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Pulmonary Typical Carcinoid on Right Middle Lobe Hypoplasia: A Case Report and Review of the Literature

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Abstract

Introduction: Pulmonary hypoplasia is common in the perinatal period and a significant cause of death in newborn infants. The majority of patients present with severe respiratory distress or repeated pulmonary infections. However, there have been some cases of pulmonary hypoplasia being diagnosed in adulthood. Furthermore, there have been some reports of lung cancer and Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNECH) developing in pulmonary hypoplasia patients.

Case Presentation: A 70-year-old man was aware of dry cough. Chest computed tomography showed a ground-glass nodule in the upper lobe of the right lung and middle lobar incomplete development of the right lung. Lung cancer of the right upper lobe and pulmonary hypoplasia of the right middle lobe were suspected, and right upper and middle lobectomy and lymph node dissection were performed. A pathological examination confirmed lepidic adenocarcinoma of the right upper lobe and a well-differentiated neuroendocrine tumor with an organoid or trabecular pattern at the middle lobe of the right lung. Based on the results of an immunohistochemical study, the tumor of the middle lobe was diagnosed as typical carcinoid.

Conclusion: We experienced a rare case of pulmonary typical carcinoid in a patient with middle lobe hypoplasia of the right lung coexisting with lung adenocarcinoma on the upper lobe of the right lung.

Keywords: Pulmonary hypoplasia; Carcinoid; Lung cancer; Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

Introduction

Pulmonary hypoplasia is common in the perinatal period and a significant cause of death in newborn infants [1]. The majority of patients present with severe respiratory distress or repeated pulmonary infections. However, there have been some reports of pulmonary hypoplasia being diagnosed in adulthood [2-4]. Furthermore, there have been some reports of Neuroendocrine Tumor (NET), tumorlets, and Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNECH) developing in cases of

pulmonary hypoplasia [5-8].

DIPNECH is defined as diffuse neuroendocrine cell hyperplasia confined to the respiratory epithelium layer without penetration of the basement membrane and is recognized by the World Health Organization (WHO) as a preinvasive precursor to carcinoid tumors and tumorlets [9-12]. Recently, there have been several reports of DIPNECH with NET [13-19].

We herein report an adult case of pulmonary typical carcinoid in a patient with right middle lobe hypoplasia and review the literature concerning lung cancer with pulmonary hypoplasia.

Case Presentation

A 70-year-old man was aware of dry cough. Chest Computed Tomography (CT) showed a ground-glass nodule in the upper lobe of the right lung (Figure 1A) and middle lobar incomplete development of the right lung (Figure 1B). 18F-fluoro-2-deoxy-glucose (18F-FDG) Positron Emission Tomography (PET) showed no significant uptake of FDG in the whole body (Figure 1C). Lung cancer of the right upper lobe and pulmonary hypoplasia of the right middle lobe were suspected, and right upper and middle lobectomy and lymph node dissection were performed. The pulmonary artery and vein were recognized intraoperatively, and then the small middle lobe of the right lung was diagnosed with pulmonary hypoplasia (Figure 2A and 2B). A pathological examination confirmed a pathological stage IA1 lepidic adenocarcinoma of the right upper lobe (Figure 3A and 3B). In addition, a well-differentiated neuroendocrine tumor with an organoid or trabecular pattern and diffuse neuroendocrine cell hyperplasia were detected at the middle lobe of the right lung.

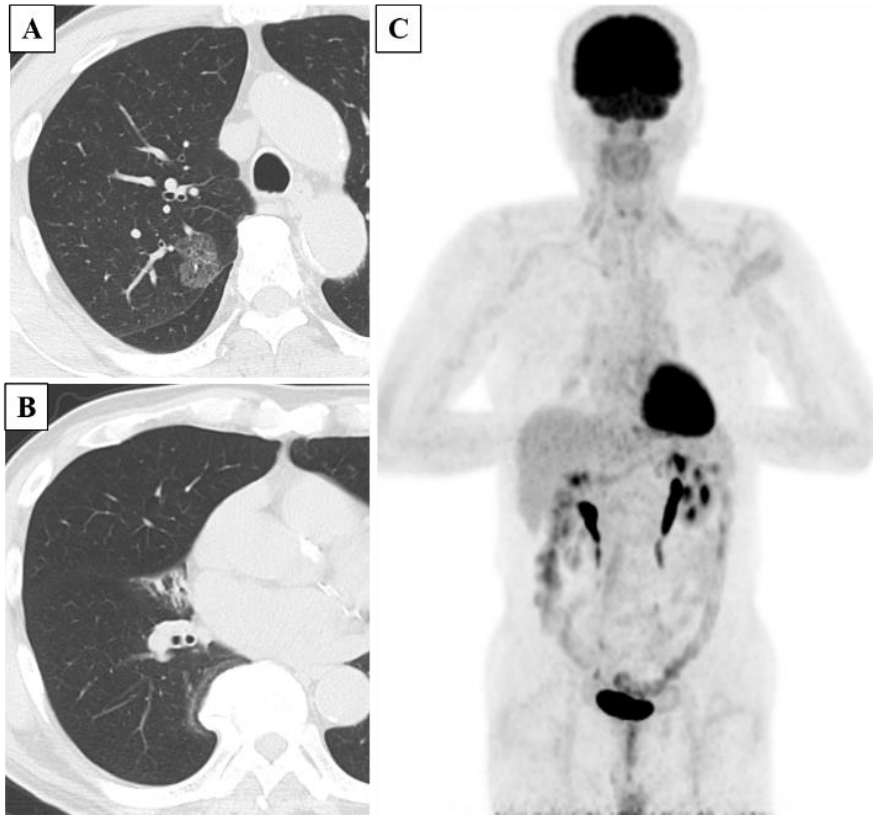

Figure 1: (A): Chest CT showed a ground-glass nodule in the upper lobe of the right lung; **(B):** Chest CT showed middle lobar hypoplasia of the right lung; **(C):** FDG-PET showed no significant uptake of FDG in the whole body.

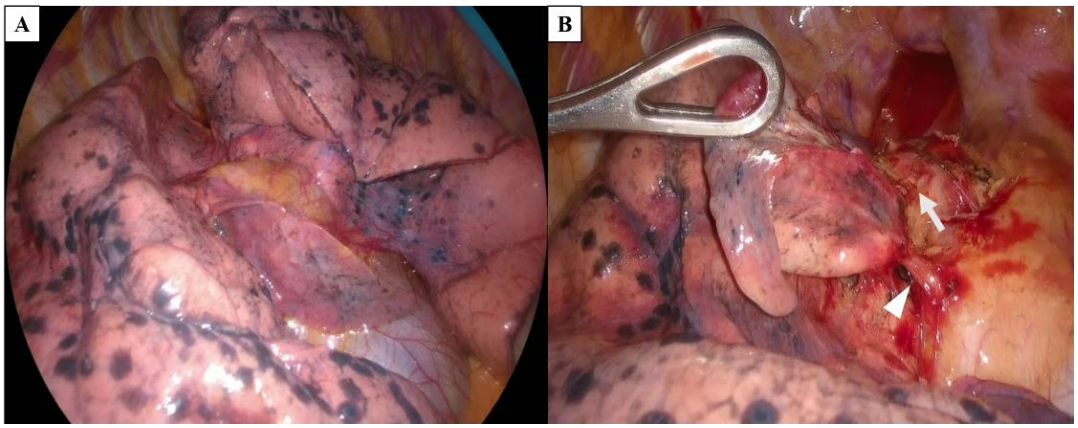

Figure 2: (A): Intraoperative findings showed middle lobar hypoplasia of the right lung; **(B):** The pulmonary artery (arrow) and pulmonary vein (triangle) were recognized.

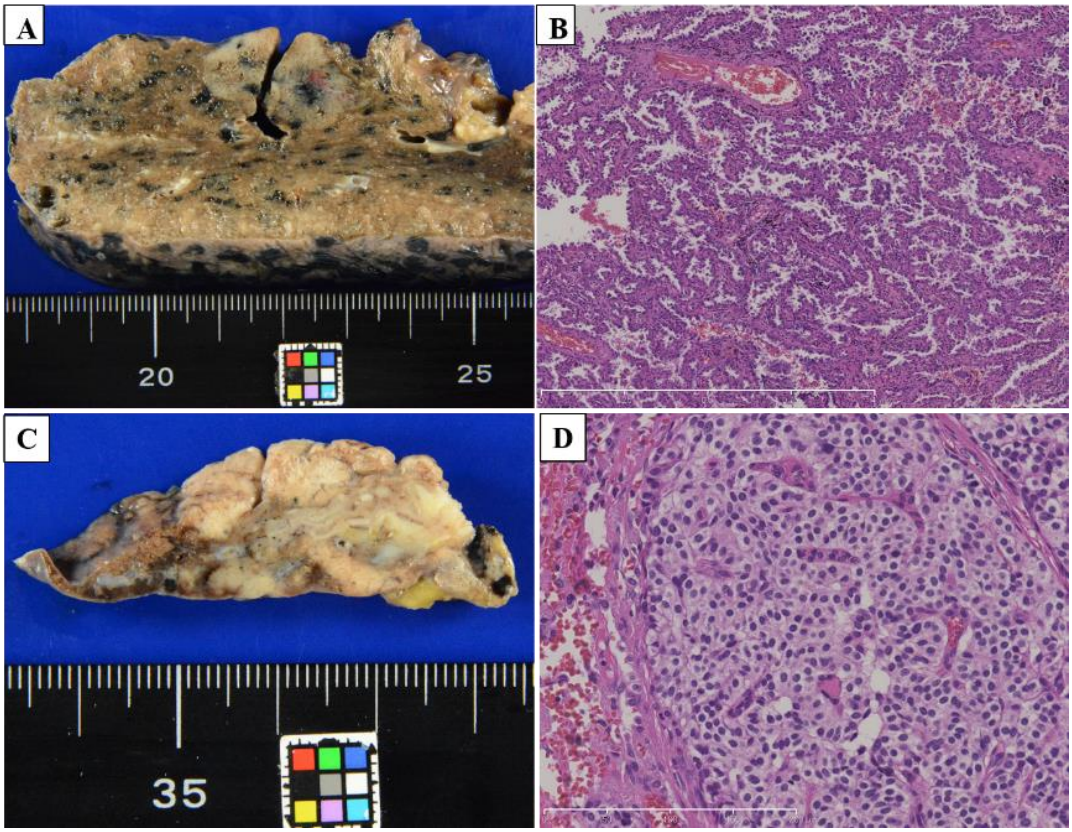

Figure 3: (A): Macroscopic findings showed a 2.6-cm-diameter nodule in the upper lobe of the right lung; **(B):** Microscopic findings of the upper lobe of the right lung showed an invasive lung adenocarcinoma; **(C):** Macroscopic findings showed a 3-cm-diameter greyish to yellowish mass in the middle lobe of the right lung; **(D):** Microscopic findings of the upper lobe of the right lung showed that the tumor cells were polygonal or elongated with round or oval nuclei and stippled chromatin and eosinophilic cytoplasm.

The tumor cells were polygonal or elongated with round or oval nuclei and stippled chromatin and eosinophilic cytoplasm (Figure 3C and 3D). There was no mitosis or necrosis. An immunohistochemical study revealed diffuse staining for Cluster of Differentiation (CD) 56, synaptophysin, and chromogranin A; Epithelial Membrane Antigen (EMA) staining was heterogeneously positive; p63 and Progesterone Receptor (PgR) were negative; MIB-1 nuclear positivity was 2.7 % (Figure 4A-D). The tumor of the middle lobe was therefore diagnosed as typical carcinoid.

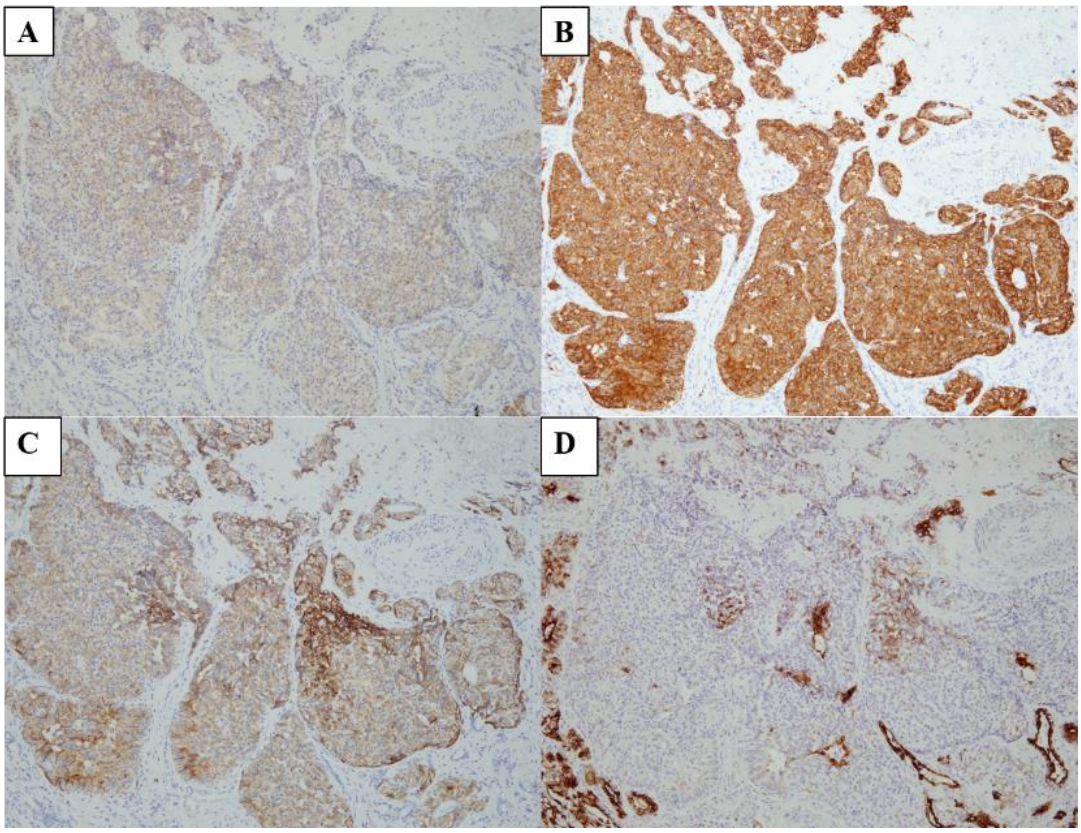

Figure 4: Immunohistochemistry showed diffuse staining for CD 56; **(A):** synaptophysin; **(B):** and chromogranin A; **(C):** EMA staining was heterogeneously positive **(D)**.

Discussion

Pulmonary incomplete development has been classified into three groups [20]: bronchus and lung are absent (agenesis), a rudimentary bronchus is present and limited to a blind-end pouch without lung tissue (aplasia), and bronchial hypoplasia with variable reduction of lung tissue is present (hypoplasia). Pulmonary hypoplasia is categorized into primary and secondary forms. Most cases are usually secondary to conditions that limit fetal lung growth, whereas primary pulmonary hypoplasia is rare and is thought to be caused by an embryologic defect of the lung or vascular tissue or an in utero vascular accident [1]. Although we did not perform bronchography, bronchoscopy and pulmonary angiography in our case, pulmonary hypoplasia was suspected by chest CT. We detected lung tissue, bronchus and pulmonary vascular without congenital fetal defects intraoperatively, so the patient was diagnosed with primary pulmonary hypoplasia of the middle lobe.

Similar to our report, there have been some reports of pulmonary hypoplasia being diagnosed in adulthood [2-8]. We searched neuroendocrine tumors developed in pulmonary hypoplasia in the middle lobe of the right lung in the PubMed, and then there

have been some cases in which NET, tumorlets, and DIPNECH developed in pulmonary hypoplasia patients (Table 1) [5-8]. Ages were in between 60 and 70 years, and there was no difference in gender, and typical carcinoids accounted for the majority. DIPNECH is defined as diffuse neuroendocrine cell hyperplasia confined to the respiratory epithelium layer without penetration of the basement membrane and is recognized by the WHO as a preinvasive precursor to carcinoid tumors and tumorlets [9-12]. Reactive neuroendocrine cell hyperplasia is commonly seen in several conditions (e.g. exposure to tobacco smoke, bronchopulmonary dysplasia, cystic fibrosis, asthma, diffuse panbronchiolitis, bronchiectasis and pulmonary fibrosis) [9].

However, DIPNECH is considered a primary neuroendocrine cell proliferation often accompanied by constrictive obliterative bronchiolitis [9]. As well as NET tends occur in DIPNECH [13-19,21], reactive neuroendocrine cell hyperplasia also induces the development of NET [12,15]. If pulmonary hypoplasia causes reactive neuroendocrine cell hyperplasia, NET might occur in pulmonary hypoplasia. Indeed, there have been some reports of NETs developing in pulmonary hypoplasia patients (Table 1). If this hypothesis is correct, pulmonary hypoplasia should need to be excised and evaluated pathologically.

Table 1: Neuroendocrine tumors developed in pulmonary hypoplasia in the middle lobe of the right lung.

Author	Age	Gender	Smoking index*	Tumor size (mm)	Histology	Pathological stage
Yoshida, et al	61	Male	1440	5	Typical carcinoid	IA1
	60	Female	0	10	Small cell lung cancer	IIB
	64	Male	880	5	Typical carcinoid	IA1
	68	Male	900	16	Typical carcinoid	IA2
Sato, et al	76	Female	200	8	Typical carcinoid	IA1
Maeshiro, et al	68	Female	200	12	Typical carcinoid with DIPNECH**	IA2
Our case	70	Male	400	30	Typical carcinoid	IA3

*Smoking index is assessed using the Brinkman index, which is calculated as the numbers of cigarettes smoked per day multiplied by the number of years for which the subject has smoked.

**DIPNECH: Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia.

Conclusion

We experienced a rare case of pulmonary typical carcinoid in a patient with middle lobe hypoplasia of the right lung coexisting with lung adenocarcinoma on the upper lobe of the right lung. It might be need to remove pulmonary hypoplasia and examined pathologically in order to assess the coexistence of NET.

Abbreviations: NET: Neuroendocrine Tumor; DIPNECH: Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia; WHO: World Health Organization; CT: Computed Tomography; FDG: FDG; PET: Positron Emission Tomography; CD: Cluster of Differentiation; EMA: Epithelial Membrane Antigen; Pgr: Progesterone Receptor.

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