INTRODUCTION

Undifferentiated pleomorphic sarcoma (UPS), formerly known as MFH, is a sarcoma with uncertain origin arising mostly in soft tissue and bone. Although MFH was previously one of the most common soft tissue sarcomas, primary UPS/MFH of the lung is now a rare clinical finding, with few reports in the literature in recent years.

Undifferentiated pleomorphic sarcoma is an aggressive mesenchymal neoplasm that was previously classified as malignant fibrous histiocytoma (MFH). Although MFH was identified as one of the most common adult soft tissue sarcomas initially by Weiss and Enzinger in 1978, the incidence of tumors diagnosed as MFH has dramatically declined in recent years following significant advances in diagnostic tools. MFH primarily occurs in the deep fascia of soft tissue in lower extremities or retroperitoneum, and the lung is the most common site of distant metastasis. Primary UPS/MFH of the lung, however, is an extremely rare clinical entity with <15 cases reported during the past two decades. In this report, we present a case of primary UPS of the lung that was considered to originate from the visceral pleura.

CASE PRESENTATION

A 71-year-old male smoker of >25 pack-year with no previous medical history presented with a 10-day history of cough. The patient had no shortness of breath, chest pain, or other pulmonary symptoms. A chest X-ray showed a nodular opacity in right middle lung field. A chest computed tomography (CT) scan showed diffuse pulmonary emphysema and a 3.0 × 3.0 cm well-defined solitary mass in the right middle lobe along the minor fissure (Figure 1A). 18F-Fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) scanning showed significantly increased uptake in the right middle lobe with the maximum standardized uptake value (SUVmax) of 18.5, but there was no significant uptake in other areas (Figure 1B). Flexible bronchoscopy revealed normal airways, and a definitive diagnosis was not provided by transbronchial biopsy. Tumor markers were within the normal range. Based on these findings, the patient underwent video-assisted thoracoscopic biopsy to obtain a histological diagnosis. A well-circumscribed solitary tumor arising from the visceral pleura of the middle lobe was observed, and an incisional biopsy was performed (Figure 2). An intraoperative frozen section was
MIYASHITA et al. reported as malignant tumor composed of atypical spindle cells and eosinophilic cells, and then, we proceeded with a right middle lobectomy and mediastinal nodal dissection by thoracotomy. The tumor strongly adhered to the pulmonary artery, but there was no direct invasion of vessels or adjacent lobes. The resected mass, measuring 3.1 × 3.0 cm in size, was well-circumscribed, firm, encapsulated, and partially necrotic without calcification. Resection margins were not clear for tumor (Figure 3A). There was no lymph node metastasis. Hematoxylin-eosin staining showed interesting fascicles of spindle cells in a storiform pattern (Figure 3B), and the tumor had originated from visceral pleura as primary lesion (Figure 3C). Immunohistochemical staining of the tumor cells revealed positive expression for vimentin, CD68, and partially smooth muscle actin (SMA), and negative expression for cytokeratin (CK), cytokeratin-7 (CK7), cytokeratin-20 (CK20),

**FIGURE 1**  A, A chest CT scan showing diffuse pulmonary emphysema and a 3.0 × 3.0 cm well-defined solitary mass in the right middle lobe along the minor fissure (arrow head). B, 18F-FDG PET/CT scanning showing significantly increased uptake in the right middle lobe with the maximum standardized uptake value (SUVmax) of 18.5

**FIGURE 2** A well-circumscribed solitary tumor arising from the visceral pleura of the middle lobe was observed (arrow heads)

**FIGURE 3** Macroscopic and pathological findings of the resected specimen. A, The mass was well-circumscribed, firm, encapsulated, and partially necrotic without calcification. B, Hematoxylin-eosin staining showing interesting fascicles of spindle cells in a storiform pattern (magnification ×200). C, The tumor was found arising from the visceral pleura as primary lesion (magnification ×50)
Desmin, S-100, CD34, mouse double minute 2 homolog (MDM2), cyclin-dependent kinase-4 (CDK4), HMB45, TTF-1, p40, p53, CD1a, CD3, CD20, CD30, Lysozyme, CAM5.2, cytokeratin-5/6 (CK5/6), epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), calretinin, and D2-40. The MIB-1 labeling index was 70% in the lesion. The final pathologic diagnosis was undifferentiated pleomorphic sarcoma of the lung arising from the visceral pleura. The patient was discharged on the fourth postoperative day, and the patient's postoperative course was uneventful except for a postoperative pneumothorax requiring endobronchial occlusion. No recurrence was detected at 15 months follow-up after surgery.

### 3 | DISCUSSION

UPS/MFH is a soft tissue sarcoma with no specific line of differentiation. MFH was first described in 1963 as a malignant soft tissue tumor arising from histiocytes, its morphology characterized by a highly ordered storiform growth pattern with less differentiated areas having a pleomorphic appearance. However, it is now known that these tumors show no evidence of true histiocytic differentiation, and the morphologic pattern may be shared by a wide variety of poorly differentiated malignant neoplasms. Furthermore, reports now show that only 13%-27% of tumors previously categorized as MFH re-reviewed using the latest immunohistochemical and electron-microscopic techniques were in fact MFH. As a result, the diagnostic term MFH was removed from the 2013 WHO Classification and replaced with a new category, undifferentiated/unclassified sarcomas (US), for tumors defined as UPS. As a consequence, the diagnosis of MFH has become less frequent in the last decade yet still remains in use practically as a synonym with UPS, describing the much smaller group of tumors that show no definable line of differentiation.

As with our case in this report, primary pulmonary UPS/MFH most commonly occurs in males between 40 and 80 years old. Typical symptoms include cough, chest pain, dyspnea, hemoptysis, weight loss, and fatigue. In patients who were asymptomatic, the tumor was relatively small in size and often found by routine chest CT examination. Therefore, to avoid inclusion of non-UPS cases, we reviewed only the latest 13 cases of previously reported primary MFH of the lung since 2002 when MFH turned to be classified within UPS/MFH (Table 1).

| Reference (yr) | Age (yr) | Sex | Location | Size (cm) | Treatment | F/U (mo) |
|----------------|----------|-----|----------|-----------|-----------|---------|
| Alhadab (2002) | 56       | M   | LUL      | UNK       | None      | DOD (4) |
| Wang (2003)    | 86       | M   | LLL      | 15        | None      | DOD (2) |
| Maeda (2007)   | 62       | M   | LUL      | 4.5       | Lobectomy | NED (24) |
| Noh (2008)     | 58       | F   | RUL      | 5.7       | Lobectomy/RT | NED (5) |
| Maitani (2010) | 18       | F   | LUL      | 2.2       | Wedge resection | NED (36) |
| Tsagaridou (2010) | 54    | M   | LUL/LLL  |           | Pneumonec tomy | AWD (168) |
| Jeon (2012)    | 55       | M   | LLL      | 5         | 1) Pneumonec tomy 2) CRT for rec. | NED (36) |
| Thomas (2013)  | 47       | M   | RUL (mets) | UNK       | Chemo     | DOD (<1) |
| Li (2013)      | 80       | F   | RUL      | 8         | None      | DOD (1.5) |
| Xu (2013)      | 55       | F   | LUL      |           | 1) CRT 2) Resection for rec. | NED (50) |
| Patel (2015)   | 86       | M   | RLL      | 9.6       | Lobectomy | NED (6) |
| Li (2017)      | 61       | M   | RUL      | 8         | Lobectomy | UNK |
| Cosgun (2017)  | 50       | M   | LUL      | 9.6       | Lobectomy | NED (36) |
| Present case (2019) | 71 | M   | RML      | 3.1       | Lobectomy | NED (15) |

Abbreviations: AWD, alive with disease; CRT, chemoradiotherapy; DOD, dead of disease; F, female; LLL, left lower lobe; LUL, left upper lobe; M, male; NED, no evidence of disease; RLL, right lower lobe; RML, right middle lobe; RT, radiation therapy; RUL, right upper lobe; UNK, unknown.
of the tumor but also tumor spread and mediastinal lymph node involvement. As previously reported, FDG PET/CT scan showed significantly increased uptake in the primary pulmonary UPS.\textsuperscript{9,13-15} It is still unclear how frequent pulmonary UPS shows high level of uptake by FDG PET/CT. However, even though this is not a characteristic finding of the pulmonary UPS, a solid pulmonary tumor with increased uptake of FDG is suggestive of possible malignancy including UPS and requires further diagnosis. Additionally, as lung is the most common metastatic site of UPS, PET/CT may be useful to identify primary or metastatic extrapulmonary lesions.

Given the extreme rarity of this disease, an optimal treatment strategy for primary pulmonary UPS has not yet been elucidated. In this case, the patient had surgical resection alone without any adjuvant treatment and 15 months postsurgery remains alive with no signs of recurrence. Previous reports described poor patient outcomes; in general, patients died within years of diagnosis without a surgical resection due to aggressive nature of the disease.\textsuperscript{12} However, for 13 cases previously reported as primary MFH of the lung since 2002 all patients underwent resection and were alive. This suggests that complete surgical resection of the tumor should be considered for patients with primary pulmonary UPS if it appears to be resectable, and close follow-up after surgery is important to find recurrence earlier. Although adjuvant chemotherapy or radiotherapy has been performed in some cases, their role remains uncertain for this malignancy.\textsuperscript{13,16}

4 | CONCLUSIONS

Primary pulmonary UPS, previously classified as MFH, is a rare malignancy. Although this tumor has been reported to be intrinsically aggressive and have a high risk of recurrence and metastasis, complete surgical resection is one of the treatment options for long-term survival.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

YM: wrote the manuscript. KH: supervised the writing of the manuscript. YM, NI, and KH: performed the operation. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data supporting the conclusions of this article are included within the article.

ETHICAL APPROVAL

The present study was conducted in accordance with the ethical standards of our institution.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for this publication.

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