Surgical treatment of primary sarcoma of the lung

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Abstract

Objective: To study the results of surgical treatment of primary lung sarcoma.

Methods: Between 1982 and 1998, we performed 18 macroscopically complete resections for primary sarcomas of the lung. The records of all patients were reviewed, as were pathological slides. Presence of symptoms, tumour size (more or less than 5 cm), complete resection, TNM stage and histology grade were analyzed for predictors of survival.

Results: Patients comprised 11 women and seven men whose age ranged from 19 to 73 years (mean 50 years). Mean tumour diameter was 8.05 cm (range 2.5–15 cm) There were one grade 1, eight grade 2 and nine grade 3 tumours. Tumours in two patients were unresectable at first presentation, and another was of doubtful resectability according to computed tomography scan. These three patients received pre-operative chemotherapy, with a partial response in the two unresectable patients allowing macroscopically complete resection in both cases. We performed 12 lobectomies (extended to the chest wall in two cases and to the diaphragm in two cases) and six pneumonectomies (extended to the chest wall in one case and the superior vena cava in one case). Operative and 30 days post-operative mortality were nil. Resection margins were invaded in two cases. Six patients received post-operative chemo- or radiotherapy and three others underwent repeat resections for pulmonary sarcoma recurrence. No patients were lost to follow-up. Pulmonary sarcomas recurred in eight patients (44%) leading to death in five cases after a mean period of 17 months. Overall median survival was 48 months, and actuarial 5-year survival 43%. Only TNM stage correlated with significantly increased survival.

Conclusion: As complete resection is the best therapeutic option for obtaining an acceptable survival rate in primary pulmonary sarcoma, pre-operative chemotherapy can be a useful adjunct in increasing the resectability of these tumours. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Primary sarcoma of the lung; Surgery; Chemotherapy

1. Introduction

Primary sarcomas of the lung are rare tumours that comprise a heterogeneous group of neoplasms whose clinical behaviour remains unclear [1]. Accordingly, many more sarcomas of the lung are metastatic than primary, and a primary pulmonary sarcoma cannot be diagnosed unless an alternate primary source has been thoroughly ruled out by clinical and radiographic examinations. Consequently, few authors describe the management of primary lung sarcomas [1–9] and furthermore, before 1975, many of them included lymphoproliferative disorders or carcinosarcomas [5]. Experience with their surgical resection is sparse, and the usefulness of neoadjuvant or adjuvant chemotherapy unknown. In this retrospective study, we reviewed the patients with confirmed primary sarcomas of the lung who were surgically treated, with a curative aim, during a 17-year period in a single institution.

2. Materials and methods

Between 1982 and 1998, 18 patients were treated for primary pulmonary sarcoma in the Thoracic Surgery Unit of Lille University Hospital, in accordance with the computer search of the surgical list, completed by a manual search. Clinical data, surgical reports, paraffin-embedded blocks and macroscopic slides were available for all patients. During the same period, 1575 patients underwent lung resection for primary malignant tumour. Primary lung sarcoma was diagnosed in 18 patients (1.1% of the 1575 lung resection cases) from the absence of sarcoma in any other site, from medical history and from clinical or radiological examinations performed pre-operatively and during follow-up, which were obtained in all cases from the referring physician. Patients with malignant lymphomas...
and carcinosarcomas were excluded from the study. All surviving patients were followed until the end point of the study (July 1999). Pathological slides were re-examined by two pathologists, experienced in the field of soft tissue tumour pathology. Immunohistochemistry and electron microscopy were also performed. Histological classification was based on the revised World Health Organization histological typing of soft tissue tumours [10] and tumour staging on the Mountain revised system for staging lung cancer [11].

Tumours were graded from 1 to 3, according to the classification of the French Federation of Cancer Centers reported by Coindre, based on tumour differentiation, mitosis count and necrosis [12]. Actuarial survival was determined by the Kaplan–Meier method, and survival differences were compared by the log-rank test. Age, sex, presence or absence of symptoms, tumour size (less or more than 5 cm), complete resection, histological cell type, stage and histology grade were analyzed as predictors of survival.

3. Results

3.1. Patient characteristics and pre-operative findings

The mean age of the 18 patients was 50 years (range 19–73 years). They comprised 11 women and seven men. Main presenting complaints were shortness of breath (seven patients), chest pain (six patients) cough (four patients), haemoptysis (one patient), fatigue and weight loss (three patients). Eight patients (44%) were heavy smokers or had a history of heavy smoking. Nine patients (50%) were asymptomatic and their tumour was discovered on a routine chest X-ray.

3.2. Radiological findings and tumour location

Pre-operative chest roentgenograms and computed tomograms (CT) were reviewed for all patients. All tumours were solitary masses. The tumour was located in the right lung in 12 patients, and in the left lung in six. In 15 patients, the tumour presented as a sharply defined density. There was a post-obstruction infiltrate in three patients. The CT showed calcification in one case of malignant histocytosarcoma, and cavitation in a leiomyosarcoma (diameter 12 cm) and a rhabdomyosarcoma (diameter 15 cm). A moderate unilateral chest effusion was discovered in four patients.

3.3. Bronchoscopy findings and pre-operative pathological diagnosis

All patients underwent sputum cytology and fiber-optic bronchoscopy. The latter showed a tumour growing in the bronchial lumen in seven cases (39%), a bronchial compression in three (16%) and a normal picture in the remaining eight (44%). Sputum cytology never helped to reach a diagnosis. A correct pre-operative pathological diagnosis was obtained in eight cases (44%): from bronchoscopic biopsy specimens in four, CT-guided percutaneous needle aspiration in two, anterior mediastinotomy in one and thorascopy in one. Mediastinoscopy was never performed. The pre-operative pathological diagnosis was false for five patients (28%). No further attempt was made to obtain a pre-operative histological diagnosis for five patients, because they were heavy smokers with peripheral nodules strongly suspected to be lung carcinoma.

3.4. Pre-operative treatments

Fifteen patients (83%) underwent surgery without any pre-operative treatment, because CT scan data indicated that their lung sarcoma was completely resectable. In two patients with pre-operative diagnoses of undifferentiated sarcoma and rhabdomyosarcoma ascertained by anterior mediastinotomy (patients 1 and 8 in Table 1), CT scan showed signs of unresectability, i.e. stenosis of the right pulmonary artery and invasion of the left auricle in patient 1, and a huge mass invading the whole chest cavity in patient 8 (Figs. 1 and 2). These two patients received six cycles of chemotherapy comprising ifosfamide, doxorubicin, dacarbazine and mesna, which reduced tumour volume by up to 50%. They underwent complete resection of their lung sarcoma 6 weeks after the end of chemotherapy, with disease-free resection margins in patient 8 and only microscopical invasion of the left auricle in patient 1.

In patient 2, complete resectability was doubtful according to CT scan, and therefore he underwent two cycles of the above chemotherapy regimen, without tumour volume reduction. Nevertheless, pneumonectomy could be performed with free resection margins.

3.5. Operative strategy and surgical results

All patients underwent macroscopically complete resection. Lobectomy was performed in 12 patients (66%). It was extended to the chest wall in two of them, and to the diaphragm in two others. Six patients (33%) underwent pneumonectomy which was extended to the chest wall in one and to the superior vena cava and partial left auricle, without cardiopulmonary bypass support, in another (patient 1). Overall, six patients (33%) had extended surgical resection including three chest wall resections (two ribs in two cases and three ribs in one case). Systematic mediastinal lymphadenectomy was done in every case. Operative and 30 days post-operative mortality were nil. Thirty days post-operative morbidity was 33% and included pulmonary infections not requiring assisted ventilation (n = 3), air leaks requiring prolonged chest drainage for more than 6 days (n = 2) and auricular fibrillation (n = 1). The mean hospital stay lasted 11 days (range 7–24 days).

3.6. Pathology results

The mean diameter of the tumours was 8.05 cm (range
2.5–15 cm). Four tumours (22%) had a diameter of less than 5 cm and one of less than 3 cm. In seven cases, tumours only invaded the pulmonary parenchyma, and in seven cases, the parenchyma and at least one large bronchial lumen. None of the tumours was restricted to the bronchial lumen. In patient 8 (rhabdomyosarcoma of 15 cm in diameter), patient 4 (malignant fibrous histiocytoma of 10 cm in diameter) and patient 13 (fibrosarcoma of 7 cm in diameter) whose tumours were invading the chest wall, the tumour was considered as primary sarcoma of the lung because over 95% of the tumoural volume was located in the lung. Two patients (11%) had positive resection margins (patients 1 and 13) and patient 13 had at least one positive hilar lymph node (N1 involvement). No patient had N2 involvement. In patient 1, who received pre-operative chemotherapy for a grade 2 undifferentiated sarcoma of uncertain resectability, the left auricle was infiltrated by some malignant cells. In patient 13, who had chest wall resection for grade 3 fibrosarcoma, parts of the chest wall margins were invaded.

### 3.7. Post-operative treatments

Patients 1 and 13, who had microscopically invaded resection margins, were treated by radiotherapy alone. Four patients had post-operative chemotherapy for presumably poor pathological prognostic factors, i.e. large undifferentiated grade 3 tumours.

### 3.8. Follow-up and recurrence

The follow-up period ranged from 2 to 144 months (mean 46 months). Sarcoma recurred in eight patients (44%) as a local relapse and metastatic spread in three, as a metastatic spread only in three, and as a local relapse only in two patients (see Table 1). Three patients (16.6%) underwent repeat surgical resection of their recurrent sarcomas: in patients 6 and 9, we resected pulmonary metastases, and in patient 15, the previous thoracotomy scar. The two patients who received neoadjuvant chemotherapy for previously unresectable tumours are alive, without recurrent disease, 20 and 58 months after surgery, respectively.

### 3.9. Survival

Five patients (27.7%) died of recurrent sarcoma after a mean period of 17 months (range 3–48 months). Four other patients (22.2%) died of non-tumour-related causes. Nine patients (50%) are still alive, six of them free of recurrent disease, and three with recurrent disease which was completely resected in two cases. The third patient who had completely resected recurrent disease died 144 months after the first intervention of non-tumour-related causes. The overall median survival period was 48 months, and actuarial 5-year survival 43%. There was a significant correlation between stage and survival: patients with stage I sarcoma had a better survival than patients with stage IIb ($P < 0.05$). Tumour grade and diameter were not found to
affect survival. Histological subtype, T factor, lymph node involvement and the presence of microscopical involvement of the resection margins comprised too few subjects to allow the calculation of statistical trends. Pathological findings and outcome are given for the 18 patients in Table 1.

4. Discussion

Primary sarcomas of the lung are rare and almost all of the descriptions of these tumours in the literature are confusing, firstly because the number of resected patients is small, ranging from 17 in the series of Nascimento and co-workers to 29 in that of MacCormack and Martini reported by Burt and Zakowski, and secondly because most series included both resected and non-surgically treated tumours [1–9]. Overall, five recent series published between 1982 and 1999 can be compared with the present study which, as far as we know, is the first report to include only surgically treated patients [3,5,6,8,9] (Table 2). Primary sarcomas of the lung include a wide heterogeneous group of neoplasms with morphological similarities to their soft tissue counterparts. Previous reports suggested that the most common types of primary sarcomas of the lung were malignant fibrous histiocytomas, leiomyosarcomas, fibrosarcomas, haemangiopericytomas and rhabdomyosarcomas. Malignant fibrous histiocytoma (MFH) displays a mixture of fibroblastic and histiocytic differentiation. Leiomyosarcomas originate from smooth muscle in the conducting or transitional airways or from blood vessels. Fibrosarcomas originate from fibroblasts and are composed of spindle cells and collagen. Rhabdomyosarcomas arise from ectopic skeletal muscle cells or result from faulty differentiation of primitive mesenchymal cells [13].

4.1. Clinical presentation and pre-operative diagnosis

Lung sarcomas may be present at all stages of life as a solitary pulmonary nodule or as a huge tumour of the chest cavity. On chest X-ray, they are known to appear as a well-circumscribed mass in the lung which tends to expand locally towards the chest wall or mediastinum. Neverthe-
less, in our series, the radiological findings were non-specific, and could have applied to any type of lung cancer [14]. A tumour growing in the bronchial lumen was found in seven of our 18 patients, compared with 13 out of 24 in the series studied by Regnard and co-workers. We obtained pre-operative tissue samples leading to correct pathological diagnosis in only 39% of the cases.

4.2. Pre-operative chemotherapy and adjuvant treatment

MacCormack and Martini showed that the 29 patients in their series who underwent complete surgical resection survived significantly longer than the eight who received radiotherapy and the five who had no treatment [5]. Regnard and co-workers confirmed that the most important predictor of survival was completeness of resection [9]. In this setting, we first report the cases of two patients with definitely unresectable primary lung sarcomas, for whom pre-operative chemotherapy allowed macroscopically complete resection in both cases, and microscopically complete resection in one case (Figs. 1 and 2). These two patients were alive and free of recurrent disease 20 and 58 months after surgery, respectively. We could not find any other series including patients who had pre-operative chemotherapy before resection of

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study period</th>
<th>Patients</th>
<th>Operated patients (n (%))</th>
<th>Complete resection (n (%))</th>
<th>Prognostic factors</th>
<th>Percentage 5-year survival (operated patients)</th>
</tr>
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<tbody>
<tr>
<td>Nascimento et al. [3]</td>
<td>1950–1978</td>
<td>18</td>
<td>17 (94)</td>
<td>17 (94)</td>
<td>Size &lt; 3 cm</td>
<td>–</td>
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<tr>
<td>Jansen et al. [6]</td>
<td>1959–1991</td>
<td>22</td>
<td>18 (82)</td>
<td>11 (50)</td>
<td>Size &lt; 4 cm; Grade</td>
<td>44</td>
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<tr>
<td>Present study</td>
<td>1982–1998</td>
<td>18</td>
<td>18 (100)</td>
<td>16 (89)(^a)</td>
<td>Stage</td>
<td>43</td>
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\(^a\) Microscopically complete resections.
primary lung sarcoma. Only Wu, in a case report, stated that pre-operative chemotherapy was used for a patient at high surgical risk for resectable haemangiopericytoma [15].

The criteria that justify post-operative radiotherapy or chemotherapy, and their impact on survival, cannot as yet be determined because they were given to different proportions of patients in the series reported in the literature. Generally, as in our series, they were justified by incomplete resection, invaded margins, lymph node involvement, and high-grade or large tumours.

4.3. Surgical management

As radical resection with pathological free margins is, when possible, the best option, segmentectomies or wedge resections when done for small peripheral tumours seem to raise the recurrence rates [6,16]. Consequently, when the tumour is unique, lobectomy or, when necessary, pneumonectomy, remains the gold standard. Due to the high percentage of large tumours in most series, resections extended to the chest wall, diaphragm, superior vena cava or auricle included six out of 18 patients in our series and six out of 19 for Bacha and colleagues [8], who reported the use of cardiopulmonary bypass in three patients with negative resection margins in two of them. Primary lung sarcomas rarely disseminate to lymph nodes, but Regnard and co-workers found N2 involvement in two out of 20 resected patients, and N1 involvement in three [9]. This justifies systematic mediastinal lymph node dissection like that performed for any lung cancer, mainly for staging purposes but also with a curative intent [9].

4.4. Pathological results

In our study, MFH was the most common histological cell type diagnosed with undifferentiated sarcoma, but in a smaller proportion of patients than in the series reported by Bacha and co-workers [8]. However, in all the other series for which pathological results were given, leiomyosarcoma was the most commonly reported form of primary pulmonary sarcoma [3,5,6]. After complete surgical resection for MFH, Lee et al. [17] reported better survival than after resection for other sarcomas, but no other data seem to support this report. It is questionable to state whether the three sarcomas which were both in the chest wall and the lung should be considered as primary sarcomas of the lung or as chest wall sarcomas. As a matter of fact, no pathological studies can rule out the precise origin of such sarcomas (malignant fibrous histiocytoma, fibrosarcoma and rhabdomyosarcoma). In accord with Regnard and associates, we considered these lesions, in whom the chest wall invasion was minimal as compared with the lung involvement, as primary sarcomas of the lung [9,18].

4.5. Prognostic factors

As already stated, complete macroscopical resection is the basis of any treatment with a curative aim in the field of primary lung sarcomas, but the impact on survival of microscopically invaded margins remains unclear, chiefly because it is rarely mentioned in the different studies. Accordingly, only Bacha and co-workers reported that six patients out of 20 had positive resection margins [8]. Tumour size was the most commonly individualized prognostic factor. A size larger than 5 cm, according to Nascimento et al. [3], and larger than 4 cm according to Jansen and co-workers [6], indicated a poor prognosis. In the series treated by MacCormack and Martini and reported by Burt and Zakowski [5], there was also a trend towards better survival for patients with tumours with a diameter of 5 cm or less. Like Regnard and Bacha [8,9], we did not find that tumour size was of prognostic significance, probably because of the few small tumours in these three series. Only Jansen and co-workers demonstrated that grade 3 sarcomas had a worse prognosis than grade 1 sarcomas [6]. The present study confirms the prognostic significance of the revised TNM international lung cancer staging system [11] when applied to primary pulmonary sarcomas, as shown by Regnard and co-workers [9]. Nevertheless, this factor was not studied in any other series.

References


