Respiratory Medicine Case Reports 31 (2020) 101225

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: http://www.elsevier.com/locate/rmcr

Case report

Pulmonary pleomorphic carcinoma presenting as undifferentiated non-small cell carcinoma with giant cells: A case report and review of literature

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ARTICLE INFO

Keywords:
Pleomorphic carcinoma
Undifferentiated
Giant cells
PD-L1
Case report

ABSTRACT

Pulmonary pleomorphic carcinoma (PPC) is a poorly differentiated non-small cell lung carcinoma, including squamous cell carcinoma, adenocarcinoma, or undifferentiated non-small cell lung carcinoma with at least 10% spindle and/or giant cells. Here, we report a case of PPC showing undifferentiated non-small cell lung carcinoma with giant cells. A 71-year-old man with dyspnea underwent right lobectomy because of a mass in the right upper lobe of the lung. A 5.0 × 3.0 × 1.5 cm-sized tumor was identified; microscopically, the tumor composed of undifferentiated large sized tumor cells admixed with syncytial tumor giant cells and emperipoletic giant cells. Immunohistochemically, the tumor cells were reactive for pan-cytokeratin, but negative for P40, thyroid transcription factor 1 (TTF-1), and vimentin. The tumor cells were also positive for 3 clones of programmed death-ligand 1 (PD-L1). The clinical and histologic findings supported the diagnosis of an undifferentiated non-small cell lung carcinoma with giant cells, which is a subtype of pulmonary pleomorphic carcinoma. Unfortunately, after surgery, multifocal lymph node metastasis was identified in radiologic examination. Only palliative chemotherapy was administered to the patient, although he was indicated for immunochemotherapy. Pulmonary pleomorphic carcinoma is known to have a poor prognosis, even in early stages of the disease, therefore, we should be careful in the diagnosis to ensure optimal treatment.

1. Introduction

Pulmonary pleomorphic carcinoma (PPC) is a rare malignant tumor of the lung and its incidence has been reported to range from 0.1% to 0.4% of all lung cancers [1]. According to the revised 2015 World Health Organization (WHO) classification [2], PPC is categorized within sarcomatoid carcinoma (SC) with spindle cell carcinoma, giant cell carcinoma (GCC), carcinosarcoma, and pulmonary blastoma. WHO defined PPC as a poorly differentiated non-small cell lung carcinoma (NSCC), which includes epithelial components comprising squamous cell carcinoma (SqCC), adenocarcinoma (ADC), or undifferentiated NSCC that contains at least 10% spindle and/or giant cells or a carcinoma consisting only of spindle and giant cells [2]. Most cases arise in tobacco smokers, and the most common presentation on radiological examination is a large peripheral mass, usually in the upper lobe of the lung [2]. Frequent mutations in Kirsten rat sarcoma viral oncogene homolog (KRAS) [3,4] and epidermal growth factor receptor (EGFR) [5–7] partially reflect the adenocarcinomatous component of the tumor, patient ethnicity, and smoking status [8]. This tumor has a poor prognosis even in early stages of the disease. Here, we report a rare case of undifferentiated NSCLC with giant cells, pathologically diagnosed as PPC.

2. Case presentation

Clinical summary. A 71-year-old male was admitted to the Department of Respiratory and Critical Care Medicine in the Department of Internal Medicine, Chosun University Hospital (Gwangju, Korea) with a presentation of dyspnea. Bronchoscopic examination showed bronchial narrowing in the right medial basal segment of the lung. Thorax computerized tomography (CT) identified a heterogeneously enhancing mass-like consolidation in the right anteromedial basal segment of the lung (Fig. 1-A). Multiple small to mildly enlarged lymph nodes (LNs)

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https://doi.org/10.1016/j.rmcr.2020.101225
Received 11 March 2020; Received in revised form 9 September 2020; Accepted 10 September 2020
Available online 14 September 2020

with somewhat heterogeneous enhancement were also observed in the right paratracheal, subcarinal, and right interlobar nodal areas. Radiologically, the lesion was diagnosed as primary lung cancer with or without distal subsegmental area of obstructive atelectasis (T2b or T3) with suspicious early metastatic LNs. Right lobectomy with LN dissection was performed.

Pathological findings. A white to grey-colored mass, 5.0 × 3.0 × 1.5 cm in size, with central necrosis was identified (Fig. 1-B). Microscopically, the tumor was mainly composed of large mononucleated cells and multifocal giant cells. Sheets of neoplastic cells were admixed with an inflammatory component consisting mainly of neutrophils (Fig. 1-C). Mononuclear tumor cells showed round to oval nuclei and prominent nucleoli. Mitotic activity was easily observed. At high magnification, 2 types of giant cells were observed (Fig. 1-D). The first type included the syncytial shaped-multinucleated giant cells showing smudged nuclei and coarsely dispersed chromatin with nuclear molding (Fig. 1-D, block arrow). The other type included emperipoletic giant cells. The multinucleated giant cells showed prominent cytoplasmic cell-in-cell features (Fig. 1-D, arrow). In the resected specimen, no LN metastasis was observed. Immunohistochemical stains revealed that these tumor cells, including giant cells expressed pan-cytokeratin (CK) (Fig. 2-A) while they were negative for vimentin, thyroid transcription factor 1 (TTF-1), and p40 expression (Fig. 2-B, C, and D). In the immunohistochemistry performed for immunotherapy, the tumor cells were all positive for SP263, SP142, and 22C3 clones of programmed death-ligand 1 (PD-L1) (Fig. 2-E, F). The clinical and histologic findings supported the diagnosis of undifferentiated NSCLC with giant cells. Unfortunately, postoperative positron emission tomography (PET-CT) revealed multifocal LN metastasis in the right mediastinum, subcarina, and right hilum. Palliative chemotherapy was administered to the patient.

3. Discussion

PPC is a rare pulmonary epithelial malignant tumor that represents 0.1–0.4% of all malignant tumors of the lung [1]. According to the definition by WHO classification of lung tumors [2], PPC is a poorly differentiated NSCLC, including SqCC, ADC, or undifferentiated NSCLC containing at least 10% spindle and/or giant cells. Due to the limitations of biopsy specimens, definite diagnosis may only be made in a resected tumor. This tumor is usually a well-circumscribed, grey/tan mass measuring >5 cm in diameter, and known as an aggressive tumor; distant metastasis is commonly observed, including metastasis to the gastrointestinal tract and retroperitoneal space [2]. The most common carcinomatous element consists of conventional ADC and SqCC and less commonly undifferentiated large cell carcinoma [9]. Lee et al. [10] reported molecular features of 61 cases of PPC (Samsung medical center, from January 1995 to March 2009), in a histologic review of malignant epithelial components of PPC. Of these, ADC was in 72%, SqCC in 25%, and large cell carcinoma in 3%. For the mesenchymal components, 72% had spindle cell tumors and 28% had giant cell tumors. The differential diagnosis for PPC includes GCC and large cell carcinoma with null immunohistochemical features. The GCC is composed almost entirely of pleomorphic tumor giant cells while PPC is a poorly differentiated NSCLC containing at least 10% of giant cells. When differentiating a PPC from a large cell carcinoma with null immunophenotype, per the WHO classification of lung tumors [2], if >10% of the tumor shows pleomorphic features (spindle and/or giant cells), then the tumor should be

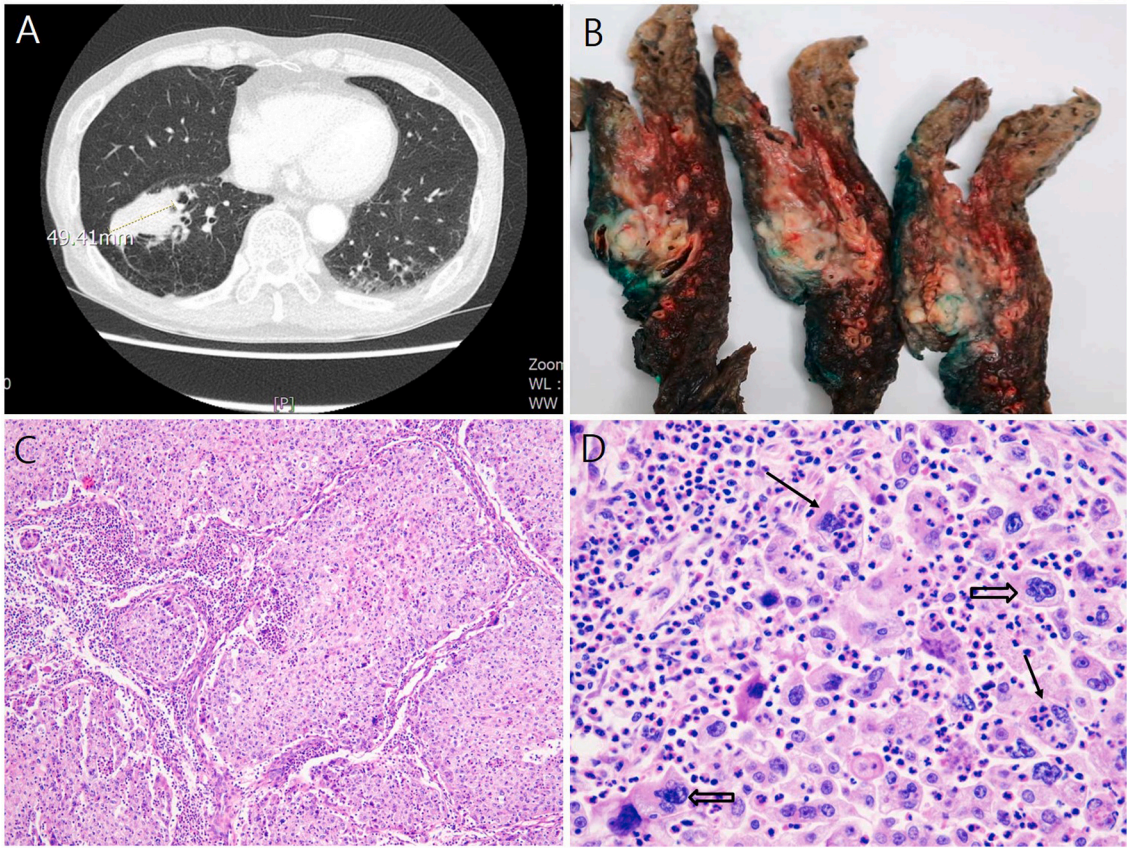

Fig. 1. A) Thorax computerized tomography (CT) showed a heterogeneously enhancing mass-like consolidation in the right anteromedial basal segment of the lung B) Grossly, a white to grey-colored mass, 5.0 × 3.0 × 1.5 cm in size, with central necrosis was identified. C) Microscopically, the tumor was mainly composed of large mononucleated cells and multifocal giant cells. Sheets of neoplastic cells were admixed with an inflammatory component consisting mainly of neutrophils. D) At high magnification, 2 types of giant cells were observed. (arrow: emperipoletic giant cells, block arrow: syncytial shaped-multinucleated giant cells).

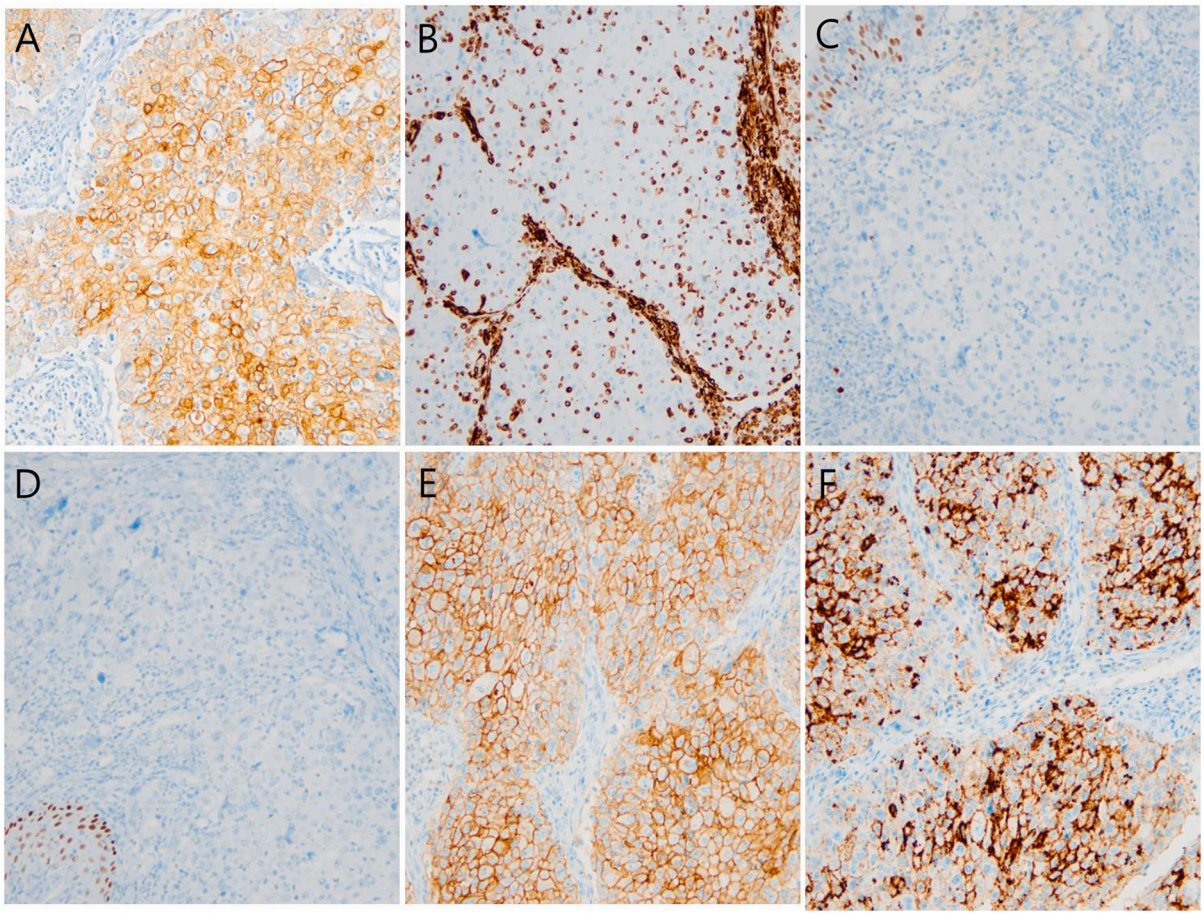

Fig. 2. Immunohistochemically, the tumor cells are positive for pan-cytokeratin (CK) (A), but negative for vimentin (B), TTF-1 (C), and p40 (D). The tumor cells were all positive for SP263 clone (E), SP142 clone (F), and 22C3 clone of PD-L1.

classified as a PPC.

A standard treatment for PPC has not been established because of its rarity [11]. Among NSCLCs, PPC is known to be very aggressive in biological behavior and resistant to conventional treatment, such as chemotherapy and radiotherapy [12–14]. It tends to show early metastasis and high relapse rate, rapid growth, and invasion into adjacent structures, therefore, more aggressive treatment strategy may be needed [15]. Until now, several prognostic factors have been suggested, such as surgical resection with tumor margin involvement, TNM stage, tumor necrosis, and pleural involvement [15]. Nakanishi et al. [16] analyzed the surgical outcome of 22 patients with PPC. Based on the epithelial component, the predominant tissue type included ADC in 15, SqCCs in 3, adenoSqCC in 1, and undifferentiated NSCLCs in 3 cases, in which only the predominantly epithelial histologic type tended to be associated with better disease-free survival, that is, the 3-year disease-free survival rate tended to be better in patients with an ADC component compared to the patients with other components ($p = 0.059$). Okuda et al. [17] also reported that type of epithelial component (ADC VS non-ADC), vascular invasion, and LN metastasis were closely correlated with survival. However, Yuki et al. [18] and Mochizuki et al. [19] reported that type of epithelial components was not a prognostic factor. Thus, predictors of the long-term survival of patients with PPC are controversial and a large-scale study is required to elucidate these factors.

Recently, immune check inhibitors (ICIs) have been approved and administrated for the treatment of NSCLC. PD-L1 expression is recognized as a predictor of the ICI effect and an indicator for choosing the patient for immunotherapy, such as ICIs. Several studies reported that PPC highly expresses PD-L1, and successful treatment with ICIs has been reported. Nakanishi et al. [16] evaluated PD-L1 expression in 8 cases of PPC. The expression of 28-8 clone of PD-L1 (for Nivolumab administration) was evaluated, in which high PD-L1 expression was frequently noted (>40%, 7 cases; 1%, 1 case). Yorozuya et al. [20] reported a case of PPC, which showed 100% PD-L1 expression and responded to durvalumab treatment. Also, Kim et al. [21] demonstrated the expression of PD-L1 and PD-L2 in 41 cases of PPC, which included ADC in 24, SqCC in 11, and adenoSqCC in 5 cases, based on histological analysis of epithelial components. PPCs frequently express PD-L1 and PD-L2 (approximately, 90%), especially higher in sarcomatous cells than in carcinomatous areas. Kim et al. suggested that targeting the PD-1/PD-L1 pathway may represent a potential therapeutic candidate for PPCs. Also, the present case showed high PD-L1 expression in 3 clones of PD-L1 antibodies (22C3, SP263, and SP142). However, due to the advanced stage of tumor in this patient, immunotherapy was not administered.

4. Conclusion

PPCs are rare lung tumors with low incidence and an aggressive biological behavior. The prognosis is still poorer than other NSCLCs. Histologically, this tumor should be differentiated from giant cell carcinoma and null cell subtype of large cell carcinoma. Recently, ICI administration has been shown to be effective for the management of lung cancer. PPCs also show high PD-L1 expression, therefore, aggressive treatment strategy, including immunotherapy should be considered for potential therapeutic candidates with PPCs.

Ethics approval and consent to participate

The study was approved by the ethics committee of Chosun university hospital (Institutional Review Board of Chosun university hospital, Gwangju, Korea), who waived the requirement for written informed consent due to the nature of the study.

Consent for publication

All data published here have consent for publication.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Funding

This study was supported by researchfund from the Chosun University, Republic of Korea, 2018.

Authors' contributions

The manuscript was designed, written, and revised by JH Jeong, HJ Seo, SH Yoon, and R Hong

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

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