Secondary spontaneous pneumothorax (SSP) caused by malignant tumors is rare, which often makes the choice of treatment difficult. In our hospital, we performed radical surgery for all pulmonary metastases arising from osteosarcoma (OS) in seven patients with SSP from February 1988 to February 2008 and retrospectively examined the clinicopathological features and postoperative outcomes. The common SSP etiology was tumor tissue rupture at the lung periphery. All patients died of OS recurrence within 18 months. A short disease-free interval (DFI) and a short interval to the second recurrence were the common clinical risk factors of poor prognosis. Curative surgery for pulmonary metastases in OS with SSP is unlikely, but in OS patients with peripheral metastatic lesions that are not accompanied by SSP and have a satisfactory DFI and few lesions, surgical resection should be strongly considered.

Keywords: lung metastases, osteosarcoma, secondary spontaneous pneumothorax

Introduction

Secondary spontaneous pneumothorax (SSP) due to metastatic sarcoma is often associated with advanced disease or systemic chemotherapy, and these patients have poor prognoses unless treated effectively. To repair SSP and prevent recurrence, we performed radical resections in seven patients with SSP caused by metastatic osteosarcoma (OS). In this case series, we retrospectively examined the characteristics, postoperative prognosis, intrathoracic recurrence and pathological findings.

Case Series

Patients and Methods

We retrospectively examined the clinicopathological features and postoperative outcomes of seven patients treated in our hospital from February 1988 to February 2008 (five males, two females; mean age, 18 years; range, 14–26 years) with OS and SSP who were without local recurrence or other distant metastasis. The SSP was right-sided in six patients and left-sided in one. Adjuvant chemotherapy for the primary osteosarcoma lesion was administered to all patients. The median duration from chemotherapy initiation to SSP development was 23 days (range, 7–95 days). In patients 1 and 2, the therapy only with drainage tube was insufficient; therefore, pulmonary resection was performed. In case 3, temporary improvement in SSP was achieved by pleurodesis with OK-432, but recurrence occurred after 11 days. The other patients had mild SSP without air drainage (Table 1). The median number of metastases
shown by preoperative computed tomography was five nodules (range, 1–32). Unilateral solitary, unilateral multiple and bilateral multiple metastases were identified in one, one and five patients, respectively. In addition to repairing SSP, our surgical indication included the possibility of complete metastasectomy by the preoperative CT image. Posterolateral thoracotomy and median sternotomy were performed in three and four patients, respectively. Partial pulmonary resection (PR) and PR plus bilobectomy were performed in six and one patients, respectively (Table 2). We could detect air leakage points in patients 1–3, who had continuous air leakage needed chest drain, by intraoperative air leakage test. However, the other patients, who had slight SSP without chest drain, did not show intraoperative air leakage by air leakage test. We completely resected all metastatic lesions found on intraoperative inspection and manipulation in all patients. We diagnosed air leaked lesions by pathological findings in cases without intraoperative air leakage. Air leakage points are shown in Table 2. Intraoperative chemical pleurodesis by dispersing talc was performed in two patients who were pleural lavage cytology (PLC)-positive and underwent wedge resection. According to the WHO classification, pleomorphic, telangiectatic and osteoblastic subtypes were identified in four, two and one patients, respectively.1) Chemotherapy following metastasectomy was performed in all patients except for case 1. The endpoint of this retrospective study was survival after metastasectomy. The disease-free interval (DFI) was defined as the period between primary therapy completion and pulmonary metastases and/or SSP diagnosis.

Results

The median DFI was 118 days (range, 90–422 days). Metastatic lesions (median maximum diameter, 12 mm; range, 6–95 mm) in all cases were identified in the lung periphery. There was no case with multiple air leaked lesions by intraoperative and pathological findings. The median number of resected tumors was five (range, 1–32). While gross pleural disseminations were not clearly identifiable, pleural effusion ipsilateral to SSP was identified. Intraoperative PLC was positive in three
patients whose histological subtype was pleomorphic (Table 3). The four PLC-negative patients were judged as requiring complete surgical and pathological resection.

The overall 1-year survival after metastasectomy was 14.3%, and all patients died within 18 months. In all patients, lung metastases recurred from 40 to 245 days (median, 129 postoperative days). Six patients also developed pleural recurrence from 116 to 258 days (median, 201 postoperative days). Postoperative events included recurrent SSP (n = 3) (Table 3). Pathologically, all patients exhibited self-disruption of the visceral pleura.

Discussion

SSP caused by metastasis represents less than 2% of all spontaneous pneumothorax cases. Approximately 80% of SSP cases are associated with metastatic sarcoma, and OS was most commonly encountered (31.4%). Moreover, 15.7% of patients had SSP as an initial finding that led to a diagnosis of pulmonary tumor.23 SSP was detected by periodic chest examinations at the same time in five of our patients who had shown no symptom.

If patients with a past history of sarcoma develop spontaneous pneumothorax, it is important to determine if the SSP is due to lung metastasis.

There are several mechanisms underlying SSP, including tumor tissue rupture at the lung periphery, a check valve mechanism due to intermittent bronchiolar obstruction by tumor tissue, and direct metastasis to a pulmonary cystic lesion.2,3 Our pathological findings indicated that the first of these mechanisms was the most common.

Some reports have suggested that chemotherapy could increase the relative risk, due to necrotic changes, from 7% to 14%, and the period from chemotherapy initiation to SSP onset ranged between 1 and 8 days.4,5 Only one patient exhibited internal necrosis, with SSP occurring 31 days after chemotherapy initiation. We presume that SSP occurred because of internal ischemic changes for the large 95-mm lesion rather than because of chemotherapy.

Three patients were PLC-positive with pleomorphic histology. The four PLC-negative patients required complete surgical and pathological resection. However, pleural recurrences were recognized in six patients except for one who was PLC negative. These recurrences presumably occurred because of dissemination caused by postoperative pulmonary recurrence or intraoperative manipulation or because of false-positive PLC due to insufficient tumor cells or difficulty in distinguishing tumor cells from pleural mesothelial cells. The intraoperative PLC could not predict postoperative pleural recurrence. Care is needed to determine the histological diagnosis except for the pleomorphic subtype.

The 5-year overall survival rate for patients who underwent a first pulmonary metastasectomy for OS was as high as 40% in several reports.6–10 To date, various parameters, including long DFI, completeness of resection, timing of metastases, limited number of pulmonary nodules (<4), tumor size, and laterality of metastases have been reported as prognostic factors in first metastasectomy.10–13 Meanwhile, Jeffrey reported that less than 10% of patients with SSP following sarcoma lived more than 2 years after the initial pneumothorax diagnosis. The poor prognosis had shown clinically progressive activity of malignant tumors with SSP of sarcoma, and SSP may be associated with increased mortality, except for Ewing sarcoma, Wilms’ tumor, and rhabdomyosarcoma.21 All our patients share the common characteristic of short DFI as a risk factor of poor prognosis before metastasectomy. Using multivariate analysis after the second recurrence, Bielack described several parameters, such as shorter interval to recurrence, multiple lesions, failure to achieve macroscopically complete
surgical remission, and no chemotherapy administered for recurrence, as adverse prognostic factors for OS. In the present study, a short interval to the second recurrence was a common characteristic and demonstrated clinically progressive activity. In OS patients with satisfactory DFI and a limited number of subpleural metastatic lesions without SSP, we should consider surgical treatment before the possible occurrence of SSP because of poor prognosis.

Conclusions

All patients died of recurrence of OS within 18 months. The SSP etiology common to all was tumor tissue rupture at the lung periphery. A short DFI and a short interval to the second recurrence were the common clinical risk factors of poor prognosis. Curative surgery for pulmonary metastases in OS with SSP is unlikely, but in OS patients with peripheral metastatic lesions that are not accompanied by SSP and have satisfactory DFI and few lesions, surgical resection should be strongly considered.

Disclosure Statement

The authors declare that they have no conflicts of interest.

References