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# A case report of successful diagnosis of a pulmonary nodule by a survey of oncogenic mutations; primary lung carcinoma or pulmonary metastasis?



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#### ABSTRACT

INTRODUCTION: The number of patients diagnosed with solid carcinomas is increasing, and the most common site of metastasis is the lungs. It is often difficult to make a differential diagnosis between primary lung carcinoma and metastatic lung tumor in using histological examination and by determining their immunohistological status.

PRESENTATION: A 64-years-old man presented with dyspnea with chest computed tomography (CT) findings of a pulmonary tumor, and afterwards suffered from a sudden bowel hemorrhaged due to colorectal carcinoma. The histological diagnosis of a pulmonary tumor was poorly differentiated adenocarcinoma. Both Thyroid transcription factor-1 (TTF-1) and Cytokeratin20 (CK20) were immunohistologically negative. Of the some oncogenic mutations investigated, a neuroblastoma RAS viral oncogen homolog (NRAS) codon13 G13D mutation was detected in both the colorectal carcinoma and the pulmonary tumor tissue samples. Based on the result, the pulmonary tumor was diagnosed as a metastasis derived from colorectal carcinoma.

DISCUSSION: Recently, examination of the oncogenes of solid carcinomas has been clinically investigated in primary lung caricnoma and in colorectal carcinomas. The clinical advantage of the oncogenic mutation survey is to identify the site, and the type, of amino acid change in detail. This case is a rare successful case of a survey of the oncogenes for giving a differential diagnosis.

*CONCLUSION*: A survey of the oncogenic genes is very useful to make a differential diagnosis between primary lung carcinoma and metastatic lung tumor.

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#### 1. Introduction

The number of patients diagnosed with solid carcinomas is increasing, and the most common site of metastasis is the lungs. It is often difficult to give a differential diagnosis between primary lung carcinoma and metastatic lung tumor [1], especially in the case of solitary pulmonary tumor with lymphadenopathy. In these cases, clinical diagnosis is made using histological examination of the tumor and by determining their immunohistological status using specific markers, such as TTF-1. However, both diagnostic methods are inexact, and so, most patients with undifferentiated pulmonary tumors are treated using empirical chemotherapy regimens.

Recently, examination of the oncogenes of solid carcinomas, including primary lung carcinoma, has been undertaken. Epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma recptor (ALK) rearrangement has been clinically investigated in

\* Corresponding author. E-mail address: aharo@surg2.med.kyushu-u.ac.jp (A. Haro). primary lung adenocaricnoma, and the Kirsten rat sarcoma viral oncogen homolog (KRAS) and NRAS mutations have been investigated in colorectal carcinomas. As such, patients with wild KRAS benefit from treatment using anti-EGFR therapies, such as panitumumab or cetuximab [2]. In the present case study, we present a case of successful diagnosis of a metastatic lung tumor derived from colorectal carcinoma by a survey of the oncogenic gene, NRAS.

#### 2. Case report

A 64-years-old man presented with dyspnea. He had acute cardiac insufficiency, and chest X-ray and chest CT showed cardiac dilatation and a right side pulmonary tumor with right mediastinal and hilar lymphadenopathy and bilateral pleural effusion. Following his recovery from the acute cardiac insufficiency, he suffered from a sudden bowel hemorrhaged due to colorectal carcinoma (Fig. 1). The hemorrhage was locally controlled using radiation therapy (40 Gy/16 Fr) combined with oral S-1. After recovery from the heart failure and bowel hemorrhage, chest CT revealed that the size of the pulmonary tumor had increased in size to 10.4 cm

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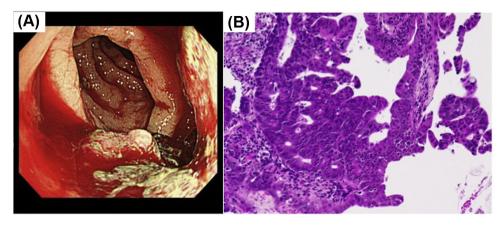


Fig. 1. Panel A: Colonoscopy revealed a bowel hemorrhage from the colorectal carcinoma. Panel B: Hematoxylin-eosin stain showed well-to-moderately differentiated tubular adenocarcinoma. (×200).

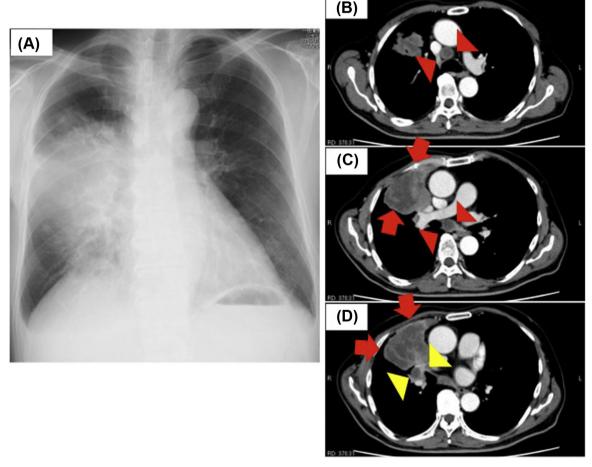


Fig. 2. Panel A: Chest X-ray revealed the right tumor and the infiltration shadows around the tumor. Panel B, and C and D: Chest CT revealed a pulmonary tumor(C and D; red arrows), hilar (D; yellow arrowheads) and mediastinal (B and C; red arrowheads) lymphadenopathy is enhanced by contrast medium.

(Fig. 2). A tissue biopsy of the pulmonary tumor was performed via bronchoscopy (Fig. 3A). The histological diagnosis was poorly differentiated adenocarcinoma (Fig. 3B). We could not make a differential diagnosis between primary lung carcinoma and metastatic lung tumor from colorectal carcinoma because both TTF-1 and CK20 were immunohistologically negative (Fig. 3C and D). As such, chemotherapy of carboplatin and irinotecan was given to the patient as irinotecan is effective for both primary lung carcinoma and colorectal carcinoma.

To make a more informed diagnosis, we furthermore investigated the EGFR mutation and ALK rearrangement of the primary lung carcinoma, and the KRAS and NRAS mutations of the colorectal carcinoma. Of the oncogenic mutations investigated, a NRAS codon13 G13D mutation was detected in both the colorectal carcinoma and the pulmonary tumor tissue samples. Based on the result, the pulmonary tumor was diagnosed as a metastasis derived from colorectal carcinoma. Four cycles of chemotherapy resulted in a partial response until a new bone metastasis appeared in the

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