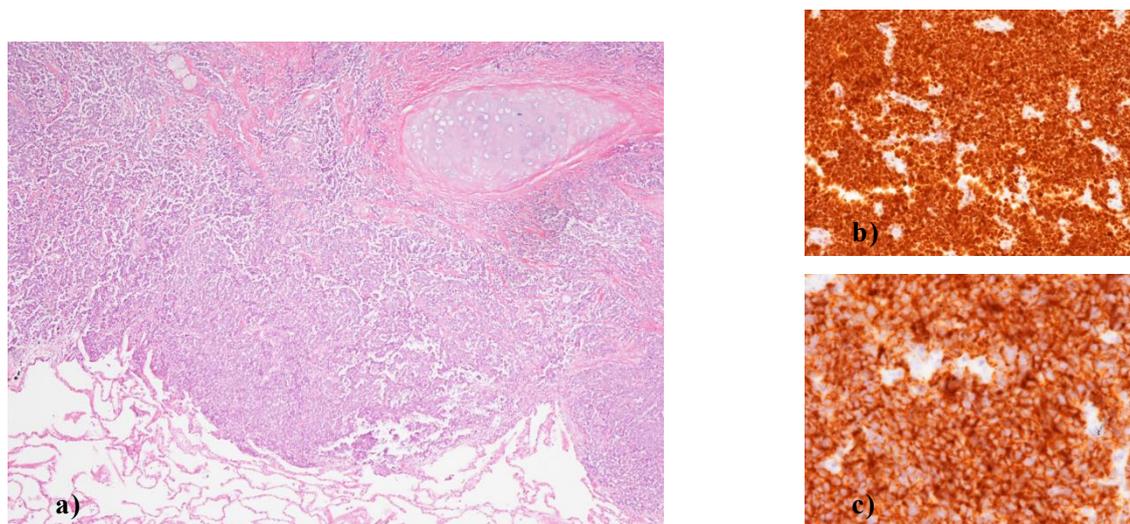
The histological identity of pulmonary lesions in breast cancer patients has major therapeutic implications, since the appropriate oncologic treatment differs significantly depending on the possibilities. Biological characteristics of ER, PgR and HER2 are very important for predicting the efficacy of therapy and patients' prognosis. Biopsy for the reassessment of these markers at the time of disease recurrence is strongly recommended [4]. Certain radiographic or clinical characteristics have also been proposed in the literature to help distinguish metastatic lesion from primary lung tumor. Metastatic lung nodules are often described as spheric or ovoid, well circumscribed, and located in the periphery [5,6], while primary lung cancer is more commonly associated with irregular borders and associated linear densities [7].

Pulmonary nodules that appear in patients who underwent mastectomy for the breast cancer may not always be pulmonary metastases, several studies reported the probability of having primary lung cancer among all solitary nodules appearing after mastectomy to range between 12 % and 48 % [8, 9]. The decision-making in the treatment should be made only after the pathologic diagnosis is confirmed. When nonsurgical diagnosis such as transbronchial biopsy and needle biopsy through the guidance of CT fails to reveal a pathological diagnosis, VATS should be considered as an option for the diagnosis [8, 9]. VATS has been demonstrated to be a useful procedure in peripheral pulmonary nodules, but in quite 20% of cases the deep location of the nodule in the



**Fig. 2 The pathological findings of the tumor of S8. The immunohistological staining showed that the cells were GCFD-15 positive, ER positive, PgR negative and HER2 positive.**

a) H & E stain ( $\times 40$ ), b) GCFD-15 ( $\times 200$ ), c) ER ( $\times 200$ ), d) PgR ( $\times 200$ ), e) HER2 ( $\times 200$ )



**Fig. 3 The pathological findings of the tumor of S3. The immunohistological staining showed that the cells were TTF-1 and NCAM positive.**

a) H & E stain ( $\times 40$ ), b) TTF-1 ( $\times 200$ ), c) NCAM ( $\times 200$ )

parenchyma requires open procedure for its localization and complete resection [10]. The distinction of a primary lung cancer from a metastatic lesion is important, because the treatment and prognosis differ for patients with these malignancies. In histological sections, the existence of acini, lepidic growth, nuclear pseudoinclusions, and scar favor the diagnosis of primary lung adenocarcinoma; on the other hand, comedo-necrosis, solid nests, trabecular architecture, and cribriform growth can be identified in metastatic breast carcinoma [11]. Such a distinction can also

be achieved by detection of special markers on the histological specimens, such as GCDFP-15 or TTF-1. GCDFP-15 is a marker for breast carcinoma [12, 13]. Overall, 55-72% of breast carcinoma studied stained positively for GCDFP-15. TTF-1 protein that regulates transcription of genes, and thus it is used as a marker to determine if a tumor arises from the lung or thyroid [14]. TTF-1 is usually positive in pulmonary adenocarcinoma or small cell carcinoma. NCAM is a cell-surface sialoglycoprotein of the immunoglobulin family involved in cell-to-cell interactions during neural development [15]. NCAM

is expressed in natural killer (NK) cells and NK-derived malignant neoplasms, but it also is found in many neural and neuroendocrine tissues and in several neuroendocrine tumors (carcinoid tumors, paragangliomas, small cell carcinomas) [16].

Pulmonary nodules in patients with prior breast cancer were usually regarded as metastatic lesions. However the possibility of primary lung cancer still cannot be excluded. When nodules are removed and diagnosed as lung metastasis combined with primary lung cancer, additional treatment should be considered following careful reassessment of CT images and the size and pathological features of the tumor.

## Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Competing interests

The authors declare that they have no competing interests.

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