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Tumor perimeter and lobulation as predictors of pleural recurrence in patients with resected thymoma

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ABSTRACT

Objectives: Recurrence of resected thymoma frequently occurs during follow-up, with pleural recurrence as the most common type. The aim of our study was to identify risk factors for pleural recurrence after complete resection of thymoma by investigating clinical, radiological, surgical, and pathological findings.
Materials and methods: Retrospective study was performed with 309 patients who had undergone complete resection of thymoma between January 2000 and December 2013. Among these cases, the patients were divided into the no pleural recurrence group (n = 285) and the pleural recurrence group (n = 24). Radiologic parameters such as maximum tumor diameter, tumor perimeter that contacted the lung (TPCL) and lobulated tumor contour were measured based on computed tomography. A multivariate analysis was performed to estimate risk factors for pleural recurrence including maximum tumor diameter, TPCL, lobulated tumor contour, World Health Organization (WHO) histologic classification, and Masaoka-Koga (M-K) stage.
Results: The median follow-up period was 62 months. The pleural recurrence rate was 7.8% (24/309). After univariate analysis, longer maximum tumor diameter ($p < 0.001$), longer TPCL ($p < 0.001$), lobulated tumor contour ($p = 0.001$), WHO histologic type B2, B3 ($p = 0.002$), and M-K stage III/IV ($p < 0.001$) demonstrated significant differences with risk factors of pleural recurrence. Multivariate analysis revealed that TPCL (per 1 cm increase: hazard ratio [HR]: 1.040, 95% confidence interval [CI]: 1.019–1.061, p < 0.001), lobulated tumor contour (HR: 5.883, CI: 1.201–28.824, p = 0.029), WHO histologic classification B2/B3 (HR: 5.331, CI: 1.453–19.558, p = 0.012) and advanced M-K stage (HR: 3.900, CI: 1.579–9.632, p = 0.003) were significantly associated with pleural recurrence.
Conclusion: TPCL and lobulated tumor contour as well as WHO histologic classification and M-K stage were independent predictors of pleural recurrence after thymoma resection. Our study demonstrated that radiologic parameters could be useful predictor of pleural recurrence in patients with resected thymoma.

1. Introduction

Thymomas are tumors of the thymus gland at the anterior mediastinum. These tumors are the most common tumors of the anterior mediastinum, but account for less than 1% of all human neoplasms. Nevertheless, recurrence of resected thymoma frequently occurs during follow-up, with pleural recurrence as the most common type [1,2]. Occasionally, pleural recurrence has been even found in the patient with complete resection of early stage thymoma.

Several studies showed that surgical resection in pleural dissemination may improve outcome [3–7]. Early detection of pleural recurrence might have influence on whether it is possible to complete resection. So that reason, prognostic indicator should be necessary for early detection of pleural recurrence.

World Health Organization (WHO) histologic classification, Masaoka-Koga (M-K) stage, tumor size, and performance of complete resection are prognostic indicators and risk factors for recurrence after surgery for thymoma [8–11]. However, these factors are not focused on pleural recurrence so that insufficient predictors of pleural recurrence.

The aim of our study was to identify risk factors for pleural recurrence after complete resection of thymoma by investigating clinical, radiological, surgical, and pathological findings.

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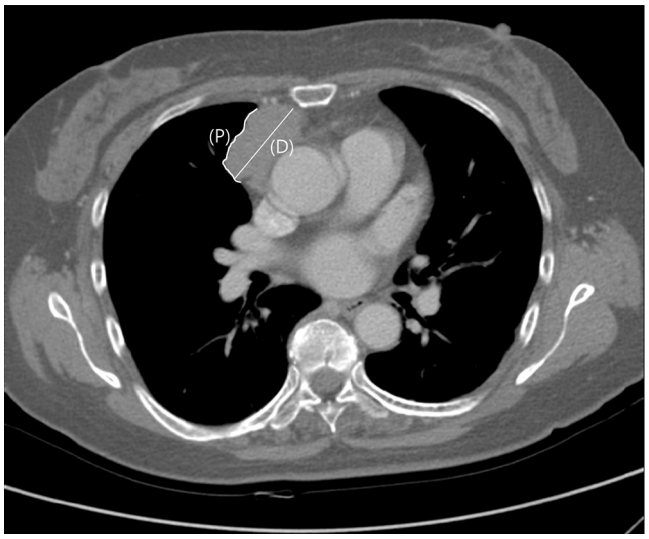

Fig. 1. Preoperative chest computed tomography showed an anterior mediastinal mass with a lobulated tumor contour. D, maximum tumor diameter (47.12 mm). P, tumor perimeter that contacted the lung (57.24 mm).

2. Materials and methods

This retrospective study was approved by our institutional review board and written informed consent was waived.

2.1. Patients

Four hundred and twenty-one consecutive patients underwent surgery for thymoma at our institute between January 2000 and December 2013. Of those, we excluded patients with WHO histologic type C or undetermined WHO histologic type (n = 61), patients with unavailable imaging data or incomplete pathology due to partial/fragmented specimens (n = 32), and patients who underwent R1 and R2 resection (n = 19). The medical records of the remaining 309 patients were reviewed retrospectively.

2.2. Radiologic parameters

Computed tomography (CT) was performed for all patients. The employed slice thicknesses for CT were 1 mm (n = 112), 3 mm (n = 45), 5 mm (n = 123), and 10 mm (n = 29). Radiologic parameters were measured by an independent single radiologist, who was blinded to the clinical details and surgical outcome. The maximum tumor diameter was measured at the largest section of the tumor on axial images. The tumor perimeter that contacted the lung (TPCL) was measured by drawing the contact surface between the tumor and the lung at the largest section of the tumor on axial images. When the tumor contacted the bilateral mediastinal pleura, only the side overhanging the pleural cavity was measured for TPCL. Tumors were classified with lobulated tumor contours when there were undulating contours where the tumor contacted the lung at the largest section of the tumor on axial images (Fig. 1).

2.3. Histology and staging

Thymomas were classified into histological types A, AB, B1, B2, and B3, according to the WHO classification system. When a tumor exhibited combined histologic type, the tumor was classified as the predominant component [12]. Based on histologic aggressiveness, patients were divided into low-risk (type A, AB, or B1) and high-risk (type B2 or B3) groups. According to the M-K system, stage was determined by review of surgical records and pathological reports. Patients were divided into an early-stage group (stages I and II) and an advanced-stage group (stages III and IV).

2.4. Surgery

The transpleural approach was defined as thymectomy through pleural incision (i.e., clamshell incision, thoracotomy, video-assisted thoracic surgery). The non-transpleural approach included a median sternotomy and transcervical incision.

Complete thymectomy was defined as resection of the entire thymus. Limited thymectomy was defined as the resection of the thymoma along with the surrounding fatty tissue, leaving residual thymic tissue.

Patients with stage IVa tumors that were completely removed macroscopically, including all of the involved pleural and pericardial lesions, were classified as R0 resections.

2.5. Definition of recurrence

According to definitions from the International Thymic Malignancy Interest Group, the time of recurrence is defined as when clinical suspicion of recurrence first occurs, regardless of whether a biopsy was done (unless the finding is subsequently demonstrated not to be a recurrence). Recurrence was divided into three categories. Local recurrence was defined as disease appearing at the site of the original tumor, or in the thymic bed including adjacent nodes. Regional recurrence was defined as intrathoracic recurrence, but not contiguous with original tumor or thymus (i.e., pleural or pericardial nodules). Distant recurrence was defined as recurrence outside the thorax, or intraparenchymal pulmonary nodules.

2.6. Follow-up

All patients were followed up at the outpatient clinic at 3-month intervals for the first year, at 6-month intervals for the subsequent year, and annually for the next 3 years. A physical examination and chest radiography were performed upon each visit to the outpatient clinic. Chest CT was performed at 6-month intervals for the first 2 years and at 1-year intervals for the subsequent 3 years. However, there was some variation in the follow-up procedure depending on the stage and histology of each tumor, as well as the surgeon's preference. After 5 years, patients were followed at our neurology or oncology department for any prevailing medical problems. Follow-up for this study was complete up to September 2015.

2.7. Statistical analysis

Patient' characteristics in no pleural recurrence group and pleural recurrence group were analyzed using Student's *t*-tests for continuous variables and chi-square tests or Fisher's exact tests for categorical variables. Continuous data are expressed as mean and standard deviation, whereas categorical variables are expressed as counts and percentages. For univariate analysis and multivariate analysis, a Cox proportional hazards regression model was used. A *p*-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 20 statistical software (SPSS Inc. Chicago, Illinois, USA).

3. Results

3.1. Pattern of recurrence

The median follow-up after the initial thymectomy was 62 months (range, 3–187 months). The recurrence rate was 8.7% (27/309). The median recurrence-free time was 59 months (range,