Case Report

Pleural and pulmonary metastases from nonseminomatous germ cell tumors successfully managed by extrapleural pneumonectomy

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Abbreviations & Acronyms
AFP = alpha-fetoprotein
$DLCO_2$ = diffusing capacity for carbon monoxide
EP = extrapleural pneumonectomy
GTS = growing teratoma syndrome
hCG = human chorionic gonadotropin
NSGCT = nonseminomatous germ cell tumor

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Introduction: Surgery for postchemotherapy residual nonseminomatous germ cell tumors may be difficult due to exceptional lesion size and location.
Case presentation: A 47-year-old man presented with swelling and pain in the left scrotum. Computed tomography revealed a solid occupied lesion in the left scrotum with huge metastases in the left lung and pleura. Results of a left high inguinal orchiectomy indicated a pathological diagnosis of germ cell tumors of several histological types. The patient declined postoperative chemotherapy but returned to our department 10 months later with dyspnea. Serum tumor marker levels were restored to normal range by adjuvant chemotherapy. Thereafter, an extrapleural pneumonectomy was performed for the remaining tumors. He has since been asymptomatic without recurrence or dyspnea for over 5 years.
Conclusion: Extrapleural pneumonectomy is a valid treatment option for the management of huge pleural and pulmonary metastases of nonseminomatous germ cell tumors.

Key words: extrapleural pneumonectomy, growing teratoma syndrome, nonseminomatuous germ cell tumors, pleural metastasis, pulmonary metastasis.

Keynote message

A 47-year-old man was diagnosed as having huge metastases of NSGCTs in the left lung and pleura. Adjuvant chemotherapy was performed after a left high inguinal orchiectomy, and subsequent EP for the remaining tumors was successful. EP is a valid option for large metastatic tumors of NSGCTs.

Introduction

Most NSGCTs are malignancies that affect young males under the age of 40 years.[1] Multimodality treatments have been effective, by which the 5-year survival rate is higher than for other malignancies.[1] Although adjuvant chemotherapy is useful for metastatic NSGCTs, 25–30% of patients harbor residual tumors.[2] Salvage surgery should be considered following decreases in tumor markers, including AFP, hCG, and serum lactate dehydrogenase, to within normal limits. However, salvage surgery is difficult for very large residual tumors and for the combined resection of multiple affected organs. We herein report a case of NSGCTs with huge pleural and pulmonary metastases that was treated successfully by EP.

Case presentation

A 47-year-old man with a history of painful testicular masses visited a local clinic. The serum tumor markers AFP, hCG, and serum lactate dehydrogenase were elevated at 8680 ng/mL, 2.9 mIU/mL, and 338 U/L, respectively. Computed tomography revealed masses in left scrotum and metastatic lesions in the left lung (Fig. 1a). A high inguinal orchiectomy was performed. The histopathological diagnosis was germ cell tumors of several histological types consisting of yolk sac tumor, embryonal carcinoma, and teratoma mixed type. The clinical diagnosis was NSGCTs with lung metastases pT2N0M1aS2 Stage IIIB, and the patient was given an intermediate prognosis according to International Germ

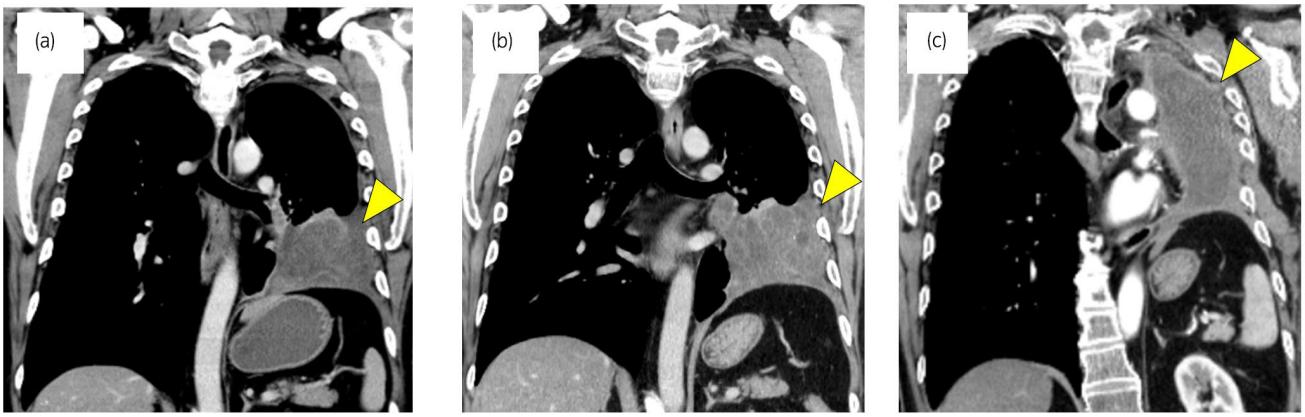

Fig. 1 Computed tomography showing the perioperative left pleura and lung. (a) Initial computed tomography of the huge pleural and pulmonary metastases (yellow arrowhead). (b) The huge metastases remained in the left pleura and lung after chemotherapy (yellow arrowhead). (c) Postoperative image 6 months after surgery showed that the pleural effusion covered the capsule and filled the left thorax (yellow arrowhead).

Cell Consensus Classification.[3] After surgery, the patient declined the adjuvant chemotherapy. Ten months later, he returned with complaints of dyspnea and significant left pleural effusion. His serum AFP level had increased to 52852.6 ng/mL. Four cycles of a bleomycin, etoposide, and cisplatin regimen were completed. After first-line chemotherapy, serum AFP and hCG levels increased again. Therefore, we selected nedaplatin 100 mg/m^2 and irinotecan hydrochloride 200 mg/m^2 regimen as second-line chemotherapy because of his renal dysfunction and anticancer activity.[4] The serum tumor markers returned to normal after second-line chemotherapy. However, the huge pleural and pulmonary tumors remained (Fig. 1b). Preoperative ventilation-perfusion scintigraphy indicated that the pulmonary metastasis of the NSGCTs caused left middle and lower lobe atelectasis. The preoperative magnetic resonance imaging showed the metastatic NSGCTs in fat tissue near the pericardium. To achieve complete removal of the tumor, EP was conducted as a salvage surgery after predicting a postoperative $DLCO_2$ of 42% by the single-breath method. The resected tumor was 23 × 17 × 6 cm in size and 1476 g in weight (Fig. 2a). The pulmonary metastatic tumor had been compressing the normal lung tissue (Fig. 2b). Histopathologically, the resected tissue was immature teratoma (Fig. 3a–c). The resected margin was negative. Postoperative imaging 6 months after surgery showed that the pleural effusion in the left thorax (Fig. 1c). The patient has shown no evidence of recurrence for 5 years since the EP and has led a daily life without the need for an oxygen inhaler.

Discussion

NSGCTs are testicular malignancy and are the most common tumor in young and middle-aged males.[1] Approximately 15% of NSGCTs metastasize to pulmonary tissue, for which 43% of patients undergo resection of remaining tumors after adjuvant chemotherapy.[5] The development of chemotherapy regimens and improvements in perioperative management have greatly extended the survival of patients with pulmonary metastasis of NSGCTs.[6] However, treatment recommendations are uncertain for huge residual pleural and pulmonary tumors requiring combined resection due to their rarity. David *et al.*

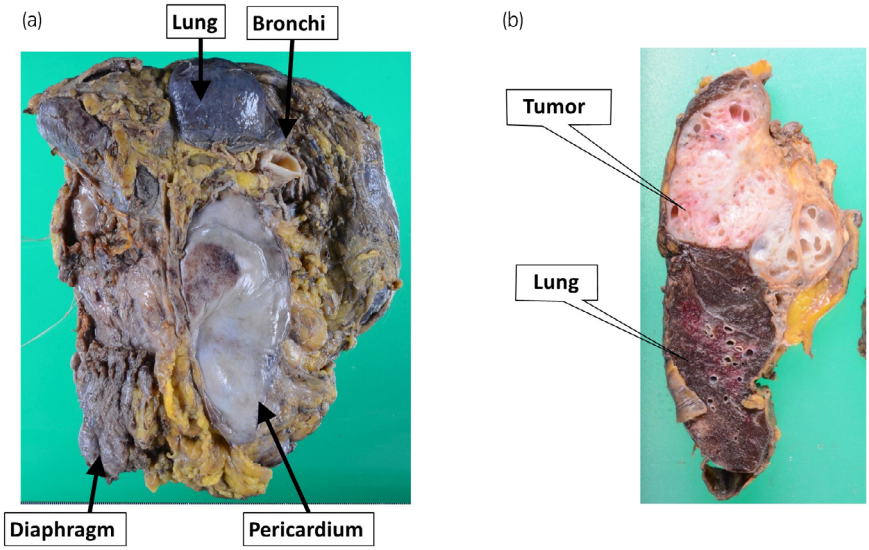

Fig. 2 Macroscopic histopathological findings of the resected left pleural tissue and lung. (a) The specimen was opened sagittally. The residual tumor was 23 × 17 × 6.5 cm in size and weighed 1476 g. Parts of the pericardium and diaphragm were adhered to the pleura. (b) The pulmonary metastasis of the NSGCTs compressed the normal lung. The tumors consisted of white solid masses, cysts, and yellow necrosis.

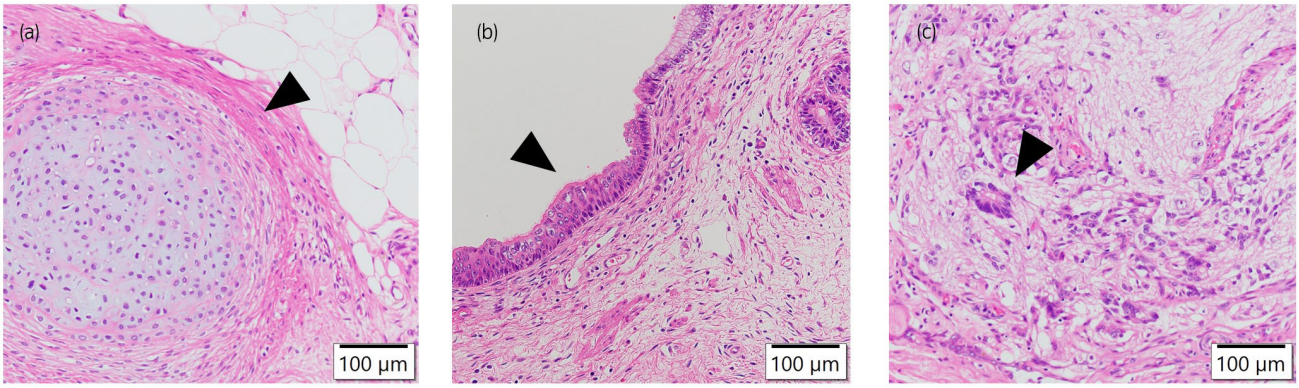

Fig. 3 Microscopic histopathological findings of the resected lung tumor revealed immature teratoma. (a) The specimen was immature cartilage tissue (arrowhead) (hematoxylin and eosin staining, original magnification ×25). (b) Bronchial epithelium with ciliated epithelium was identified (arrowhead) (hematoxylin and eosin staining, original magnification ×25). (c) The tumor had an immature tissue-like neural canal surrounded by similar nerve tissue (arrowhead) (hematoxylin and eosin staining, original magnification ×25).

analyzed 157 cases of testicular germ cell tumors that required pulmonary resections.[7] Seventy-one cases (45%) exhibited primary and metastatic tumors at the first diagnosis and 43 cases (28%) displayed a single metastasis.[7] Regarding the histological type of the pulmonary metastases of the NSGCTs, 68 cases (43%) were viable tumors, 45 cases (29%) were fibrosis/necrosis, and 40 cases (25%) were mature teratoma.[7] Recurrence in patients with differentiated teratoma after the first metastasectomy was 38%, and the survival of those patients was 87% at 5 years, 85% at 10 years, and 67% at 15 years.[7]

Several factors should be considered prior to EP. It is especially critical to estimate the remaining respiratory function and quality of life after surgery. Cagini *et al*. described the long-term survival and prognostic factors of 141 patients with thoracic metastasis for germ cell tumors. However, pneumonectomy was performed for only three cases (2%), and details on the prognosis were absent.[1] Another report indicated that postoperative respiratory function was related to perioperative mortality.[8] Keigo *et al*. recommended that EP should be avoided due to the possibility of perioperative acute myocardial infarction in nonseminomas in the mediastinum.[9] A predicted postoperative $DLCO_2$ of <40% has been associated with a diminished prognosis after lung resection.[10] In the present case, the estimated postoperative $DLCO_2$ was 42%. Accordingly, he could retain sufficient respiratory function for daily life following surgery without the need of an oxygen inhaler. It is important to evaluate perioperative general status including respiratory function, when considering EP. In contrast, observation without salvage surgery also has its pitfalls. First, it is possible that residual masses contain viable tumor cells. Prognosis was significantly worse in case of malignant lung metastasis.[1,7] Second, GTS might occur without salvage surgery. The prevalence of GTS with metastasis of NSGCTs ranges from 1.9% to 7.6%.[11] Insufficient initial surgery and chemotherapy-resistant metastasis may be contributing factors to this complication.[12]

In summary, a patient with NSGCTs underwent chemotherapy after a left high inguinal orchiectomy. Subsequent EP was performed for huge pleural and pulmonary metastases. As a result of the treatment, he could return to daily life, avoid GTS, and has been recurrence free for over 5 years. Although EP is a treatment option carrying considerable risk, it may be a treatment option pending favorable results of careful perioperative examination. Further research is needed to establish safe and valid treatments for huge NSGCT metastases.

Conflict of interest

The authors declare no conflict of interest.

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