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CASE REPORT

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Autopsy findings in a rare case of pleomorphic carcinoma in a patient on dialysis

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Key Clinical Message

Pleomorphic lung cancer is a very rare type of cancer and very few cases have been reported in the literature. We present a case of pleomorphic lung cancer in a patient with history of IgA nephropathy on hemodialysis.

KEYWORDS

autopsy, hemodialysis, lung pleomorphic cancer, pleural effusion

1 | INTRODUCTION

In Japan, malignancy is the leading cause of death in the general population and is the third leading cause of death among patients on dialysis. Approximately 90% of malignancies are diagnosed within 5 years of starting dialysis, but in these cases, lung cancer is uncommon and pleomorphic carcinoma is extremely rare.[1] Patients on dialysis regularly undergo chest X-ray examinations to evaluate body fluid volume based on the cardiothoracic ratio and to assess arteriosclerosis. Pleural effusion is a relatively common abnormal finding in dialysis cases and is often secondary to fluid overload. However, in cases of unilateral pleural effusion or pleural effusion that does not respond to fluid management, the possibility of malignancy should be considered. In this study, we report a case, including autopsy findings, of an extremely rare lung pleomorphic carcinoma that was discovered because of a unilateral pleural effusion in a patient on dialysis. The tumor grew rapidly and metastasized to various organs in the body.

2 | CASE HISTORY/EXAMINATION

The patient was a 73-year-old man with chief complaints of cough and dyspnea for the past 2 months. He has a 30 pack-years of smoking history and a 5-year history of asbestos exposure at work in his 20s. He started hemodialysis at the age of 66 years because of IgA nephropathy. After 6 years of dialysis, he developed cough and dyspnea. Chest X-ray showed a marked increase in the right-sided pleural effusion, which persisted even after addressing the fluid

overload. Therefore, the patient was admitted to our department for further investigation.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT)

Physical findings on admission were as follows: height of 173 cm, weight of 63.2 kg (baseline weight after dialysis was 61.8 kg), blood pressure of 104/70 mmHg, pulse rate of 104 beats/min, respiratory rate of 18/min with an O_2 saturation of 97% with nasal cannula oxygen at a flow of 2 L/min, temperature of 36.3°C, moist rales on the right lower lung field, and pitting edema on both lower extremities. Laboratory data on admission were as follows: hemoglobin of 9.7 g/dL and white blood cell count of 10,330/μL and increased tumor markers levels, with cytokeratin (CK) 19 fragment at 4.2 ng/mL and progastrin-releasing peptide at 174 pg/mL (Table 1).

Chest computed tomography (CT) revealed a new heterogeneous mass extending from the right lower lobe to the posterior mediastinum and carina, as well as enlarged mediastinal and hilar lymph nodes, compared with the chest CT scan 1 year earlier. Positron emission tomography (PET)-CT revealed significant accumulation (SUVmax 25) in the right lower lobe mass and in the right lung pleura (Figure 1).

Pleural fluid analysis showed a bloody character and high levels of hyaluronic acid (17,200 ng/mL), but cytology revealed no malignant cells. Endobronchial ultrasound-guided transbronchial needle aspiration biopsy of a mediastinal lymph node revealed proliferation of large round-like and spindle-shaped cells. Immunostaining was positive for Thyroid transcription factor-1 (TTF1) and CK 7 (Figure 2) but was negative for sarcoma. Based on these clinical findings, we diagnosed as primary pleomorphic carcinoma of the lung with multiple metastases to the mediastinal lymph node and pleura, clinical stage IV (TMN classification: T4N2M1).

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

In the subsequent 3 months, the tumor growth was aggressive. He developed anemia that was thought to have been caused by tumor bleeding. During dialysis, the patient began to have seizures, and head CT showed multiple metastatic brain tumors. Eventually, the fast-growing metastatic brain tumor led to his death after 93 hospital days.

TABLE| 1 Laboratory findings on admission.

Parameter	Value	Unit	Reference range
Blood cell counts			
White blood cells	10,330	/L	3,300-8,600
Neutrophil	65.3	%	44-74
Lymphcyte	10	%	20-50
Red blood cells	327	$\times 10^4/\mu L$	430-570
Hemoglobin	9.7	g/dL	11.6-14.8
Hematocrit	31	%	35.1-44.4
Platelet	5.9	$\times 10^4/L$	15.8-34.8
Serum chemistries			
Sodium	141	mEq/L	138-145
Potassium	4.1	mEq/L	3.6-4.8
Chlorine	104	mEq/L	101-108
Calcium	9.6	mg/dL	8.6-10.1
Phosphorus	5	mg/dL	2.5-4.5
Blood urea nitrogen	46	mg/dL	8.0-20.0
Creatinine	10.37	mg/dL	0.50-1.00
Total protein	5.4	g/dL	6.7-8.3
Albumin	2.7	g/dL	3.9-4.9
Lactate dehydrogenase	156	U/L	168-470
Aspartate aminotransferase	8	U/L	13-30
Alanine aminotransferase	4	U/L	10-42
C-reactive protein	8.6	mg/dL	0.00-0.30
Brain natriuretic peptide	98.5	pg/mL	0.00-18.4
Thyroid stimulating hormone	1.08	U/mL	0.35-4.94
Free triiodothyronine	1.47	pg/mL	1.68-3.67
Free thyroxin	1.06	ng/dL	0.7-1.48
Tumor marker			
Carcinoembryonic antigen	7.7	ng/mL	0.00-5.00
Carbohydrate antigen 19.9	32.2	U/mL	0.0-37.0
Carbohydrate antigen 125	21.4	U/mL	0.0-35.0
Squamous cell carcinoma antigen	1.4	ng/mL	0.0-1.5
Cytokeratin 19 fragment	4.2	ng/mL	0.0-3.5
Pro-gastrin releasing peptide	174	pg/mL	0.0-81.0
Pleural effusion			
Appearance	Bloody		
Total protein	3.9	g/dL	
Albumin	2.2	g/dL	
Lactate dehydrogenase	483	U/L	
Adenosine deaminase	18.6	U/L	
Hyaluronic acid	17200	ng/mL	
Carcinoembryonic antigen	3.3	ng/mL	
Carbohydrate antigen 19-9	7.5	U/mL	

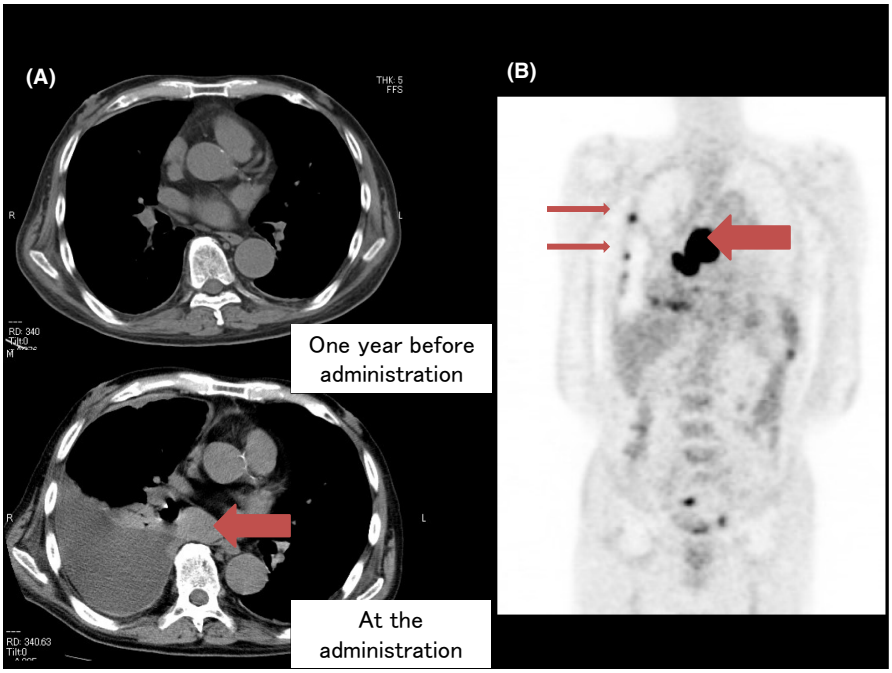

FIGURE 1 (A) Chest computed tomography (CT) reveals a big tumor on the right lower lobe extending to the carina. (B) Positron emission tomography (PET) CT shows high accumulation in the right lower lobe mass and the pleura.

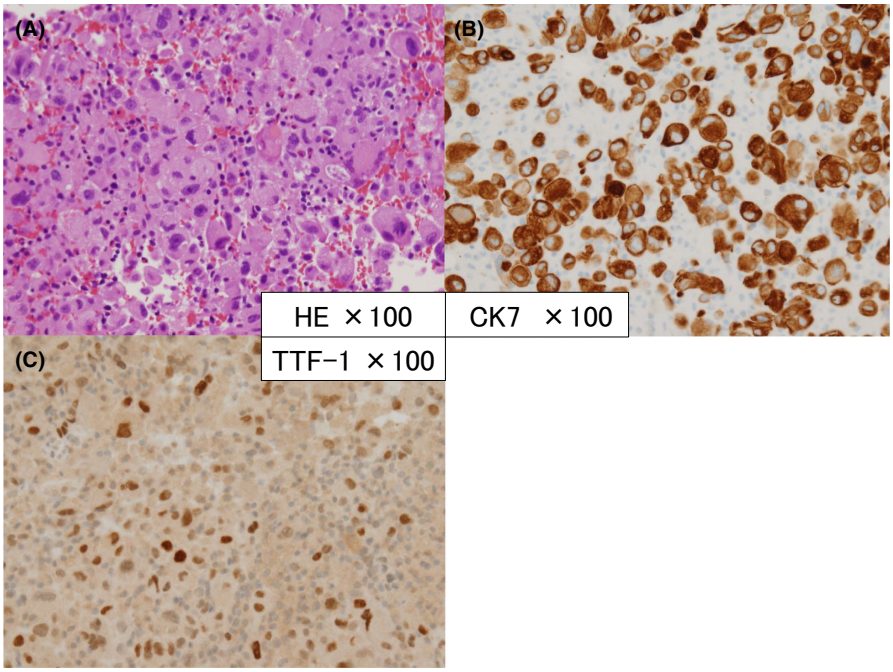

FIGURE 2 (A) Mediastinal lymph node biopsy shows proliferation of large round cells and spindle-shaped cells. Immunostaining staining with (B) Cytokeratin (CK) 7 and (C) Thyroid transcription factor (TTF)-1.

On autopsy, the primary tumor was located in the right lower lobe; measured 8 cm in diameter; and was grayish-white, hard, and with irregular margins. Similar to the mediastinal lymph node biopsy findings, microscopic examination of the primary tumor showed proliferation of large round and spindle-shaped cells. In addition to the mediastinal, hepatic hilum, peripancreatic, and splenic hilum lymph nodes showed metastasis. Moreover, there were metastases in the heart, mediastinum, thyroid, stomach, duodenum, small intestine, large intestine, pancreas, gallbladder, bilateral adrenal glands, mesentery, peritoneum, and retroperitoneum (Figure 3). In addition, the presence of asbestos body-like structures in the right lower lobe was confirmed using Berlin blue staining. These autopsy findings confirmed the diagnosis of pleomorphic lung cancer with multiple metastases.

5 | DISCUSSION

We reported a dialysis case of pleomorphic lung cancer that was discovered because of a rapid increase in unilateral pleural effusion. The primary and multiple metastatic tumors grew rapidly, and the patient died after 93 hospital

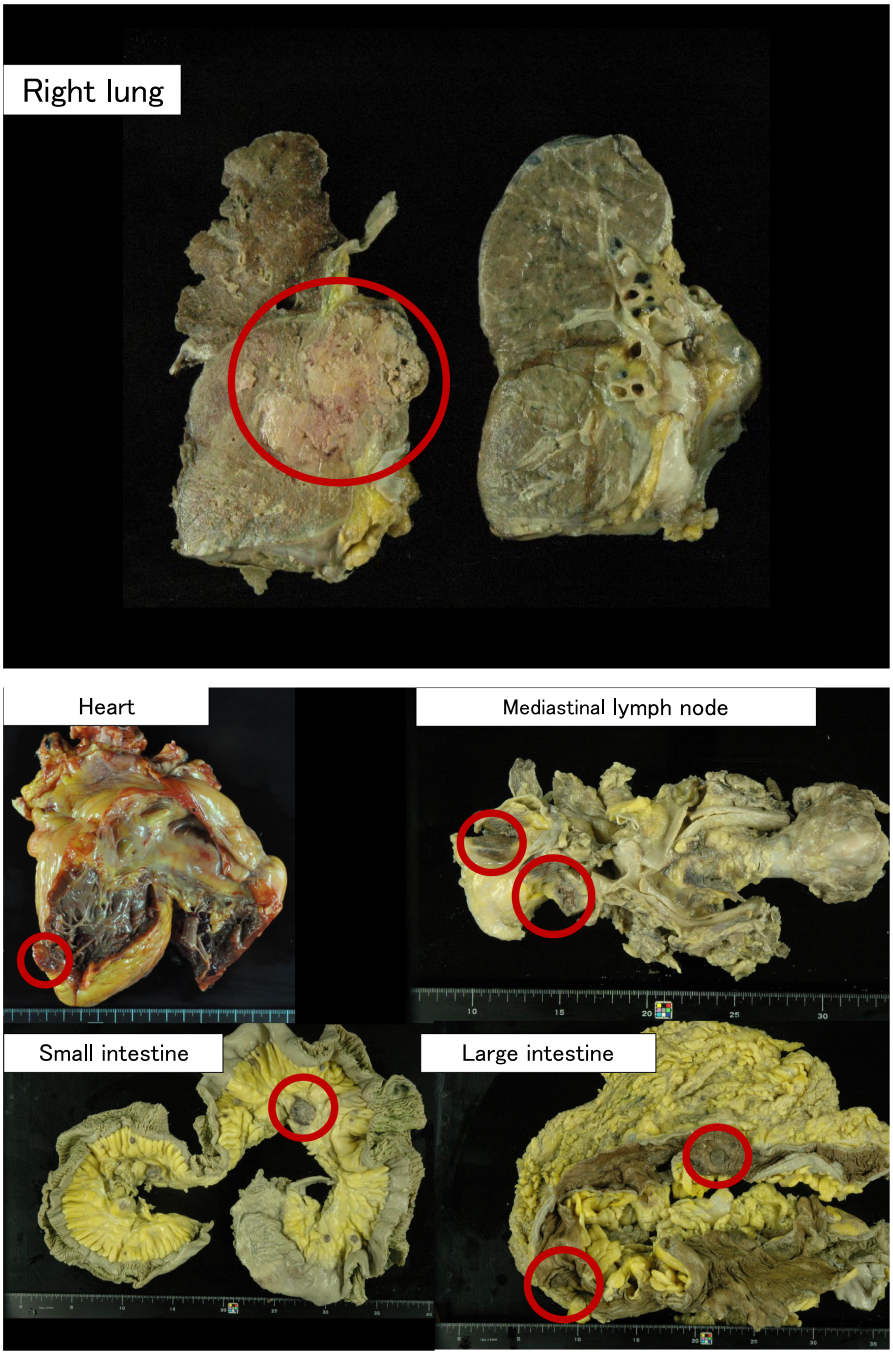

FIGURE 3 Autopsy findings. The primary tumor is located in the right lower lobe; measures 8 cm in diameter; and is grayish-white, hard, and with irregular margins. There are metastases in the heart, mediastinum, thyroid, stomach, duodenum, small intestine, large intestine, pancreas, gallbladder, bilateral adrenal glands, mesentery, peritoneum, and retroperitoneum.

days. Autopsy revealed metastases to various organs and lymph nodes, some of which were not confirmed during the clinical course. Pleomorphic carcinoma of the lung is extremely rare, accounting for approximately 0.1% to 0.4% of lung tumors,[1,2] and had been reported in very few dialysis cases. The prognosis of pleomorphic lung cancer is poor, with a reported median survival time of 22.8 months.[3] It is relatively common in older men and had been linked to smoking and asbestos.[4,5] In this case, the autopsy findings suggested that the patient had been exposed to asbestos. The most common histological types of asbestos-related lung cancer are squamous cell carcinoma, adenocarcinoma, and small cell carcinoma, and only two cases of pleomorphic carcinoma had been reported.[6] To our best knowledge, this was the first report on lung pleomorphic carcinoma in a patient on hemodialysis. We reported this pleomorphic lung cancer case with the autopsy findings in order to add to literature data on this disease.

In this case, the rapid clinical course made treatment of the pleomorphic lung cancer not feasible. The reported prognostic factors include tumor diameter of 4 or 5 cm or more, pleural invasion, pathologic stage II or higher, presence of lymph node and distant metastases, high uptake (SUVmax ≥15) of the primary tumor on PET-CT, and the presence of massive necrosis.[1,3,4,7] Many of these poor prognostic risk factors were present in this

case. Pleomorphic lung cancer has a poor response to conventional chemotherapy and radiotherapy[8,9] but was reported to have a PD-L1 expression in the sarcomatoid areas.[10] In fact, the effectiveness of immune checkpoint inhibitor therapy for pleomorphic lung cancer had been demonstrated in some case reports,[11,12] although not in studies on multiple cases. Moreover, studies on the effectiveness of immune checkpoint inhibitor therapy for pleomorphic lung cancer, in comparison with other treatments, are needed. Further additional case reports that include therapy are required to understand pleomorphic lung cancer. Patients on dialysis are prone to congestive heart failure and commonly present with dyspnea and pleural effusion. In this case, the pleural effusion was unilateral, and the cancer was advanced at the time of admission.

AUTHOR CONTRIBUTIONS

Keiichiro Okada: Conceptualization; writing – original draft; writing – review and editing. **Serina Kita:** Conceptualization. **Hirotaka Yamanouchi:** Data curation. **Shinichiro Nakao:** Formal analysis. **Yuto Matsuda:** Formal analysis. **Yui Kusuno:** Investigation. **Kazutoshi Nomura:** Investigation. **Tomohisa Yabe:** Investigation. **Norifumi Hayashi:** Supervision; writing – review and editing. **Keiji Fujimoto:** Supervision; writing – review and editing. **Kengo Furuichi:** Project administration; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors state that the study was conducted without any commercial or financial relationships that could be interpreted as a conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

All procedures performed in studies involving human participants were by the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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