


# The first case of micropapillary adenocarcinoma associated with cystic airspace in a non-smoking man

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## Keywords

BRAF mutation, EGFR mutation, lung cancers associated with cystic airspaces, micropapillary adenocarcinoma.

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## Introduction

Lung cancers associated with cystic airspaces are typically adenocarcinoma with lepidic, papillary, and/or acinar patterns and are usually found in smokers. To date, there has been no report of those cancers revealing micropapillary patterns. Pulmonary micropapillary adenocarcinoma was added to the 2015 World Health Organization (WHO) classification as a major histological subtype of adenocarcinomas owing to its association with a poor prognosis.

Here, we describe the first case of pulmonary micropapillary adenocarcinoma associated with cystic airspaces in 79-year-old non-smoking man.

## Case Report

A 79-year-old non-smoking man with a history of colon polyps and premature ventricular contractions presented with progressive circumferential thickening of a cyst wall in his left lower lung (Fig. 1). The cyst had been diagnosed one year previously, but he declined further examinations at that time. He had worked at a Yakitori restaurant for 50 years and had retired at the age of 70 years.

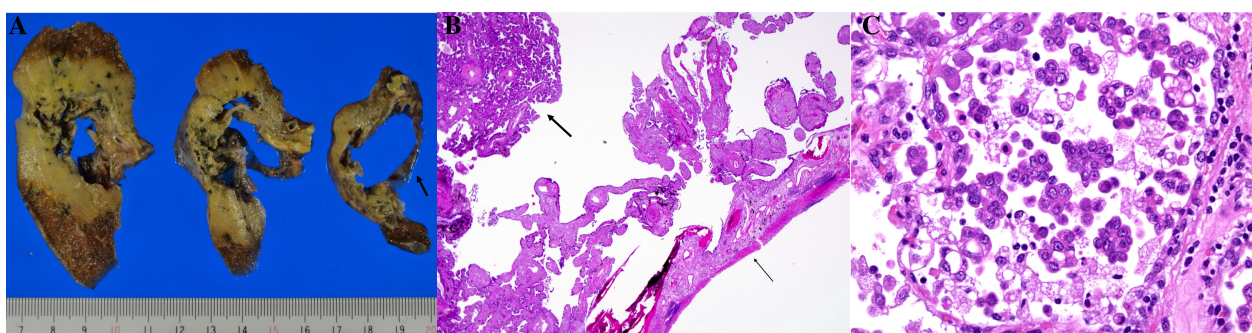
## Abstract

Lung cancers associated with cystic airspaces are attracting increasing attention because of delayed diagnosis. The cancers that usually occur in smokers comprise lepidic, papillary, and/or acinar adenocarcinoma, but a micropapillary type has not been described to date. Pulmonary micropapillary adenocarcinoma was added to the 2015 World Health Organization (WHO) classification system as a new subtype with a notably poor prognosis. We describe the first micropapillary adenocarcinoma of the lung associated with cystic airspaces in a 79-year-old non-smoking man.

On admission, computed tomography (CT) revealed a cyst with a circumferentially thickened wall and granular shadows in the periphery. His vital signs, physical findings, and blood test results were normal. His carcinoembryonic antigen (CEA) level was 2.4 ng/mL and sputum cytology revealed adenocarcinoma cells. Preoperative staging with positron emission tomography (PET)/CT and brain magnetic resonance imaging (MRI) indicated cT3N0M0 Stage IIB, and he underwent a left lower lobectomy. Post-operative staging revealed pT3N1M0 Stage IIIA. Whole thickened cystic wall was uniformly involved by the cancer but no cancer was found in the thin-wall part indicated by the arrow in Figure 2A. Specimens of cancer tissues showed adenocarcinoma with papillary (60%), micropapillary (35%), and lepidic (5%) components (Fig. 2B, C). Spread through air spaces (STAS) were evident around the primary tumour and metastatic lesions were also identified in the same lobe. Epidermal growth factor receptor (EGFR) exon 19 deletion was observed and programmed cell death ligand 1 (PD-L1) expression was negative. No emphysema is visible in the resected lung tissue. Tissue culture findings were also negative.



**Figure 1.** Chest computed tomography images acquired 12 (A) and six (B) months before, and during (C) admission. Cancer has progressed along the wall of cyst in left lower lobe.



**Figure 2.** Gross specimen of surgically resected lung cancer tissue. Whole thickened cystic wall was uniformly involved by the cancer, but thin-wall part indicated by the arrow was not (A). Cyst wall (small arrow) adjacent to the adenocarcinoma consists of mixed papillary and micropapillary patterns (large arrow) (haematoxylin and eosin (HE), 40 $\times$ , B). Histological section of pulmonary adenocarcinoma showing micropapillary components, defined as papillary tufts without fibrovascular cores (HE, 400 $\times$ , C). No emphysema is visible in the resected lung tissue.

## Discussion

Lung cancers associated with cystic airspaces were first described by Womack and Graham in 1941 and they are known to be associated with delayed diagnosis. The frequency of such cancers ranges from 0.46% to 3.7% and they are highly prevalent among smokers [1]. High incidences of positive PD-L1 expression and Kirsten rat sarcoma viral oncogene homologue (KRAS) mutation have been observed in cancer tissues [2]. The most common types of lung cancer associated with cystic airspaces are lepidic, papillary, and/or acinar adenocarcinoma [3], although data regarding morphologic subtypes are limited.

Pulmonary micropapillary adenocarcinoma has attracted increasing attention because of its association with a poor prognosis, including a tendency towards recurrence and metastasis. It is now classified by the WHO as a major histological subtype of adenocarcinomas. It is characterized by dominance in males who do not smoke, and a high incidence of EGFR or v-raf murine sarcoma viral oncogene homologue B1 (BRAF) mutations [4]. Although micropapillary adenocarcinoma and adenocarcinoma with acinar

and/or papillary patterns have been reported, pure micropapillary adenocarcinoma has not been reported to date. The proportion of micropapillary patterns in cancer tissues does not affect prognosis. As partial lung resection is associated with a poor prognosis, lobectomy followed by adjuvant chemotherapy is recommended [5].

To our knowledge, this is the first description of a micropapillary lung cancer associated with cystic airspaces. Physicians must also consider that lung cancers associated with cystic airspaces can develop in non-smokers.

## Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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