Chin J Clin Oncol (2008) 5: 379~382
DOI 10.1007/s11805-008-0379-6

Clinical Analysis of 15 Patients with Adult-Type Pulmonary Blastoma

Lei Wang
Qingyi Liu
Ming He
Xianli Meng
Yuekao Li
Yumin Ping
Yanning Chen

[1] The Second Department of Thoracic Surgery; [2] CT Room; [3] Pathology Department, the Fourth Hospital of Hebei Medical University, Shijiazhuang 050011, Hebei Province, China.

Correspondence to: Lei Wang
E-mail:yuankundu@163.com

The work was supported by the Hebei Provincial Fund for Development of Oncology Faculty, based on High Scholarship and Creative Research Potential (No.[2005]52).

Received Feburary 22, 2008; accepted June 17, 2008.

CJCO http://www.cjco.cn
E-mail: 2008cocr@gmail.com
Tel (Fax): 86-22-2352 2919

OBJECTIVE To study the clinical and histopathological characteristics of pulmonary blastoma (PB), and to review the diagnostic criterion and treatment methods.
METHODS Clinical and histopathological data from 15 cases of PB in this hospital, from 1990 to 2006, were retrospectively analyzed.
RESULTS Surgical procedures were conducted in all 15 patients, including pulmonary lobectomy in 9, lobectomy of the 2 right pulmonary lobes in 2, excision of pulmonary segments in 1, lobectomy and bronchoplasty in 1, lobectomy and angioplasty in 1, and excision of the whole left lung in 1. Of the 15 cases, 11 were misdiagnosed as lung cancer, 2 were doubted to be a benign tumor before surgery, 1 was suspected to be a malignant mesenchymoma, and only 1 was diagnosed as a PB.
CONCLUSION Preoperative final diagnosis of PB is very difficult, since the clinical symptoms of the disease are nonspecific. To confirm the diagnosis, comprehensive consideration of the factors, such as the clinical manifestations, morphological characteristics and immunohistochemical tumor markers, should be taken. Surgery is the treatment of choice for PB, and a thorough removal is the key to a cure. PB has a high malignancy and often recurs and metastasizes, usually with a poor prognosis.

KEY WORDS: pulmonary blastoma, adult type, diagnosis, therapy.

Introduction

Pulmonary blastoma (PB) is a rare malignant tumor with a pulmonary or pleural origin. Similar to the structure of an embryonic lung, it consists of mesenchymal and epithelial constituents, and accounts for 0.25% to 0.5% of primary malignant lung tumors[1]. Based on different ages of onset, PBs can be divided into 2 types, i.e. adult and child types. In our study, data from 15 cases with adult PB, from August 1990 to April 2006, were collected. The clinicopathologic features of the PB cases were retrospectively analyzed, and the methods of diagnosis and treatment reviewed.

Materials and Methods

Clinical data

Among the 15 patients, 9 were male and 6 female. Their ages ranged from 35~72 years, averaging 55.1; case histories were between 1 week and 2 years. Clinical symptoms included the following: cough-

ing was seen in 10, chest-back pain in 3, bloody phlegm in 5, hemoptysis in 1, fervescence in 6, and asthma and obstructive respiration in 2. One PB case was found during a physical examination. A left upper lobe (LUL) tumor was seen in 5 cases, a left lower lobe (LLL) in 1, right upper lobe (RUL) in 3, and right lower lobe (RLL) in 5. In 1 case, the tumor stretched over the right upper and middle lobes.

Bronchofibroscopy was performed in 10 cases. A nodus in the lobes of the LUL, and hyperemia and edema were shown in 1, with bloody phlegm and a negative result. A stricture caused by pressure of the tumor at the anterior segment of the RUL was shown in another, with a pathological result of a disintegrated heterologous cyst. It was shown in the examination that a neoplasm could be seen at a bronchial opening on the parietal region of the LUL in 1 case, which was fragile and hemorrhagic, indicating disintegrated cancer cells. A neoplasm at the opening of the RLL was identified in 1 and pathological confirmation of a prickle cell adenocarcinoma in 1. There was a neoplasm at the opening of the RUL in another, with a bite biopsy demonstrating that there was a heterologous cyst in the fibrous tissue, expected to be cancer. In 1 case there was a neoplasm at the opening in the front lateral basal segment of the RLL, with the pathological result of severe dyskaryotic cells. In another case, a cauliflower-like neoplasm obstructing the lumens was found at the opening of the LUL, which was fragile in quality, suggesting a squamous cancer by pathology. Other pathological results were negative. Results of a phlegm smear examination were negative in 5 cases.

Methods

Of the 15 patients lung cancer was preoperatively confirmed in 11, a benign tumor in 2, malignant mesenchymoma in 1, and PB in 1. Surgical resection was conducted in all patients of our group, among which pulmonary lobectomy was performed in 9, lobectomy of the 2 right pulmonary lobes in 2, excision of the lobe in 1, lobectomy and bronchoplasty in 1, lobectomy and angioplasty in 1, and excision of the whole left lung in 1. No intraoperative deaths occurred in our patients. A 10%-formalin fixation of the surgical specimens was conducted, with paraffin imbedding. Following H&E staining and light microscopy, immunohistochemical SP staining was conducted in 6 cases. EMA, Vim, CK, S100 and Act antibody and kits were bought from the Beijing Zhongshan Co.

Results

Image analysis

Of the total cases, 5 were central-type and 10 peripheral-type PB. Tumors with homogeneous density were found in 7 of the 15 cases, and that of heterogeneous density in the other 8. A regular margin of the neoplasm could be observed in 7 cases, and irregular and blurry verge in 8. Among the 8 cases, a fine burr around the tumor fringe was seen in 2. Of the 15 cases, a superficial sub-lobe was seen in 3 cases, an excentric cavity in 1, concomitant pulmonary atelectasis and obstructive pneumonia in 4, adhesion of the tumor to the chest wall in 4, and mediastinal lymphatic swelling (short diameter > 10 mm) in 3. Intensified CT scanning using iopromide contrast medium was conducted in 5 cases, with the lesion of a moderate to high intensity. After a ^{99}mTc-MIBI i.v. was conducted, a chest imaging indicated an abnormal radioactive enrichment shadow at the superior lobe of the right lung in 1 patient, suggesting it to be a malignant lesion. A whole-body PET imaging using an ^{18}F-FDG i.v. showed an obviously enhanced glycometabolic lesion at the inferior lobe of the right lung in 1 patient. The standard uptake value (SUV) was 3.6, showing it to be a malignant lung tumor in the hilum of the right lung. A tumor metastasis was displayed as an enhanced glycometabolic focus at the higher-middle mediastnum.

Pathological examination

Based on an analysis of the gross specimens, all the tumors were solitary, without a capsule in most of the cases. There were incomplete pseudocapsules in a few cases. Of the 15 cases, there were no corrugated visceral pleura on the tumor surface in 5, a slight corrugation in 4, and a severe corrugation in 6, where an encroachment of the parietal pleura occured in 4. A moderate hardness of the mass was seen in most of the cases, and a soft fish-like neoplasm in a few. Most of the tumors were firm, with a greyish or greyish-yellow cross section, and hemorrhage and necrosis inside some tumors. The diameters of the tumors were < 5 cm in 3 cases, 5 cm to 9 cm in 7, and ≥ 10 cm in 5. The minimum tumor size was 3 × 3 × 2 cm, and the maximum 14 × 14 × 14 cm.

Microscopic results

A biphase-type PB was found in 13 of the 15 cases, comprising a malignant mesenchymal and epithelial composition. The mesenchymal cells presented with a dispersed distribution, and no obvious differentiation was seen. Most of the cell nuclei assumed a fusiform shape, and an occasional orbicular-ovate shape. The nuclei were big and dark-stained, and nuclei could be seen, with a commonly-seen nuclear fission, less cytoplasm and acidophilia. In the cell-rich primitive undifferentiated mesenchymal tissues, there were glandular organelles formed by the malignant epithelial cells of various differentiations. A well-differentiated cartilage and hemorrhagic necrosis zone could be seen in a few cases. Immature or embryonic characteristics were shown in the main body of the tumors. There were 2 epithelial-type PB cases in the total, showing only malignant epithelial compositions, and a lack of sarcoma constituents. A well-differentiated conferted branching glandular tube

construction could be seen, with a pseudostratified high-columnar shape in the epithelium, and a lucency in part of the cytoplasm. There was a slight increase in the nucleoplasmic ratio, and the cytoplasmic shape was similar to an endometrioid glandular organ, with a monostratal cubical shape in part of the glandular epithelium. Morula was seen. Positive lymph nodes were found in 5 cases.

Immunohistochemical outcomes

CK (+) and EMA (+) were shown in 6 cases, Vim (+) in 5, S100 (+) in 1, and (-) in the other 5.

Prognosis

PB tumors often relapse and metastasize. In our cases, metastases were found in the brain, thoracic cavity, liver and adrenal gland etc. Follow-up was conducted in 11 cases, with a follow-up rate of 73.3% using the time of death as the end point of the follow-up. The follow-up time ranged from 5 to 61 months, with the survival time of over 5 years in 1 case, of 2 years in 1 case, of 1 year in 5, and of less than 1 year in 4 cases. The 2-year survival rate reached 18.2%.

Discussion

The origin of PB tissue is not clear at the present time. Most authors believe that the tumor originates from a primitive multipotent mesenchymal lung blastema. The adult-type PB has been divided into biphase and epithelial types. The biphase-type PB is the classical PB, which was included in the WHO (2004) new classifications as pulmonary carcinoma sarcomatodes, considering it to be a poorly-differentiated non-small cell carcinoma containing fleshy tumor or sarcomatoid constituents. The epithelial-type PB is a unidirectional tumor with primitive epithelium, but without primitive mesenchymal contents, which is similar to a well-differentiated fetal adenocarcinoma. It was included as a variant-type adenocarcinoma in the WHO new classification[2].

This disease can be found in patients of any age, ranging from 2 months to 80 years, with an average of 35[3]. The site of onset is more frequently seen in the right lung compared to the left, and more commonly found in the superior lobe than in the inferior. Also the incidence rate is higher in males compared to females[4]. In our group, the mean age of onset was 55.1 years, with a male-female ratio of 1.5 : 1. Most of the PBs are distributed in the subpleural peripheral part of the lung, with a late presence of respiratory symptoms, and early chest pain when the parietal pleura is involved. The symptoms such as cough, shortness of breath or bloody phlegm might occur, if there is a tumor at the hilum of the lung, or the peripheral tumor is big enough to oppress or infiltrate the ambient tissues, such as the trachea and great vessels.

The PBs had no obvious specificity in imageology. The main clinical manifestations in our patients were a solid tumor in the lung, with a solitary tumor in all of the cases. Some characteristics were shown, after an analysis of the CT imaging manifestations in our group, as follows: a. the PB was usually found at the peripheral part of the lung, with a roundish form and large volume, and a 5 cm diameter in most cases; b. usually there was no coarse burr and in-depth sublobe at the verge of the tumor; c. no apparent intumescent lymph nodes were found in the mediastinum and the hilum of the lung (short diameter < 10 mm) d. when an intensified CT scanning was conducted, the images were heterogeneous owing to a frequently seen hemorrhage and necrosis in the tumor, with several necrotic foci. In our group perfusion scans and PET examinations were respectively conducted in 1 case, showing an abnormal radioactive enrichment shadow and thus indicating a malignancy. It was of a confirmative benefit for diagnosis, but adequate data are still lacking.

A preoperative diagnosis of PB is rather difficult. It is our point of view that a bronchofibroscopy can be conducted if the tumor is close to the lung hilum, and a biopsy should be conducted if there is a neoplasm in the lumen. If there is no neoplasm in the lumen, this disease can be differentiated from a central-type bronchiogenic cancer. It is hard to make a conclusive diagnosis of PB because of limited specimens, though the tumor can be found by bronchoscopy. Therefore a bite biopsy combined with brush cytology can be conducted and multifocal sampling can be helpful for preoperative diagnosis. CT-guided percutaneous lung needle biopsy is preferred with a minor trauma and a rather high positive rate, if the tumor localizes at a verge of the lung. Most researchers do not believe that dissemination or implantation of lung cancer would occur. Huang et al.[5] mentioned a report by Sinner et al. in which 1,264 cases were subject to a needle biopsy. They found, after a long term follow-up, that tumor implantation occurred in only 1 case. In the 3 cases who underwent a needle biopsy in our group, adenocarcinoma cells were found in 1 (epithelial type), malignant mesenchymoma in 1 (biphase type), and PB in the other 1 (biphase type).

Recently extensive development of immunohistochemical determinations have made it much easier to determine a final diagnoses of PB. Joint application of the immunohistochemical indices, such as AE1/AE3, Vim, CK and calretinin etc., have been used to differentiate between PB and epithelioma or other types of sarcoma [6,7]. Differentiations are needed among PB and the tumors and cancers, such as carcinosarcoma of the lung, pleomorphic carcinoma of the lung, pulmonary adenocarcinoma and malignant mixed tumor, as well as mixed cellular-type mesothelioma.

The key for treating PB lies in early discovery and timely treatment, and ideal therapeutic efficacy depends on correctness and thoroughness of the treatment. Sur-

gery is the main treatment for PB, with the choice of surgical procedures best based on the size and site of the tumor, and the patient's physical condition, i. e., wedging, pulmonary lobectomy or excision of the total lung[8,9]. It was found in our study that PB presented with an infiltrative growth. No pseudo capsules were formed by an intertexture between the capsules or tumor rim and the normal tissues. However the actual diseased region had infiltrated into the peripheral tissues. This results in aggressiveness, recurrence and metastasis.

Past studies have shown that there were less lymphatic metastases in PB cases. Nevertheless, in our study we found a rather high node metastatic rate, with preoperative CT examinations showing mediastinal lymphatic swelling in 3 cases, and all postoperative pathological results confirmed the presence of metastasis. CT scanning indicated that there was no lymphatic swelling in 2 patients. Metastases were also found after lymphadenectomy, with a node metastatic rate of 33.3% in the total group (5/15). The number of cleared nodes amounted to 112 in our group, with a positive rate of 11.6%. PB is quite aggressive, with a rather high lymph-node metastatic rate, therefore a conservative surgery is inadvisable, and a wedging should be cautiously performed, with a pulmonary lobectomy plus lymphadenectomy as the conventional mode of surgery. Since some of the tumors were small, with a smooth verge and a pseudocapsule, these tumors were easily misdiagnosed as a benign lung lesion, with a wedging excision. Rapid frozen section diagnosis, after an intra-operative excision of the tumor, can aid in determining the mode of surgery.

Radiotherapy and chemotherapy can be used as an adjuvant treatment for PB, however there are various reports concerning efficacy. In our group, preoperative new adjuvant chemotherapy was conducted in 2 patients and preoperative radiotherapy in 1 patient. The effects were unsatisfactory, and tumors failed to significantly diminish. In 8 patients who underwent postoperative chemotherapy, only 2 achieved a survival of over 2 years, indicating that it is hard to confirm the efficacy of chemotherapy.

There have been various reports on the prognosis of PB in the past. Some authors have insisted that the prognosis is good in some of the patients who undergo surgery, but most suggest that the prognosis is rather poor[10]. PB prognosis relates to the site of the primary tumor, tumor size, metastasis and pathologic type etc. The prognosis was poor in the patient with the biphase-type PB and a tumor close to the pleura with a tumor diameter of > 5 cm, and a mediastinal nodular metastasis. A 2/3 of the patients died within 2 years, after the final diagnosis. Koss et al.[11] reported that the 5-year survival rate was 16% in 52 PB patients, and the 10-year survivals was merely 8%. Follow-up was conducted in 11 cases of our group, with the shortest survival time (ST) of 5 months, and the longest ST of 61 months. The mean ST was 6 months in the group with lymph node metastasis, and 24.4 months without. The mean ST achieved 11.1 months in the patients with a diameter of ≥ 5 cm, and 34 months in those with the size of < 5 cm.

References

1 Rosai J. Acherman's Surgical Pathology (9th Eds). 2004: 398-399.
2 Huo Z. Development of clinicopathologic studies on pulmonary blastoma. Zhen Duan Bing Li Xue Za Zhi 2005; 12: 382-3840 (Chinese).
3 Lee HJ, Goo JM, Kim KW, et al. Pulmonary blastoma: radiologic findings in five patients. Clin Imaging 2004; 28: 113-118.
4 Li QM, Liu JW, Zhan ZL, et al. Pulmonary blastoma: a report of 2 cases. Zhongguo Zhong Liu Lin Chuang 2004; 31: 360 (Chinese).
5 Huang JF, Huang CJ, Zhan YZ. Clinical application of CT-guided transcutaneous lung puncture biopsy. Zhongguo Fei Ai Za Zhi 2002; 5: 58-60 (Chinese).
6 Huo Z, Liu HR. Clinicopathologic and immunohistochemical study of adult-type pulmonary blastoma. Zhongguo Yi Xue Ke Xue Yuan Xue Bao 2005; 27: 475-478 (Chinese).
7 Yu H, Wu YL, Rong TH. Pulmonary blastoma: a clinical analysis of 4 cases and review of literature. Zhongguo Zhong Liu Lin Chuang 2001; 28: 64-66 (Chinese).
8 Yao GG, Yang MT, Wang SY. Adult pulmonary blastoma: a report of 5 cases with review of literature. Zhongguo Fei Ai Za Zhi 2005; 8: 132-135 (Chinese).
9 Zhuo YM, Wang RH, Yang ZY. A case report of pulmonary blastoma. Zhongguo Zhong Liu Lin Chuang 2004; 31: 751 (Chinese).
10 Zhang ZF, Wang R, Gao F. Pulmonary blastoma: a report of 3 cases. Zhonghua Xiong Xin Xue Guan Wai Ke Za Zhi 2004; 6: 340 (Chinese).
11 Koss MN, Hochholzer L, O'Leary T. Pulmonary blastomas. Cancer 1991; 67: 2368-2381.