Pulmonary tumors of embryonic origin are rare, in which pulmonary blastomas (PB) are probably the most uncommon. The two types of PB, biphasic and monophasic, are also known as well-differentiated fetal adenocarcinoma (WDFA). We recently encountered one patient with PB in a young adult. The histopathologic findings was consistent with the monophasic type of pulmonary blastoma – WDFA. There are no specific clinical or radiological features of WDFA, although young age, peripheral location of well circumscribed mass and large tumor size are often characteristic findings. The histopathological and immunohistochemical techniques play an important role and are the only reliable way to establish a definite diagnosis. The surgical resection is the treatment of choice.

Key words: Biphasic pulmonary blastoma; Computed tomography; Pulmonary blastoma; Well differentiated fetal adenocarcinoma

Well-differentiated fetal adenocarcinoma is a distinct clinicopathologic entity. However, preoperative diagnosis for WDFA is difficult because of nonspecific clinical and radiological findings. So far, less than fifty cases have been reported before [1]. We report one case of WDFA. The imaging findings, pathologic features, clinical presentation, management and prognosis are described, along with a review of the literatures. The awareness of this rare malignancy may alert the radiologists to include this disease in the differential diagnosis.

CASE REPORT

A 28-year-old nonsmoking female visited our chest clinic because of productive cough for three weeks, but not responding to antibiotics. She denied having any previous serious medial problem. Her physical findings were unremarkable. Chest radiographs (PA and lateral view) revealed a large, spherical homogeneous opacity in the right middle lung field, showing smooth well defined borders with collapse of the medial segment (Fig.1a & 1b). Hemogram and blood biochemistry values were all within normal limits. CT of the chest disclosed a solitary well circumscribed mass, measuring 8 x 5 x 5.6 cm, in the right middle lobe and some non-enhancing areas suggestive of necrosis (Fig. 2). No cavitation, calcification, pleural effusion, hilar or mediastinal adenopathy was evident on CT. An associated inhomogeneous opacity with air-bronchogram in the medial segment of the right middle lobe was suggestive of atelectasis. Occlusion of the lateral segment of the right intermediate bronchus was also found (Fig.3). The bronchoscopy revealed bronchial compression with mild stenosis in the lateral segment branch of right intermediate bronchus. Sputum examinations for fungi, neoplastic cells, and acid-fast bacilli yielded negative findings. The result of the pulmonary function test was within normal limit. The serum tumor markers, CEA, AFP, and CA-125, were also within the normal range. Accordingly, malignant tumor was
suspected on the basis of the imaging findings. At tho-
racotomy, a firm mass was palpated. The patient
underwent right middle lobectomy. The resected
tumor, measuring 8.0 x 6.5 x 4.0 cm in dimension, was
well demarcated in the right middle lobe. The tumor
invaded the adjacent visceral pleura but did not
penetrate. The remaining lung parenchyma of this lobe
was atelectatic without involvement. The gross
specimen of the tumor showed necrosis and hemor-
rhage on the cut end and a polypoid mass protruding
into the adjacent branch of the right intermediate
bronchus. Microscopically, all margins were free and
all mediastinal lymph nodes and peribronchial lymph
nodes did not show evidence of metastasis. The mass
consisted of branching tubules or cribriform pattern
lined by pseudostratified nonciliated columnar cells
containing clear or slightly eosinophilic cytoplasm.
The nuclei of the tumor cells were oval or round. The
cells were characterized by subnuclear and supranu-
clear vacuoles, producing a distinctive endometrioid
appearance. In the lesion, numerous solid epithelial
nests, also known as morules, was seen beneath the
glandular epithelium with solid nests of round
optically clear nuclei. Immunohistochemical analysis
revealed the tumor cells were reactive against cytoke-
atin (CK) antibody and some of the tumor cells espe-
cially in morule area were reactive against
Chromogranin A, Factor VIII, neuron-specific enolase

Figure 1. Chest radiographs (PA and
lateral view) showed a well circumscri-
bed mass in the right middle lobe.

Figure 2. Chest CT revealed a mass in the right middle
lobe with inhomogeneous enhancement and large areas of
necrosis.

Figure 3. CT scan in lung window setting showing
occlusion of lateral segment of right middle lobe (arrow).
(NSE) and calcitonin antibodies. The stromal cells between tumor cells were reactive against Vimentin antibody. Mucincarimine stain showed presence of mucin in the luminal border of tumor cells. PAS and D/PAS stains showed there was glycogen in the cytoplasm of tumor cells. Both histological picture and immunohistochemical profile were characteristic of WDFA because it lacked the sarcomatous features of pulmonary blastoma. The patient was clinically staged as IB (T2N0M0). The post-operative course was uneventful, and there were no complications. At the lastest follow-up, 10 months postoperatively, the patient was clinically and radiologically free of the disease.

**DISCUSSION**

Pulmonary blastomas (PB) are rare malignancy, representing less than 1% of all lung cancers. This tumor mimic the embryonic elements of the lung in early fetal development between 10 and 16 gestational weeks. The pathogenesis of this tumor is controversial. Initially, pulmonary blastoma was thought to be analogous to nephroblastoma and some investigators also believed it to be a variant of carcinosarcoma with coincidental resemblance to the fetal lung. However, now the entities have been separately classified and also known, the PB usually arise peripherally in the lungs, while pulmonary carcinosarcoma arises centrally in the lung in associated with large bronchus. Also, in PB the epithelial component is always glandular, whereas in carcinosarcoma it is usually squamous [2,3,4].

The 2 types of PB are biphasic and WDFA. Biphasic PB (BPB) contains both neoplastic glandular tissue and adult sarcomatous or embryonic mesenchymal tissue, whereas a WDFA contains solely malignant glandular tissues of embryonic appearance. According to the recent WHO classification, however, WDFA is a variant of pulmonary adenocarcinoma[5]. The pediatric variant of pulmonary blastoma is known as pleuropulmonary blastoma, in which there is no recognizable neoplastic epithelium, and was a distinctive high grade sarcomatous malignancy, and observed not only in lung but also in extrapulmonary tissue [6,7].

Little information is available on genetic changes, lack of $P^53$ mutation seen in WDFA, whereas presence of mutation in the $P^53$ gene in BPB (42%), were reported [7]. The incidence of WDFA is estimated to comprise only 0.5% of all pulmonary neoplasms. WDFA occur at any age, with the mean age at diagnosis being 35 to 40 years and gender ratio favoring women or equal in distribution. In 80% of patients, there is a history of tobacco use suggesting that the same agents that are thought to have a role in the pathogenesis of bronchogenic carcinomas may also be involved in the development of the PB. Approximately 25% to 40% of patients are asymptomatic at presentation, with incidental diagnosis by chest radiography, suggesting the mass may be present as long as several years before the patient seeks medical attention. Hemoptysis and cough are the most common symptoms in patients with tumors affecting the bronchi, whereas chest pain is common when pleura is involved. Pleural effusion occur occasionally.

On plain radiographs, PB typically presents as well defined homogeneous radiopacities in the middle and peripheral zone but without preference for any lobe. On ultrasound examination, they show heterogeneous appearance with solid and few cystic areas which indicate necrotic component. On computed tomography, it usually depicts as a well demarcated mass composes of solid tissue and nonenhancing area associated with compressing atelectasis, from ranges 5 cm to 10 cm in the maximum dimension. Some lesions tend to be lobulated and cavitated. In majority, they are spherical peripheral tumors, less frequently in midlung location or as polyoid intrabronchial mass (27%). Occasionally they are present as multiple pulmonary nodules. In both WDFA and BPB, lymphadenopathy is rare. In WDFA pleural effusion are rare; whereas in BPB pleural effusion are present in about 50% of cases. Cytological examination and endobronchial biopsies yield a correct or suggestive diagnosis in only one-third of the cases. This low yield rate is probably due to peripheral and extrabronchial location

**Figure 4.** WDFA. High magnification of microphotograph shows pseudostratified non-ciliated columnar epithelium and central morule with round nuclei. (H & E; × 100)
of the tumor and the histologic resemblance of the tumors to other neoplasms and small size of the lesion presenting with complex histologic features [1,5,7-11]. As in the majority of the reported cases, our case was also diagnosed on the basis of a histological examination of a resected specimen. Although a correct diagnosis may be achieved after resection, but adequate sampling is essential because BPB may contain a pattern of WDFA in the epithelial part of PB. Therefore on the small biopsy, a BPB cannot be excluded if the patient of WDFA is presented.

Grossly, these lesions are usually solitary, well-circumscribed, and variegated in color, 50% of them show necrosis. Microscopically, the epithelial glands often have sub- and supranuclear vacuoles, producing an endoemtrioid appearance. The histologic characteristic of morular metaplasia, solid balls of cells with ample eosinophilic cytoplasm at the bases of well ordered glands, are seen in 43% of biphasic tumor and 86-100% of cases of WDFA, is also presented in our case.

The reported clinical course of WDFA varies. Some patient had a fulminant course with widespread metastasis. Other patients, including the present case, were free of disease several months or years after surgical resection. The presence of thoracic metastasis and tumor size (< 5cm) were related to outcome, additionally; recurrence, nodal metastasis, pathological stage are included into prognostic factor. Also, histological differentiation between WDFA and PBP is important because of differences in prognosis and therapy. This rare tumor appears to carry a more favorable prognosis in the absence of metastasis following adequate surgical resection than for biphasic pulmonary blastoma and other pulmonary malignancies of similar stage. According to the previous study, the 10 year survival for WDFA is about 75% versus about 15% for BPB [1,4,5,11]. Treatment is primarily surgical, although, combination chemotherapy and radiotherapy have been reported to result in objective responses in inoperable tumors or after incomplete resections.

Our case of WDFA is similar to the reported case in the aspect of the clinical history, image and histological findings. The final surgical pathologic stage in this patients was stage IB (T2N0M0). We believe that the possibility of a primary lung tumor should be considered for any adult case with space occupying lesion. A primary lung malignancy should not be excluded only on the basis of the patient’s age, and should receive the detail and vigorous diagnostic evaluation and appropriate treatment. In our case, this allowed a complete resection of the tumor.

REFERENCE

分化良好的肺臟胎兒腺癌：病例報告

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肺母細胞瘤是一種發生於年輕人極為罕見的惡性腫瘤。其組織學影像類似胎兒期肺組織，主要是由腺管樣排列或濺漫樣分佈的間葉樣的腫瘤細胞所構成。肺母細胞瘤有兩種類型，分別為複相及單相的，即所謂的分化良好的肺臟胎兒腺癌。在此我們敘述一位 28 歲女性病患的臨床和影像表現。電腦斷層攝影顯示一邊緣清楚的腫瘤在右肺中葉，伴隨著壞死區域。最後經手術切除及病理檢查後證實為分化良好的肺臟胎兒腺癌。對於這種腫瘤，手術切除還是為主要治療方式。至於化療和電療所伴演的角色，仍待商確。雖然此病例極為罕見，臨床上沒有特殊的症狀，手術前診斷也比較困難。然而，若一年輕患者其影像特徵為一界定清處的腫塊時，分化良好的肺臟胎兒腺癌必須列入鑑別診斷。

關鍵詞：複相的肺母細胞瘤；電腦斷層攝影；肺母細胞瘤；分化良好的肺臟胎兒腺癌