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Primary Pulmonary Angiosarcoma Presenting with Hemoptysis and Ground-Glass Opacity: A Case Report and Literature Review

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Angiosarcoma originates from the vascular endothelium and accounts for only 1-2% of all sarcomatous malignancies. The skin is one of the most common primary sites. However, primary pulmonary angiosarcoma is rare, and only 31 cases of primary pulmonary angiosarcoma have been reported. A 79-year-old Japanese female developed bloody sputum, and chest X-ray and chest computed tomography (CT) showed consolidation with ground-glass opacity (GGO) on the right middle and lower lung fields. The bronchoscopic findings demonstrated bleeding from the right B^4 and B^5, and bronchial arterial embolization was subsequently performed. However, the CT findings demonstrated new pulmonary nodules with GGO in the left lung, and she presented with hemosputum and a progression of anemia. Right hemothorax also occurred, and surgical lung resection was performed to control the bleeding. The pathological analysis of the resected lung revealed the focal growth of atypical alveolar epithelioid-like cells that were positive for CD31 and negative for epithelial membrane antigen, and these atypical cells were replacing the endothelium of the pulmonary artery. Based on these findings, the patient was diagnosed with pulmonary angiosarcoma, which might originate from the endothelium of the pulmonary artery. No abnormal findings were observed except for the pulmonary involvement on systemic CT scanning. However, the patient passed away due to respiratory failure with compression of the brainstem caused by brain metastasis three months after the first visit. Early surgical resection is the important treatment for patients with angiosarcoma. In addition, we review the literature reporting the patients with primary pulmonary angiosarcoma.

Keywords: angiosarcoma; hemoptysis; lung cancer; pathology; thoracic surgery
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Introduction

Angiosarcoma is a sarcoma originating from the vascular endothelium which accounts for only 1-2% of all sarcomatous malignancies (Young et al. 2010). The skin is one of the most common primary sites, and metastatic pulmonary lesions are frequently observed with or without pneumothoraces and hemothoraces (Kitagawa et al. 1987); however, angiosarcoma is seldom observed in the lung as the primary lesion. Primary pulmonary angiosarcoma is rare, and only 31 cases of primary pulmonary angiosarcoma have been reported thus far. A diagnosis of angiosarcoma depends on immunohistochemical findings (Yang et al. 2012), and effective treatments for this tumor have not yet been established (Obeso Carillo et al. 2013). Primary pulmonary angiosarcoma has a poor prognosis, with most patients dying within months after their first presentation of symptoms (Obeso Carillo et al. 2013). We herein report a case of primary pulmonary angiosarcoma presenting with hemoptysis as the chief complaint and ground-glass opacity (GGO) with a review of the pertinent literature.

Case Presentation

A 79-year-old Japanese female developed bloody spu-

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tum in November 2013 and was referred to our hospital for an evaluation of an abnormal chest X-ray. The patient was a never-smoker and had no history of drinking, and she did not take any regular medications. She was a housewife and had no inhalation history of toxic materials. She had been diagnosed as having nodular goiter when she was 73 years of age and had been observed with no treatment. On admission, her height was 151.2 cm, body weight was 42.9 kg, blood pressure was 108/60 mmHg, pulse rate was 95 beats/min, transcutaneous oxygen saturation was 97% (room air, rest), and body temperature was 36.0ºC. Chest auscultation revealed inspiratory coarse crackles in the right middle and lower lung fields. Swelling of the thyroid gland, 5 cm in size, was palpable. She had no skin abnormality including scalp. The laboratory findings on admission demonstrated an elevation of the peripheral white blood cell count (12,200/μl), lactate dehydrogenase (330 IU/l), surfactant protein-D (463 ng/ml), fibrinogen degradation product (FDP) (62.2 μg/ml) and D-dimer (26.1 μg/ml) levels, and a slight decrease of the serum hemoglobin (Hb) level (11.0 mg/dl). Tumor markers, such as carcinoembryonic antigen, carbohydrate antigen 19-9, cytokeratin 19 fragment and pro-gastrin-releasing peptide, were within normal limits. Another blood examination data such as myeloperoxidase anti-neutrophil cytoplasmic antibody (ANCA), proteinase-3 ANCA, beta glucan and anti-double stranded DNA IgG antibody were normal levels. A chest X-ray (Fig. 1A) on admission showed consolidation with GGO in the right middle and lower lung fields and tracheal deviation to the right due to the goiter. Chest computed tomography (CT) on admission demonstrated consolidation and GGO in the right middle and lower lobes and localized GGO in the left S^{1+2} and S^{8} (Fig. 1B, C). Other obvious abnormal findings were not observed on her head, chest and abdominal CT. Fine needle aspiration of nodular goiter performed on the 2th day after admission, and a cytological examination demonstrated cyst and no malignant findings. Bronchoscopic findings (Fig. 2A) performed on the same day demonstrated bleeding from the right B^{4} and B^{5}, and a cytological examination of bronchial washing demonstrated no malignant findings. Bronchial angiography was performed on the same day, and bronchial arterial embolization (BAE) for the middle branch of the right bronchial artery was performed. Thereafter, her CT findings and symptoms of hemoptysis showed a slight improvement and the patient was discharged from the hospital on the 7th day after admission.

Four weeks after discharge, the patient began to produce bloody sputum and her CT findings demonstrated new pulmonary nodules with GGO in the left S^{1+2} (Fig. 1D) and S^{8}, and the laboratory findings showed a progression of

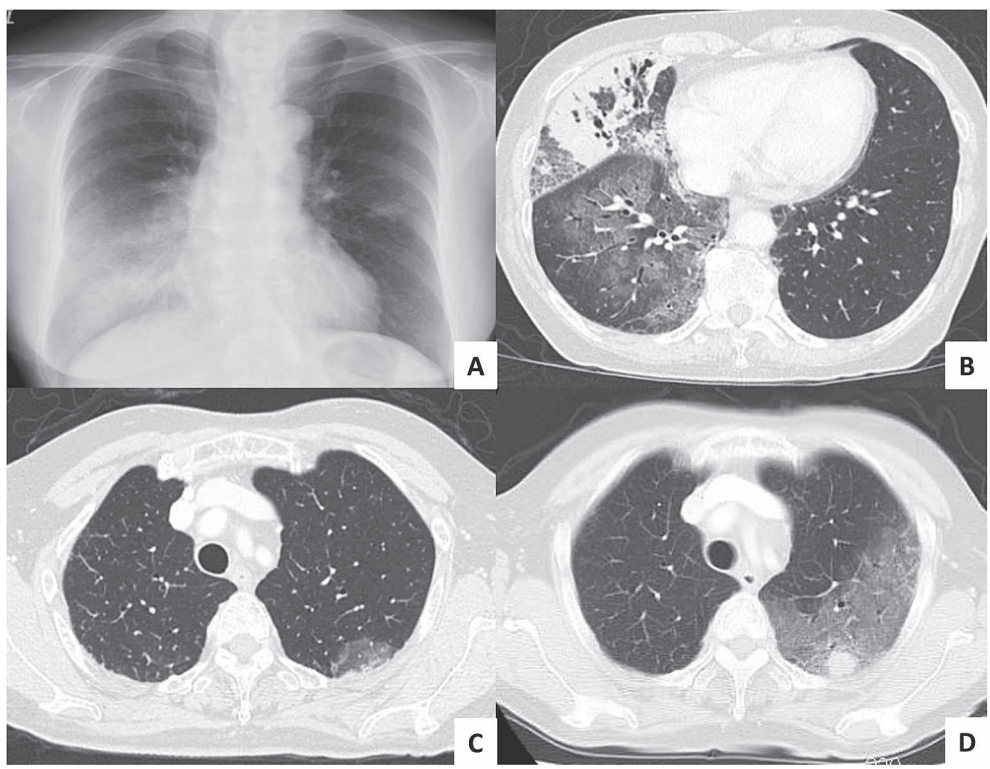

Fig. 1. The radiological findings of the present patient.
A chest radiograph on admission (A) shows consolidation with ground-glass opacity (GGO) in the right middle and lower lung fields and tracheal deviation to the right due to a goiter. The lung window of chest computed tomography (CT) on admission demonstrates consolidation and GGO in the right middle and lower lobes (B) and localized GGO in the left S^{1+2} (C). The lung window of chest CT four weeks after discharge demonstrates a new pulmonary nodule with GGO in the left S^{1+2} (D).

anemia (Hb 8.5 g/dl). BAE was performed again for the middle-lower branch of the right bronchial artery and left bronchial artery, however, her symptom of hemoptysis and the CT findings did not improve. A right hemothorax occurred on 18th day of hospital readmission; therefore, surgical resections of the right middle lobe, left upper lobe and a portion of the left lower lobe were performed to control the bleeding.

The pathological findings of the resected lung specimens obtained from the right middle, left upper and lower lobes revealed focal growth of atypical alveolar epithelioid-like cells with hyperchromatic nuclei and light-eosinophilic cytoplasm arranged in a cord-like fashion, partially forming irregular small vascular channels (Fig. 2B). The vascular channels of the pulmonary artery around the bronchial and bronchiolar areas were often lined by atypical tumor cells (Fig. 2C). The immunohistochemical findings demonstrated that these atypical cells were positive for CD31, which is a specific marker for tumors derived from the endothelium (Fig. 2D), and that they were negative for epithelial membrane antigen, cytokeratin CAM5.2 and cytokeratin AE1/AE3. Left hilar lymph node metastasis was also observed. According to these findings, the patient was diagnosed with pulmonary angiosarcoma, which might originate from the vascular endothelium of the pulmonary artery. No abnormal findings were observed except for the pulmonary involvement on systemic CT scanning; therefore, a diagnosis of primary pulmonary angiosarcoma was made. The patient became unconscious on the 14th day after surgery, and head CT findings revealed a new cerebellar mass that was 5 cm in diameter and subcortical multiple nodules that were not observed on the first admission. She eventually passed away due to respiratory failure by compression of the brainstem induced by brain metastasis three months after the first visit.

Discussion

Angiosarcoma is a rare disease entity and accounts for only 1-2% of all sarcomatous malignancies (Young et al. 2010). A report of 99 patients with angiosarcoma demonstrated that primary lesions originated from the skin of the head and face (29 cases), liver (17 cases), trunk (13 cases), heart (12 cases), pleural cavity/chest wall (8 cases), extremities (7 cases) and other sites (Naka et al. 1995). The primary lesion of the present patient was thought to originate from the lung according to the clinical, pathological and radiological findings; however, pulmonary lesions are typically secondary and metastatic lesions from other primary lesions in patients with angiosarcoma (Kitagawa et al. 1987). Primary pulmonary angiosarcoma is rare, and

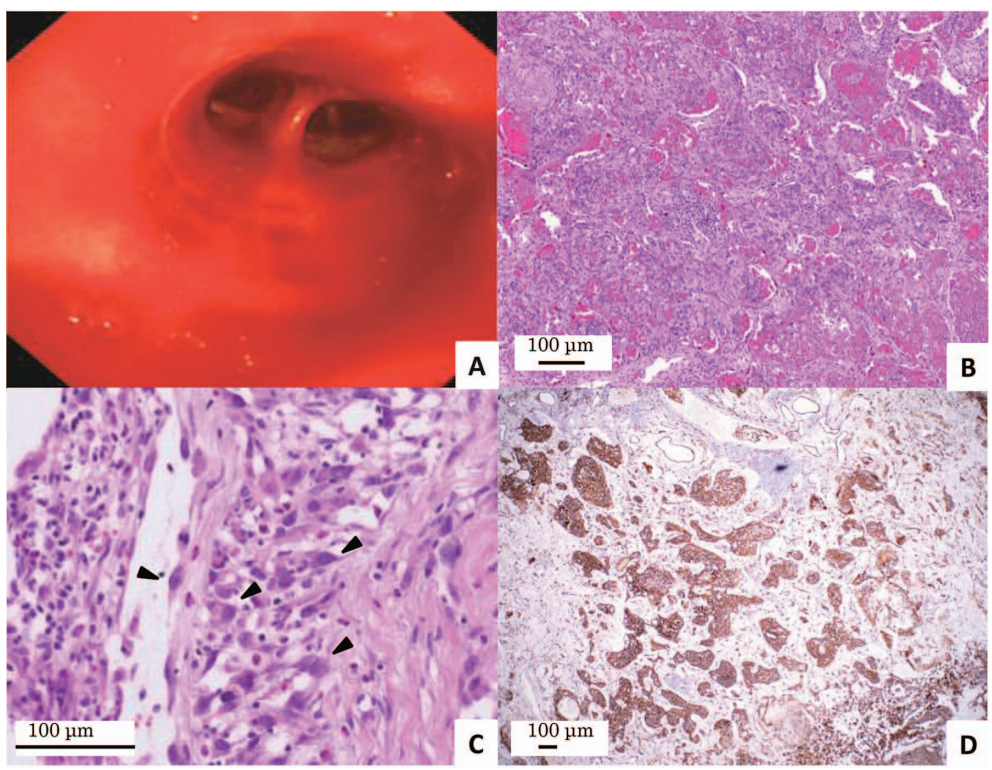

Fig. 2. The bronchoscopic findings and pathological findings.
(A) The bronchoscopic findings of the 2th day after admission show bleeding from the right B^4 and B^5. Panels B, C, and D show the pathological findings of the resected lung specimens obtained from the right middle lobe. Hematoxylin-eosin staining reveals focal growth of atypical alveolar epithelioid-like cells arranged in cord-like fashion (original magnification, ×100) (B), and higher magnification shows that atypical cells (arrowheads) are observed, replacing the vascular endothelium of the pulmonary arteries (original magnification, ×400) (C). (D) The immunohistochemical findings demonstrate that these atypical cells are positive for CD31 (original magnification, ×40).

there have been only 32 case reports, including the present patient, six case reports in the Japanese literature (Oka et al. 1981; Sasaki et al. 1992; Ogura et al. 1993; Kinoshita et al. 2000; Asari et al. 2003; Ogawa and Takaya 2014) and 25 reported cases in the overseas literature (Ott et al. 1987; Sheppard et al. 1997; Keel et al. 1999; Atasoy et al. 2001; Junge et al. 2001; Kojima et al. 2003; Maglaras et al. 2004; Bouhaouala et al. 2005; Corpa-Rodriguez et al. 2005; Pandit et al. 2005; Ozcelik et al. 2006; Herrak et al. 2007; Wilson et al. 2008; Kuroda et al. 2009; Chen et al. 2010; Wan Musa et al. 2010; Alayon-Laguer et al. 2011; Eichner et al. 2011; Kakegawa et al. 2012; Yang et al. 2012; Obeso Carillo et al. 2013; Treglia et al. 2014) reported thus far. Table 1 represents the clinical characteristics of the reported 32 patients with primary pulmonary angiosarcoma. The average age was 55.9 (23-82) years, and the female/male ratio was 1:5. Hemoptysis and/or hemosputum (15 cases) were the most frequently observed symptoms at the first visit, followed by a cough (11 cases) and chest pain (9 cases).

The clinical features of angiosarcoma are typically based on the pathological characteristics that the progression of tumor cells tends to occur in the blood vessel, and thus bleeding, progressive anemia and coagulation abnormality are frequently observed (Tateishi et al. 2003). The progression of the tumor may cause hemoptysis, chest pain, pneumothorax or hemothorax in patients who have sarcoma with pulmonary lesions including primary pulmonary angiosarcoma (Kinoshita et al. 2000). The progression of the tumor aggravated the clinical symptoms of respiratory failure and hemoptysis induced by an intrapulmonary hemorrhage, the progression of anemia and coagulopathies, such as an elevation of FDP and D-dimer, in this patient. Similar to our patient, the reported prognosis of patients with primary pulmonary angiosarcoma is poor, and the median survival time of 22 reported cases with available data in Table 1 was 5 months. Obeso Carillo et al. (2013) reported that patients treated with curative resection of the pulmonary tumor showed a median survival time of 16.8 months; therefore, early treatment with surgical resection may be crucial to the treatment of primary pulmonary angiosarcoma.

The previously reported chest radiological findings of primary pulmonary angiosarcoma include pulmonary nodules (27 cases), infiltrations (7 cases), GGO (4 cases), pleural effusion (5 cases), pulmonary nodules surrounded by GGO (3 cases), and the invasion of other organs (6 cases). However, it is difficult to make a precise diagnosis of pulmonary angiosarcoma according to the radiological findings alone. A hemothorax was reported in four patients (Maglaras et al. 2004; Eichner et al. 2011), and hemothoraces were observed during the progression of the disease in these cases. In patients with metastatic pulmonary lesions of angiosarcoma, pulmonary involvement of angiosarcoma is characterized by multiple subpleural distributions of pulmonary nodules and/or infiltrations with surrounding GGO (Goto et al. 2008). These radiological features were also observed in the clinical course of the present patient.

Most of the cases of primary pulmonary angiosarcoma were diagnosed by surgical resection of the lung or at autopsy, and only 9 patients were diagnosed by transbronchial lung biopsy or CT-guided lung biopsy (Ogura et al. 1993; Keel et al. 1999; Junge et al. 2001; Kojima et al. 2003; Herrak et al. 2007; Wan Musa et al. 2010; Alayon-Laguer et al. 2011; Ogawa and Takaya 2014). Relatively large lung specimens are necessary for the precise diagnosis of primary pulmonary angiosarcoma, and the histopathological features of the tumor cells and immunohistochemical findings are important. CD31-, CD34- and factor VIII-positive tumor cells are characteristic findings (Chida et al. 2012), which was also observed in the present patient.

Angiosarcoma generally tends to demonstrate hematologic metastasis to the lung, bone, liver, lymph node and adrenal gland (Naka et al. 1995). The brain is a rarely the site of primary or metastatic lesions of angiosarcoma (Jung et al. 2012), and there have been only two case reports that showed brain metastasis from primary pulmonary angiosarcoma thus far (Ogura et al. 1993; Maglaras et al. 2004). The pathological features of the brain lesions in the present patient were not evaluated, however, abnormal findings were not observed on initial head CT, and the characteristics of the intracranial mass lesions with surrounding brain edema and hemorrhage (Jung et al. 2012) and its rapid growth were compatible with metastatic lesions of angiosarcoma. Brain metastasis leads to a poor prognosis of patients with angiosarcoma, and an early diagnosis using neurological examinations in addition to a radiological survey may be important when patients with angiosarcoma show clinical clues of intracranial involvement.

The most effective treatment of angiosarcoma is surgical resection of the affected lesions, and other treatment modalities are thought to be less effective. There has been only one case report where the combined treatment of radiotherapy and interleukin-2 administration was effective (Kojima et al. 2003), however, systemic chemotherapy and radiotherapy are ineffective in most patient with angiosarcoma, and surgical resection of the affected lesions should be considered as early as possible.

In conclusion, we herein reported a rare case of primary pulmonary angiosarcoma presenting with hemoptysis and GGO complicating brain metastasis, which was diagnosed based on the findings of a lung surgical resection using video-associated thoracic surgery. Early surgical resection is the most important modality for making a prompt diagnosis and performing appropriate treatment, because systemic chemotherapy and radiotherapy are often ineffective in patients with angiosarcoma.

Table1. Reported cases of primary pulmonary angiosarcoma.

Authors	Age/sex	Symptoms	Chest CT findings	Treatment	Outcome
Alayon-Laguer et al.	77/M	Abdominal pain, weight loss	A 86-mm mass in LLL	ChemoT and RT	Died
Asari et al.	78/M	Cough, hemoptysis	Bilateral multiple nodules	No treatment	Died
Atasoy et al.	50/M	Chest pain, malaise, hoarseness	A 100-mm mass in LUL	ChemoT	Alive (9M)
Bouhaouala et al.	46/M	Hemoptysis	Diffuse consolidation in RLL	Lobectomy	Died (11M)
Chen et al.	50/M	Hemoptysis	Left multiple nodules	Lobectomy and ChemoT	Alive
Corpa-Rodriguez et al.	42/M	Chest pain, cough, malaise	A 150-mm mass in RUL	Lobectomy	Died (2M)
Eichner et al.	69/M	Shortness of breath, hemoptysis	Bilateral reticular and alveolar patterns with small nodules	No treatment	Died (4D)
Eichner et al.	81/F	Spontaneous bilateral hemothorax	Bilateral diffuse consolidation and pleural effusion	No treatment	Died
Herrak et al.	48/M	Chest pain	A mass in RUL	No treatment	N/A
Junge et al.	41/M	Shortness of breath	A 100-mm mass in LLL	Lobectomy, ChemoT and RT	Alive
Kakegawa et al.	45/M	Hemoptysis, cough	A 12-mm nodule in left main bronchus	Pneumonectomy	Alive (1Y)
Keel et al.	N/A	N/A	Bilateral masses	ChemoT	Died (2M)
Keel et al.	N/A	N/A	A mass	N/A	N/A
Kinoshita et al.	82/M	Cough, hemoptysis	A 50-mm mass in RUL	Lobectomy	Died (6M)
Kojima et al.	25/M	Chest pain, cough	A 55-mm mass in left hilum	RT and IL-2	Alive (1Y)
Kuroda et al.	43/M	Cough	A mass in LLL	Lobectomy	Alive (15M)
Maglaras et al.	46/M	Hemoptysis	Patchy consolidation in RUL, bilateral diffuse GGO	ChemoT	Died (1M)
Obesco Carillo et al.	56/M	Hemoptysis	A 25-mm nodule in LLL	ChemoT	Died (7M)
Obesco Carillo et al.	35/M	Bone and joint pain	A solid lesion in RLL	Lobectomy and ChemoT	Died (6M)
Ogawa and Takaya	69/M	Chest pain	A 44-mm mass in LUL, bilateral multiple nodules	N/A	N/A
Ogura et al.	64/F	Cough, shortness of breath, hemoptysis	A 32-mm mass in left hilum	Pneumonectomy, RT and IL-2	Died (9M)
Oka et al.	46/M	Hemoptysis, cough	A left mass	Pneumonectomy	Died (2M)
Ott et al.	60/M	Shortness of breath, chest pain, cough	A right 130-mm mass and pleural effusion	Pneumonectomy	Died (68D)
Ozcelik et al.	62/M	Hemoptysis, cough, chest pain, weight loss	A 35-mm nodule in RUL	Lobectomy, ChemoT and RT	Died (5M)
Pandit et al.	79/F	Shortness of breath, chest pain	Bilateral multiple nodules and pleural effusion	No treatment	Died (18M)
Sasaki et al.	65/M	Hemoptysis	Bilateral patchy consolidation	Steroid therapy	Died
Sheppard et al.	65/M	Hemoptysis	Bilateral multiple nodular Consolidation	No treatment	Died (2D)
Treglia et al.	54/F	No symptoms	A 40-mm mass in LLL	Lobectomy	N/A
Wan Musa et al.	23/M	Shoulder and chest pain	A 50-mm mass in LUL, left pleural effusion	ChemoT	Died (0.5M)
Wilson et al.	56/M	Hemoptysis	A 39-mm mass in LUL	Lobectomy, ChemoT and RT	Died (39M)
Yang et al.	41/M	Cough	A 17-mm nodule in LUL	Wedge resection	Died (a few days)
Present case	79/F	Hemoptysis	Consolidation and GGO in RLL and RML	Lobectomy	Died (21D)

M, male; F, female; N/A, not applicable; GGO, ground-glass opacity; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; ChemoT, chemotherapy; RT, radiotherapy; IL-2, interleukin 2; M, months; D, days; Y, year.

Conflict of Interest

The authors declare no conflict of interest.

References

Alayon-Laguer, D., Padua, I.J., Arroyo, N., Caceres, W. & Conde-Sterling, D. (2011) Hispanic with a primary pulmonary angiosarcoma: case report and literature review. *Bol. Asoc. Med. PR*, **103**, 34-40.

Asari, T., Nara, K., Hosobe, S. & Saito, K. (2003) A case of angiosarcoma of the lung. *Nippon Rinsho Saibo Gakkai zasshi*, **42**, 96-97.

Atasoy, C., Fitoz, S., Yigit, H., Atasoy, P., Erden, I. & Akyar, S. (2001) Radiographic, CT, and MRI findings in primary pulmonary angiosarcoma. *Clin. Imaging*, **25**, 337-340.

Bouhaouala, M.H., Charfi, M.R., Fajraoui, N., Bouaziz, N., Boukhris, A. & Kilani, T. (2005) Primary pulmonary angiosarcoma. *Rev. Pneumol. Clin*., **61**, 115-118.

Chen, Y.B., Guo, L.C., Yang, L., Feng, W., Zhang, X.Q., Ling, C.H., Ji, C. & Huang, J.A. (2010) Angiosarcoma of the lung: 2 cases report and literature reviewed. *Lung Cancer*, **70**, 352-356.

Chida, S., Nagasawa, H., Shimada, Y. & Okada, K. (2012) Angiosarcoma. *Kansetsu Geka*, **31**, 217-219.

Corpa-Rodriguez, M.E., Mayoralas-Alises, S., Garcia-Sanchez, J., Gil-Alonso, J.L., Diaz-Agero, P. & Casillas-Pajuelo, M. (2005) Postoperative course in 7 cases of primary sarcoma of the lung. *Arch. Bronconeumol.*, **41**, 634-637.

Eichner, R., Schwendy, S., Liebl, F., Huber, A. & Langer, R. (2011) Two cases of primary pulmonary angiosarcoma as a rare cause of lung haemorrhage. *Pathology*, **43**, 386-389.

Goto, H., Watanuki, Y., Miyazawa, N., Kudo, M., Inoue, S., Kobayashi, N., Kaneko, T. & Ishigatsubo, Y. (2008) Clinical and pathological analysis of 10 cases of secondary pneumothorax due to angiosarcoma of the scalp. *Nihon Kokyuki Gakkai Zasshi*, **46**, 85-91.

Herrak, L., Alaziz, S. & Benosmane, A. (2007) Primary pulmonary angiosarcoma. *Rev. Mal. Respir*., **24**, 73-76.

Jung, S.H., Jung, T.Y., Joo, S.P. & Kim, H.S. (2012) Rapid clinical course of cerebral metastatic angiosarcoma from the heart. *J. Korean Neurosurg. Soc.*, **51**, 47-50.

Junge, K., Toens, C., Peiper, C., Hermanns, B. & Schumpelick V. (2001) Primary angiosarcoma of the lung. *Chirurg*, **72**, 969-972.

Kakegawa, S., Kawashima, O., Ibe, T., Ujita, M., Iwashina, M., Nakano, T. & Shimizu, K. (2012) A case of primary angiosarcoma of the lung presenting as a hemorrhagic bronchial tumor. *Ann. Thorac. Cardiovasc. Surg.*, **18**, 347-351.

Keel, S.B., Bacha, E., Mark, E.J., Nielsen, G.P. & Rosenberg, A.E. (1999) Primary pulmonary sarcoma: a clinicopathologic study of 26 cases. *Mod. Pathol.*, **12**, 1124-1131.

Kinoshita, T., Maebeya, S., Kato, M. & Naito, Y. (2000) A case of surgically resected pulmonary angiosarcoma. *Haigan*, **40**, 297-300.

Kitagawa, M., Tanaka, I., Takemura, T., Matsubara, O. & Kasuga, T. (1987) Angiosarcoma of the scalp: report of two cases with fatal pulmonary complications and a review of Japanese autopsy registry data. *Virchows Arch. A Pathol. Anat. Histopathol.*, **412**, 83-87.

Kojima, K., Okamoto, I., Ushijima, S., Yoshinaga, T., Kitaoka, M., Suga, M. & Sasaki, Y. (2003) Successful treatment of primary pulmonary angiosarcoma. *Chest*, **124**, 2397-2400.

Kuroda, N., Hamaguchi, N., Inoue, K., Ohara, M., Mizuno, K., Hayashi, Y. & Lee, G.H. (2009) Application of immunocytochemistry to the diagnosis of primary epithelioid angiosarcoma of the lung. *Med. Mol. Morphol.*, **42**, 250-253.

Maglaras, G.C., Katsenos, S., Kakadelis, J., Katsanos, C., Metafratzi, Z., Stefanou, D.G., Vassiliou, M.P. & Constantopoulos, S.H. (2004) Primary angiosarcoma of the lung and pleura. *Monaldi Arch. Chest Dis*., **61**, 234-236.

Naka, N., Ohsawa, M., Tomita, Y., Kanno, H., Uchida, A. & Aozasa, K. (1995) Angiosarcoma in Japan. A review of 99 cases. *Cancer*, **75**, 989-996.

Obeso Carillo, G.A., Garcia Fontan, E.M., Canizares Carretero, M.A. & Perez Pedrosa, A. (2013) Primary pulmonary angiosarcoma, an exceptional neoplasm with a poor prognosis: reports of two cases and review of the literature. *Gen. Thorac. Cardiovasc. Surg.*, **61**, 643-647.

Ogawa, K. & Takaya, H. (2014) Angiosarcoma of the lung. *Kokyu*, **33**, 386-390.

Ogura, Y., Shimotakahara, T., Nishijima, H., Matsumoto, H., Yanagi, M. & Shimazu, H. (1993) Resected angiosarcoma of the lung: a case report. *Nippon Kokyuki Geka Gakkai zasshi*, **7**, 157-164.

Oka, S., Hirabayashi, T., Hayashi, K., Kondou, S., Matsui, K. & Yoshimatsu, A. (1981) A case of malignant hemangioendothelioma of the lung. *Nippon Kyobu Shikkan Gakkai Zasshi*, **19**, 63-67.

Ott, R.A., Eugene, J., Kollin, J., Kanas, R.J., Conston, D.E. & Chi, J.C. (1987) Primary pulmonary angiosarcoma associated with multiple synchronous neoplasms. *J. Surg. Oncol.*, **35**, 269-276.

Ozcelik, C., Onat, S., Yaldiz, M. & Ozcelik, Z. (2006) Primary epithelioid angiosarcoma of the lung presenting as pulmonary hemorrhage. *Asian Cardiovasc. Thorac. Ann.*, **14**, 69-71.

Pandit, S.A., Fiedler, P.N. & Westcott, J.L. (2005) Primary angiosarcoma of the lung. *Ann. Diagn. Pathol.*, **9**, 302-304.

Sasaki, Y., Kawano, O., Sakata, T., Matsumoto, M., Kohrogi, H., Sugimoto, M., Ando, M., Araki, S., Higashi, K. & Takahashi, K. (1992) A case of intractable hemoptysis due to malignant hemangioendothelioma. *Nippon Kyobu Shikkan Gakkai Zasshi*, **30**, 123-127.

Sheppard, M.N., Hansell, D.M., Du Bois, R.M. & Nicholson, A.G. (1997) Primary epithelioid angiosarcoma of the lung presenting as pulmonary hemorrhage. *Hum. Pathol.*, **28**, 383-385.

Tateishi, U., Gladish, G.W., Kusumoto, M., Hasegawa, T., Yokoyama, R., Tsuchiya, R. & Moriyama, N. (2003) Chest wall tumors: radiologic findings and pathologic correlation: part 2. Malignant tumors. *Radiographics*, **23**, 1491-1508.

Treglia, G., Cardillo, G. & Graziano, P. (2014) A rare case of primary pulmonary epithelioid angiosarcoma detected by (18) F-FDG PET/CT. *Clin. Nucl. Med.*, **39**, 450-452.

Wan Musa, W.R., Abdulwakil Elraied, M.A., Phang, K.S., Kwah, Y.G., Tan, S.P., Harun, R. & Ban, A.Y. (2010) Primary epithelioid angiosarcoma of the lung presenting as left-sided shoulder pain. *Ann. Acad. Med. Singapore*, **39**, 658-659.

Wilson, R., Glaros, S., Brown, R.K., Michael, C. & Reisman, D. (2008) Complete radiographic response of primary pulmonary angiosarcomas following gemcitabine and taxotere. *Lung Cancer*, **61**, 131-136.

Yang, C.F., Chen, T.W., Tseng, G.C. & Chiang, I.P. (2012) Primary pulmonary epithelioid angiosarcoma presenting as a solitary pulmonary nodule on image. *Pathol. Int.*, **62**, 424-428.

Young, R.J., Brown, N.J., Reed, M.W., Hughes, D. & Woll, P.J. (2010) Angiosarcoma. *Lancet Oncol.*, **11**, 983-991.