Solitary Fibrous Tumor with Rapid Progression after 16 Years’ Follow Up

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Abstract

A 79-year-old woman was admitted to our hospital for an investigation of a large 13-cm tumor in the chest and treatment for dyspnea in January 2010. The tumor had been observed on chest X-rays since 1992. It had measured 7 cm in 2008, then started to grow rapidly. Further investigations revealed that it was a malignant solitary fibrous tumor that was strongly suspected to have transformed from a benign to malignant state. Resection was not possible, and the patient died one month later. Benign solitary fibrous tumors of the pleura may become malignant during long-term follow-up. All suspected or proven solitary fibrous tumors of the pleura should be resected.

Key words: malignant solitary fibrous tumor, transformation

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Introduction

Solitary fibrous tumor of the pleura (SFTP) is a rare primary tumor arising from submesothelial mesenchymal cells. Only approximately 800 cases have been reported to date (1). These tumors are benign and present as asymptomatic masses in over 80% of patients (2). Although surgical resection is the first selective treatment, we experienced a case of an SFTP that became malignant and inoperable after 16 years of follow-up.

Case Report

A 79-year-old woman was referred to our hospital for a further investigation and treatment of dyspnea in January, 2010. In 1992, a chest X-ray obtained at a local hospital had shown a tumor in the left lower lung field measuring 7 cm (Fig. 1A). The patient declined further examinations, including computed tomography (CT), a biopsy and resection and was accordingly followed with annual X-rays without further investigations for 16 years, during which time, the size of the tumor did not change (Fig. 1B). On an examination performed in December, 2008, however, the tumor was shown to have grown to approximately 9 cm (Fig. 1C). Nevertheless, the patient again declined further investigations. However, she became aware of general fatigue in August, 2009 and dyspnea in December, 2009, with both symptoms being progressive, and was admitted to her local hospital for dyspnea associated with massive pleural effusion. The dyspnea worsened despite treatment, and she was transferred to our hospital for further investigations and treatment for suspected malignant disease.

A physical examination performed on admission revealed inaudible left breath sounds and digital clubbing. The patient’s vital signs indicated hypoxemia (SpO2: 92% O2 1 L/
dom arrays. The mitotic activity was not aggressive, with solid spindle cell growth and fusiform cells arranged in random arrays. The mitotic activity was not aggressive, with 1.4 mitoses in 10 high-power fields (HPF). However, the proliferative index (positivity for Ki67) was high, with 50% of the nuclei being labeled positively. In addition to the preoperative biopsy findings, tumor necrosis was also observed. The final diagnosis was a malignant solitary fibrous tumor.

**Discussion**

We herein described the case of a 79-year-old woman admitted to our hospital with a large 13-cm tumor in the chest that had been first observed 18 years previously. The tumor had remained quiescent for 16 years, then began to grow rapidly. Our investigation conducted at 18 years revealed the mass to be a malignant solitary fibrous tumor that was strongly suspected to have transformed from a benign to malignant state. Resection was not possible, and the patient died one month later. This case emphasizes the need to resect all suspected or proven SFTP lesions.

SFTP is a rare primary tumor arising from submesothelial mesenchymal cells, with only approximately 800 cases having been reported to date (1). It occurs in a wide age range, predominantly in the sixth and seventh decades of life, and with a fairly equal sex distribution (2). Patients commonly exhibit few physical signs, of which clubbing is the most frequent (2). Large tumors may cause sufficient lung compression to result in wheezing, dullness to percussion and/or decreased breath sounds in the affected hemithorax.

Microscopically, SFTPs typically display zones of both hypercellular and hypocellular collagenized stroma in a so-called patternless architecture. Malignant SFTPs are characterized by greater cellularity with an infiltrative growth pattern, moderate to marked cellular atypia and a high mitotic activity (>4 mitoses per 10 HPF) (3). Both benign and most malignant SFTPs are positive for CD34, CD99 and bcl-2 (1).

With respect to the diagnosis of SFTP, the diagnostic accuracy of preoperative fine-needle aspiration biopsies is not satisfactory (4-7). In the present case, we performed a core needle biopsy of the tumor. The mass displayed greater cellularity with an infiltrative growth pattern and cellular

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**Figure 1.** Previous chest X-ray films obtained before admission to our hospital. The oldest available X-ray (October, 2001) showed a tumor in the left lower lung field (A). No growth was observed until February, 2007 (B). The tumor was subsequently found to have grown on an investigation conducted in December, 2008 (C).
Figure 2. Chest X-ray film, contrast CT and bone scintigraphy performed on admission. The chest X-ray film showed a large tumor and pleural effusion (A). Contrast CT revealed an approximately 15-cm tumor with necrosis and a mediastinal shift (B). Bone scintigraphy demonstrated no evidence of bone metastasis or findings suggestive of hypertrophic pulmonary osteoarthropathy (C).

Figure 3. Staining of the tumor with Hematoxylin and Eosin staining reagent (A), CD99 (B), CD34 (C) and bcl-2 (D). CD99, CD34 and bcl-2 were positive. The histopathological findings were consistent with those of a solitary fibrous tumor (original magnification x100).

atypia, although the mitotic activity was not aggressive. However, the proliferative labeling index was 50%, which is in contrast with the less than 2% reported by Yokoi et al. in benign cases, indicating that the tumor was a malignant solitary fibrous tumor. Yokoi et al. also proposed that malignant SFT lesions may arise de novo or by transformation within benign or low-grade tumors (8). In the present case, the tumor was quiescent for the first 16 years following detection,
but then proceeded to grow rapidly over the next year. The microscopic and macroscopic findings described above suggest that the tumor was malignant. Based on a comprehensive consideration of the patient’s clinical course and pathological findings, we consider that the tumor underwent malignant transformation after having been benign for 16 years.

Several previous studies suggesting malignant transformation of SFT are summarized in Table. In cases 2 and 3, although most regions of the primary tumors were benign, each contained a malignant portion, suggesting malignant transformation within a benign tumor (8). Cases 6, 7 and 9 involved the recurrence of a benign tumor following curative resection of the primary tumor before subsequent malignant transformation (9-11), cases 1, 4, 5, 8 and 10 involved malignant recurrence without a preceding benign tumor (8, 10, 12-14) and cases 4, 7 and 9 involved malignant transformation more than 10 years after initial surgery to treat the primary benign tumor (8, 10, 11). Therefore, although the malignant transformation of SFTP has been reported, transformation occurring after more than 10 years of follow-up without curative surgery is very rare. In cases of recurrence after curative surgery, it is very difficult to distinguish de novo carcinogenesis from the transformation of a residual tumor. The present case followed the natural course of an SFTP that was thought to have transformed from a benign to malignant state. The data in Table suggest that there are many different types of recurrence, with some cases occurring within several months of curative resection and others developing more than 10 years after resection. Yokoi et al. reported an association between the p53 level and malignant transformation (8), while Walters et al. found that BCL-6 contributes to such transformation (15). In the present case, although we did not examine the influence of these molecules on the observed transformation, we speculate that the involvement of several key mutations due to hypoxia or inflammation induced the lesion to become malignant. SFTP is considered to be an unstable premalignant tumor, and a degree of genetic change over the 16 years of quiescence may have occurred.

Resection of benign SFTPs carries an excellent prognosis. Malignant SFTP is more rare than its benign counterpart, accounting for 13% to 37% of cases (5, 6, 16-18). England et al. reported that 55% of 82 patients with malignant tumors died of their disease secondary to invasion, recurrence or metastasis (18). Resectability is the most important indicator of the clinical outcome (19). For example, Lococo et al. reported that the 5-year survival rate was 87.1% in 46 patients whose tumors were completely resected versus 0% in four patients treated with incomplete resection. In that study, the presence of malignant pleural effusion had a substantial negative impact on survival, with an estimated hazard ratio of 3.44 (19). The present patient’s tumor must have been benign at the time of detection and could have been curatively resected. We therefore recommend performing curative resection as soon as possible after the detection of a suspected SFTP.

Several limitations of the present study warrant mention. First, this is a case report of one patient. Second, no pathological examinations were conducted prior to the enlargement of the tumor. Nevertheless, the patient’s clinical course clearly indicates the transformation of the tumor from a benign to malignant state.

The diagnostic accuracy of preoperative fine-needle aspiration biopsies for detecting SFTP is not satisfactory, and tumors may transform from a benign to malignant state during follow-up. All cases of SFTP should be resected, even if the diagnosis is not confirmed and the tumor is only suspected of being an SFTP.

The authors state that they have no Conflict of Interest (COI).

References