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Case report

Analysis of significantly mutated genes as a clinical tool for the diagnosis in a case of lung cancer

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ABSTRACT

Bronchoendoscopic examination is not necessarily comfortable procedure and limited by its sensitivity, depending on the location and size of the tumor lesion. Patients with a non-diagnostic bronchoendoscopic examination often undergo further invasive examinations. Non-invasive diagnostic tool of lung cancer is desired. A 72-year-old man had a 3.0 cm × 2.5 cm mass lesion in the segment B1 of right lung. Cytological examination of sputum, bronchial washing and curetted samples were all "negative". We could confirm a diagnosis of lung cancer after right upper lung lobe resection pathologically, and also obtained concordant results by genomic analysis using cytological negative samples from airways collected before operation. Genetic analysis showed mutational profiles of both resected specimens and samples from airways were identical. These data clearly indicated the next generation sequencing (NGS) may yield a diagnostic tool to conduct "precision medicine".

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1. Introduction

Patients with a non-diagnostic bronchoendoscopic examination often undergo further invasive examinations. Bronchoendoscopy is relatively safe, with less than 1% of procedures complicated by pneumothorax [1]. However bronchoendoscopic examination is not necessarily comfortable procedure and limited by its sensitivity, which ranges from 34 to 88%, depending on the location and size of the lesion [2]. In this study, we report a case of lung cancer diagnosed by genomic analysis, but not by usual bronchoendoscopic examinations including cytological and pathological measures.

2. Case presentation

A 72-year-old man was pointed out to have an abnormal mass lesion by computed tomography of the chest by a routine health check-up. He was referred to our hospital and underwent the clinical examinations and surgery. During these procedures, we collected several specimens for diagnosis and genomic analyses (Table 1).

The abnormal mass lesion was located in the upper lung field and the size of mass was 3.0 × 2.5 cm in diameter (Figs. 1 and 2). He had a smoking history of 50 pack-year. Interstitial lung fibrosis was also pointed out but he had no respiratory symptom. The result of laboratory examination of hematology and blood chemistry was within normal ranges including several tumor markers. Bronchoendoscopy was performed to confirm a diagnosis of the mass lesion. Because the introducible bronchus to mass lesion was not identified, we could not use endobronchial ultrasonography (EBUS) using a guided sheath (EBUS-GS) [3]. Instead, by an angulated curette forceps, we obtained a small amount of liquid samples from bronchus adjacent to the mass lesion. We also obtained bronchial washing, bronchial brushing samples and sputum. A report from cytological examination of bronchial washing and curetted samples indicated there were no apparent tumor cells in these specimens (all "negative").

Imaging findings including local invasion to adjacent vessels

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Table 1
The timeline of clinical examinations, collection of samples and genomic analyses was exhibited.

Date	Events	Results
5/26/2015	First visit	Symptom free
5/26/2015	Chest X-P	A mass of right upper lung field was found.
6/12/2015	Chest CT	Local invasion to innominate vein was found.
6/25/2015	Sputum Collection	No apparent tumor cells were detected.
	Bronchial brushing/washing	No apparent tumor cells were detected.
	Bronchial curetting	No apparent tumor cells were detected.
	Blood sample collection	Collection for genomic analysis
7/7/2015	Bone Scintigraphy	No metastasis was found.
7/8/2015	Brain MRI	No metastasis was found.
8/10/2015	Surgical Resection	No invasive findings were revealed.
9/25/2015	Genomic analysis	

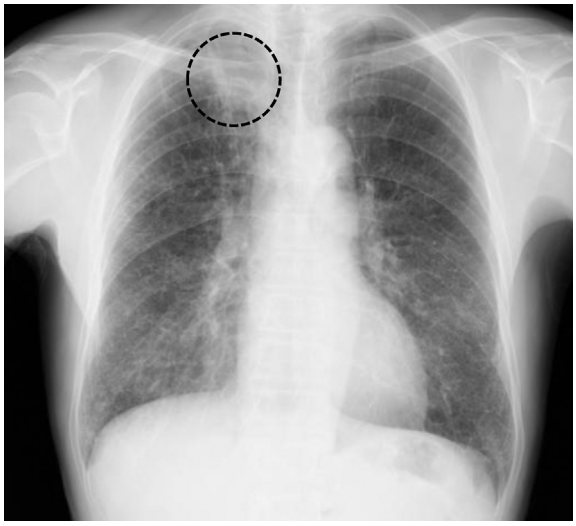

Fig. 1. Chest radiography revealed a mass lesion in mediastinal right upper lung field. Tumor lesion was indicated by dotted circle.

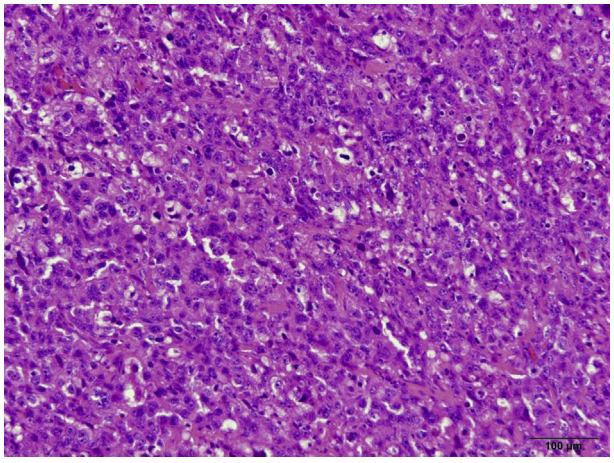

Fig. 3. A pathological diagnosis of a resected tumor was solid type of adenocarcinoma by new WHO classification.

and mediastinal nodal swelling was compatible with lung cancer as the stage of cT3N2M0 (stage IIIA) clinically. Because an innominate vessel was located over the tumor, we could not find the route of percutaneous CT guided needle biopsy (Fig. 2). Upper lung lobe resection was performed to confirm the diagnosis and the stage of the tumor. A pathological diagnosis of a resected tumor (3.0 × 2.5 cm) was solid type of adenocarcinoma by new WHO classification (Fig. 3) [4]. After surgery, we could confirm the non-invasiveness of the tumor to adjacent innominate vessel and no mediastinal lymph node metastasis. (pT2aN0M0, stage IB). However, because of local recurrence of mediastinal lymph nodes metastases with malignant pleural effusion, radiation therapy and chemotherapy with carboplatin and nab-paclitaxel was administered as advanced stage of lung cancer.

Recent international collaborative studies from The Cancer Genome Atlas (TCGA) identified a set of 53 significantly mutated genes (SMGs) by studying the whole exons of 230 cases of lung adenocarcinoma and 178 of squamous cell carcinoma [5,6]. Instead of analyzing approximately 20,000 genes of whole exons, these SMGs will be able to disclose principal mutations and signaling

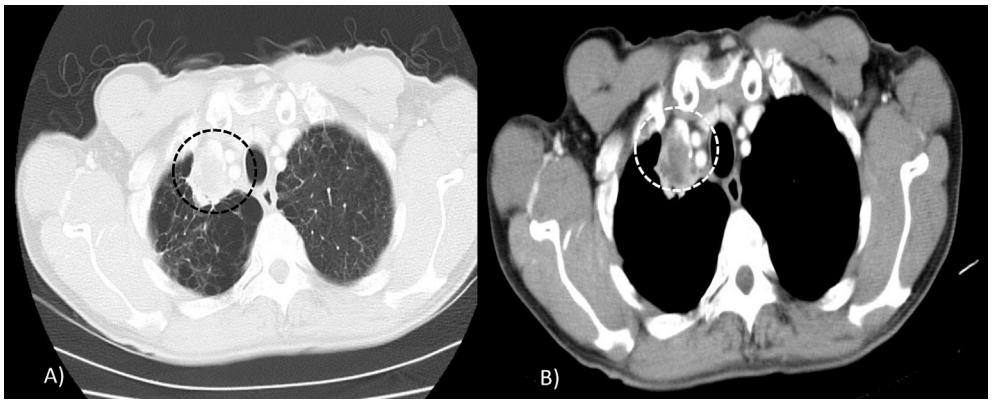

Fig. 2. Computed tomography of the chest revealed a mass lesion adjacent to vessels in mediastinum. Tumor lesion was indicated by dotted circle. A) The introducible bronchus to mass lesion was not identified. B) Because an innominate vessel was located over the tumor, we could not find the route of percutaneous CT guided needle biopsy.

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