

CASE REPORT

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A CASE OF MEDIASTINAL EMBRYONAL CARCINOMA SUCCESSFULLY TREATED BY INTEGRATIVE THERAPY

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ABSTRACT

Mediastinal embryonal carcinoma is rare, and the life prognosis of this disease is assumed to be relatively short. We encountered a case of mediastinal embryonal carcinoma for which we could perform radical surgical resection. The patient was male, aged 16 years, and acutely aware of back pain. Because the pain increased during the same year, he visited a local doctor, and an expanding neoplastic lesion was detected in the right thoracic wall by computed tomography (CT). Then he was referred to our institution. Magnetic resonance imaging (MRI) showed a dumbbell type tumor (Eden type 3) at the Th7/8 level. Malignant disease was suspected, so the authors planned and performed CT-guided biopsy. The result showed that this tumor pathologically corresponded to malignant peripheral nerve sheath tumor (MPNST). Therefore, chemotherapy was considered the main treatment. After 2 courses of chemotherapy, the tumor size decreased dramatically. The authors thought that radical resection is possible if there is no intrathoracic tumor dissemination as a result of a favorable response to chemotherapy. We thus performed surgical resection after we confirmed by a thoracoscopic exploratory thoracotomy that there was no intrathoracic tumor dissemination. Pathological findings were consistent with an embryonal carcinoma. Both the cutting ends of the thoracic wall and the epidural lateral sides of the excised lesion were negative for tumor cells. There is no image finding from the MRI and PET-CT suggesting metastasis or recurrence in the MRI and PET-CT 18 months after surgical resection. Therefore, the long-term vital prognosis can be expected in this patient.

Key Words: Mediastinal embryonal carcinoma, Integrative therapy, Radical resection, Surgical treatment, Life prognosis

INTRODUCTION

Germ cell tumors are classified as seminoma or non-seminoma. Non-seminoma is histologically classified as embryonal carcinoma, choriocarcinoma, yolk sac tumor, teratoma, or combined germ cell tumors. The original sites of germ cell tumors after puberty (except for gonads) include those close to the retroperitoneum and pineal body. The tumors originate most frequently in the mediastinum, and in most cases are male patients. In particular, non-seminomatous germ cell

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tumors, for which the primary lesions are in the mediastinum, are known to result in extremely poor vital prognoses⁸).

In the case described here, we encountered a case of mediastinal embryonal carcinoma for which we could perform radical surgical resection. We describe an integrative therapy including the surgical resection of a mediastinal embryonal carcinoma.

CASE REPORT

Patient: Male, 16 years aged

Chief complaint: Back pain

Disease history: No special history observed

History and presentation

The patient was a 16-year-old male who was acutely aware of back pain. Because the pain increased during the same year, he visited a local doctor, and an expanding neoplastic lesion was detected in the right thoracic wall by CT. Then he was referred to our institution.

Present medical condition

Although the patient complained of tenderness on the right side of his back, there were no skin findings such as swelling or burning sensations.

Blood examination

The alkaline phosphatase (ALP) level was mildly elevated to 389 U/L, but no other abnormal findings were observed.

Image findings

MRI revealed a great expansion of tumor inside and outside the right intervertebral foramen at the Th7/8 level. The longitudinal size was about 33mm. The lesion was isointense to slightly hyperintense on a T1-weighted image, isointense to hyperintense on a T2-weighted image, and heterogeneously enhanced by contrasting on both T1 and T2 images.

Thoracic invasion was suspected because of a partially unclear border between the tumor and parietal pleura. There was no clear intensity change that appeared suspicious of an invasion to the vertebral body and arch laminae (Fig. 1). Positron emission tomography (PET)-CT showed a high standardized uptake value (SUVmax 10.73) in the tumor area (Fig. 2a), as well as in the left clavicular lymph node (SUVmax 4.14) (Fig. 2b). Then, CT-guided needle biopsy was performed on the tumor suspected to be malignant.

Pathological findings (CT-guided needle biopsy)

Highly malignant tumor was suspected, because nucleic size and shape showed pleomorphic and part of specimen was composed of higher nuclear/cytoplasmic (N/C) ratio cells. Immunohistochemically, tumor cells were positive for CD99, INI-1, vimentin, and epithelial membrane antigen (+), and negative for B-cell lymphoma 2 (BCL-2), α -smooth muscle actin, desmin, actin, CD34, CD56, S-100, glial fibrillary acidic protein (GFAP), and leukocyte common antigen (LCA) staining. Ki-67 staining showed an MIB-1 index of 80–90%. Although tumor cells were negative for S-100 and GFAP, MPNST was suspected.

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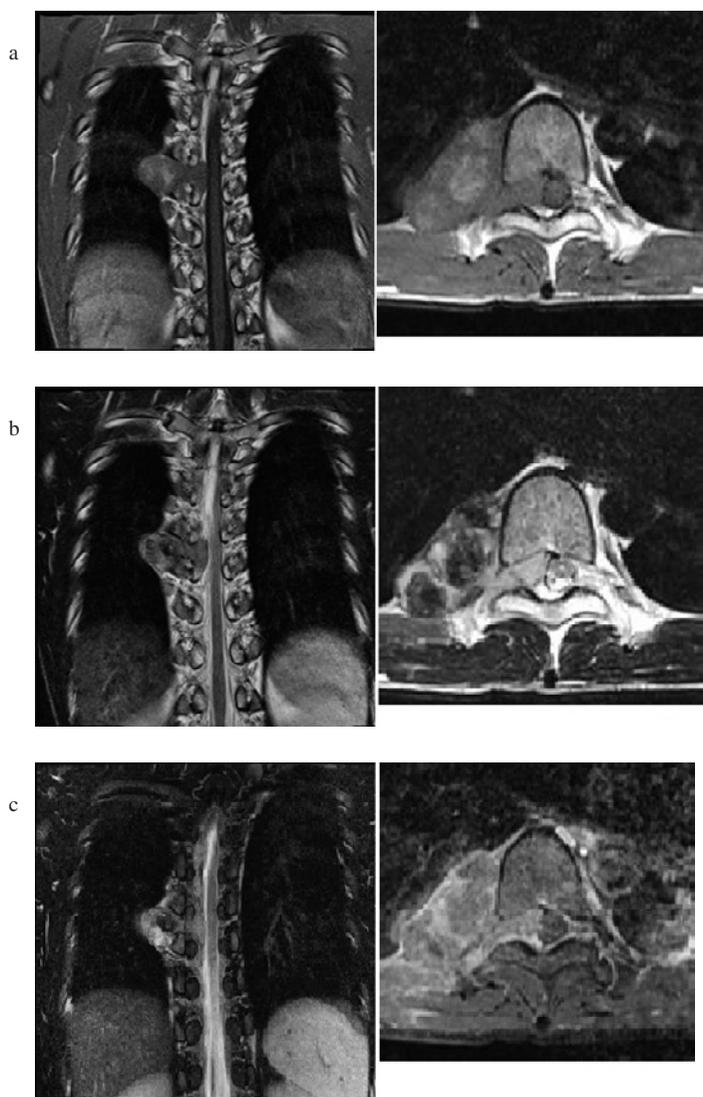


Fig. 1 MRIs revealing a lesion at the Th7/8 level.

Fig. 1a T1-weighted image revealed a great expansion of tumor inside and outside the right intervertebral foramen, isointense to slightly hyperintense.

Fig. 1b T2-weighted image revealed isointense to hyperintense.

Fig. 1c Heterogeneously enhanced by contrasting.

Clinical course

Based on the results of a CT-guided needle biopsy, we adopted the standard chemotherapy regimen for malignant tumors of soft tissues that had been used in our institution. We performed the following treatment: 1 course of 35 mg/m² doxorubicin (DOX) on days 1–2 and 100 mg/m² cisplatin (CDDP) on day 1. After drug withdrawal, 1 course of 3 g/m² ifosfamide (IFM) and 50 mg/m² etoposide (VP-16) were administered from days 1 to 4. Since MRI images after the 2 above courses showed tumor size reduction, 2 additional courses were performed. While

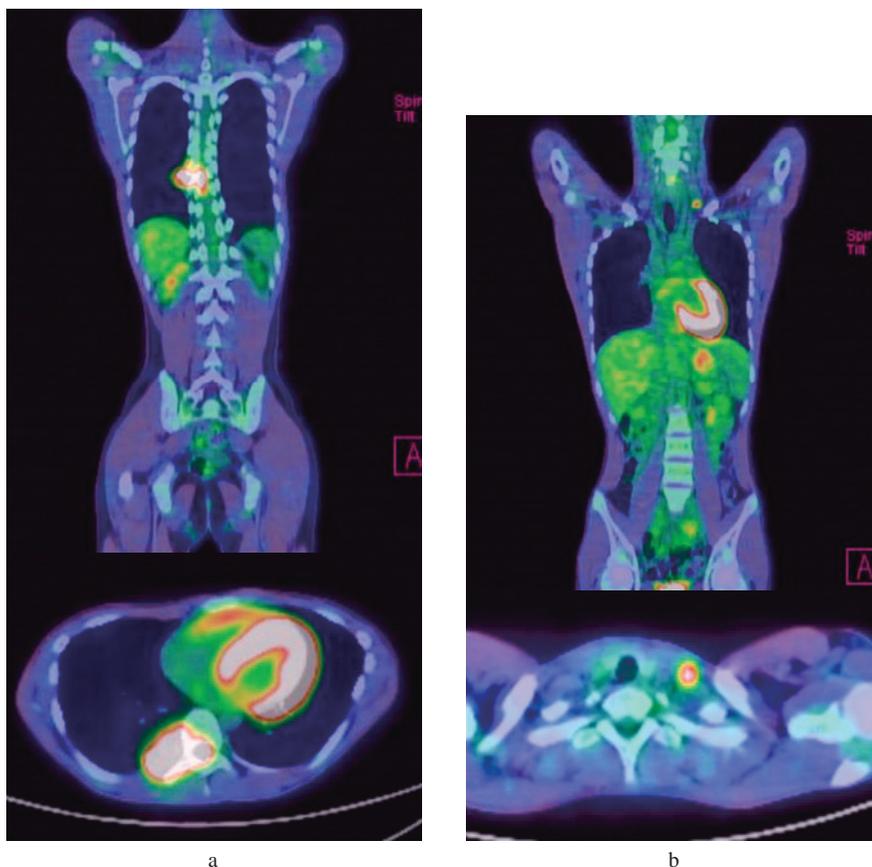


Fig. 2 PET-CT images.

Fig. 2a PET-CT showed high SUV in the tumor area.

Fig. 2b PET-CT showed high SUV in the left clavicular lymph node.

the size of the tumor before chemotherapy was 48×25 mm, it shrank to 40×14 mm after the completion of the 4 courses. Both the lesions inside and outside the intervertebral foramen were observed to have shrunk (Fig. 3). In addition, PET-CT imaging showed the shrunken tumor and reduced SUV (Fig. 4a). The area under the left clavicle that had showed a high SUV was absent after chemotherapy (Fig. 4b).

In order to confirm the tumor's intrathoracic dissemination, a thoracoscopic evaluation (Fig. 5) was performed under general anesthesia between the third and fourth courses of chemotherapy, followed by cytodiagnostic examination of the lavage fluid. From the result, we judged that there was no intrathoracic dissemination because tumor cells were not observed clearly. Tumor progression to the epidural space was difficult to judge from the image.

Surgical treatment

The surgery was designed to achieve total extirpation with a greater than 1-cm peripheral margin, including the biopsy scar. First, the rib was resected at a position 7-cm away from the median in the lateral direction, centering on the biopsy scar. The Th6/7 and Th9/10 facet joints were resected in the craniocaudal direction until the intervertebral disk could be seen. The parietal

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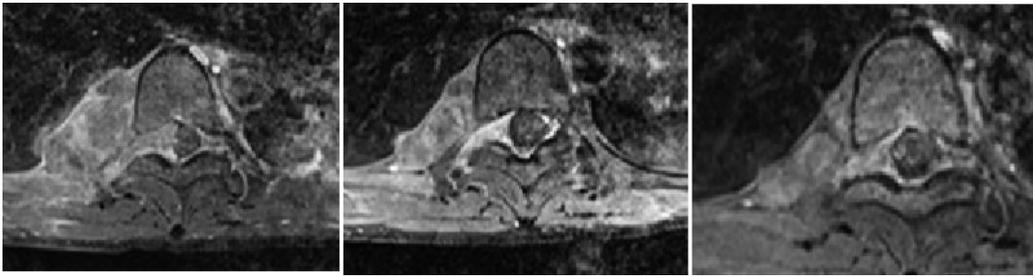


Fig. 3 Change of tumor size by chemotherapy. MRIs demonstrated the lesion at the moment before chemotherapy, and after 2 weeks and 4 weeks of chemotherapy from the left side. The size of the tumor before chemotherapy was 48×25 mm, but it shrank to 40×14 mm after completion of the 4 courses.

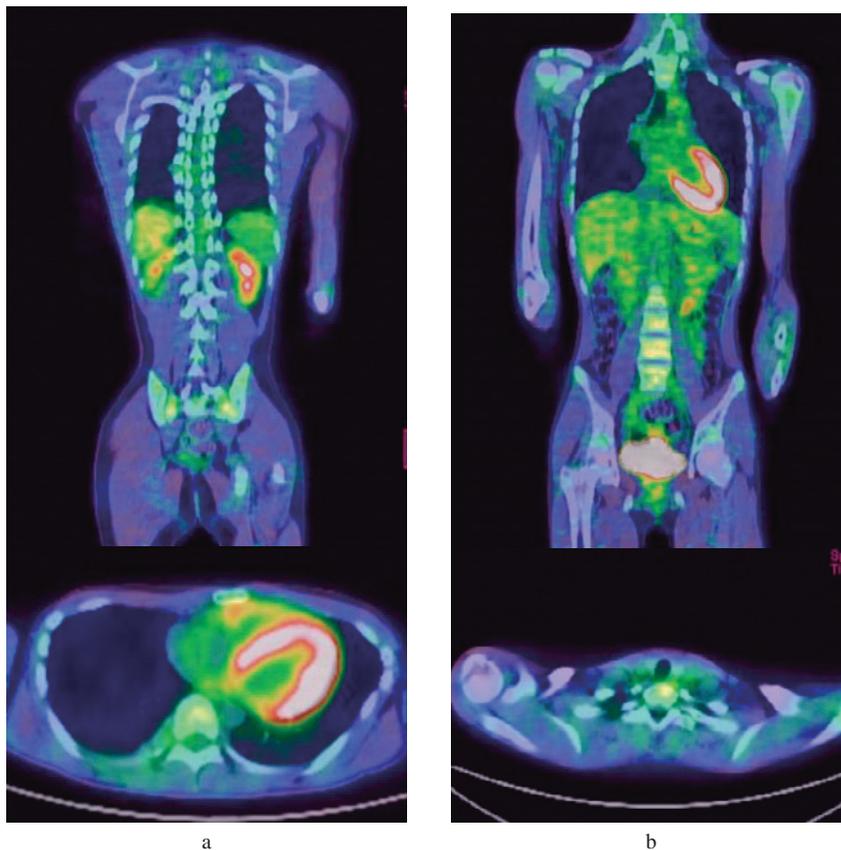


Fig. 4 PET-CT imaging before chemotherapy.

Fig. 4a PET-CT imaging showed the shrunken tumor and reduced SUV before chemotherapy.

Fig. 4b The area under the left clavicle that showed high SUV was absent after chemotherapy.

pleura was perforated from the upper and lower margins of the rib to provide an index. Next, the patient was maintained in the left lateral position to perform thoracotomy at the seventh intercostal space. The thoracic wall was resected based on the landmark which was made posterior



Fig. 5 Intrathoracic findings. We confirmed that a parietal pleura was not ruptured.

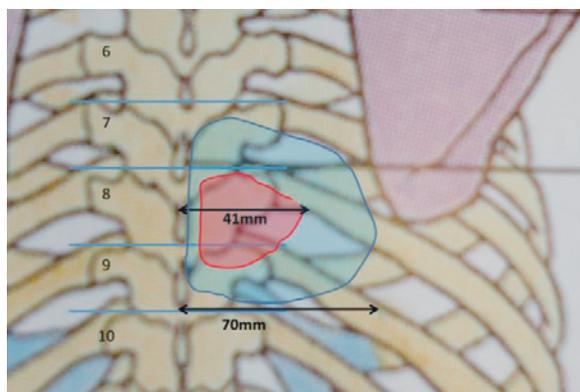


Fig. 6 Extent of resection.

We resected Th7, 8, and 9 parietal pleura, and the ribs.

approach. Then, the segmental arteries of the seventh, eighth, and ninth thoracic vertebral bodies were ligated, followed by curettage of the intervertebral discs where possible. Pedicle screws were inserted in both sides of Th5, 6, 10, and 11, and in the left side of Th7, 8, and 9. This was followed by left rodding, and the seventh, eighth, and ninth thoracic laminae were resected. A part of the epidural tissue was submitted for pathological examination to confirm the absence of contamination with tumor cells. After identifying and ligating the nerve root, pediclectomy was performed from the inner periphery of the pedicle using a chisel until reaching the 2-cm incision in the front vertebral body that was placed in advance. Then the extirpation of the vertebral body, thoracic wall, and tumor en bloc was performed (Fig. 6). Finally, a right fibular graft was transplanted in the enucleated area of the vertebral body, followed by posterior fixation (Fig. 7).

Pathological findings (excised sample)

The enucleated tumor was located in the soft tissue bordered by thoracic vertebra, the ribs, and parietal pleura. More than 95% of the tumor was a necrotic focus. Immunohistochemically, the tumor cells were positive for CD30, and placental alkaline phosphatase (PLAP) and negative for alpha-fetoprotein (AFP), human chorionic gonadotrophin (HCG), and INI-1. Additional

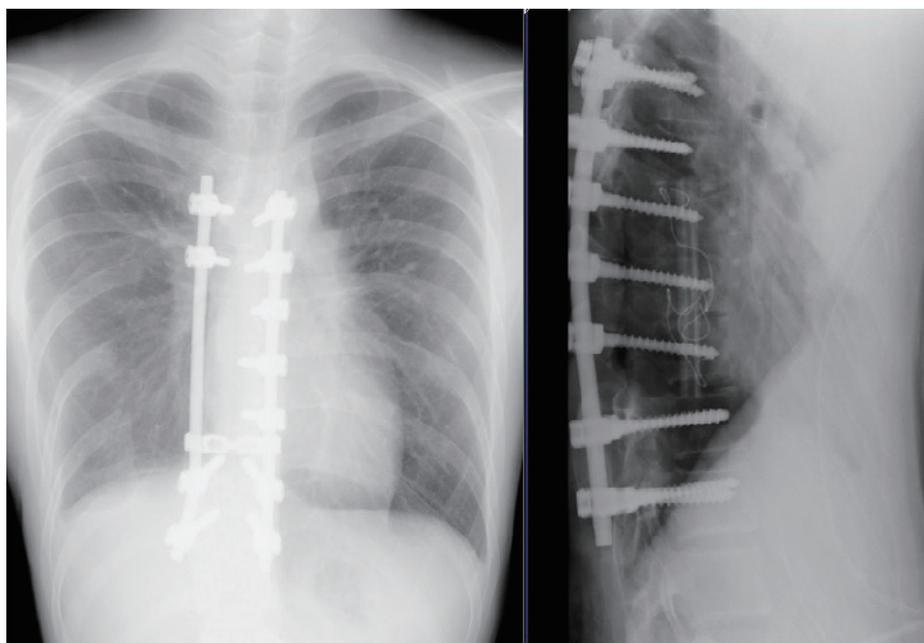


Fig. 7 X-ray immediately after the operation.

immunochemistry analysis revealed the expression of CD117 and OCT3/4 staining. Therefore, germ cell tumor with embryonal carcinoma component was diagnosed.

CT-guided needle biopsy's specimen is not consistent with this diagnosis.

Both the cutting ends of the thoracic wall and the epidural lateral sides of the excised lesion were negative for tumor cells.

DISCUSSION

In particular, non-seminomatous germ cell tumors, for which the primary lesions are in the mediastinum, are known to result in extremely poor vital prognoses. The 5-year survival rate is approximately 40%, although this varies among studies⁴. This is because these tumors often infiltrate the adjacent organs during their progress, and as a result they are difficult to completely excise surgically². We did not expect this germ cell tumor to be present at the beginning of this patient's treatment because the preoperative MRI showed a dumb-bell type tumor, and highly-specific special immune-staining provided no significant results because of the remarkable necrosis of the biopsy tissue.

With regard to the preoperative diagnosis, neurogenic tumors including neurinoma, gangliocytoma, ganglioglioma, and MPNST were first differentially diagnosed by the preoperative imaging findings. Since the MIB-1 index was extremely high (80–90%) and the amount of necrotic tissue in the tumor tissue was considerable according to the preoperative CT-guided biopsy, we suspected MPNST and chose the corresponding therapeutic strategy. Thereafter, we obtained the results of additional postoperative staining that showed CD30 (+), PLAP (+), CD117 (+), and OCT3/4 (+). Therefore, a final pathological diagnosis of embryonal carcinoma was made. CD30, CD117, PLAP, and OCT3/4 are the immunostaining markers highly specific for embryonal

carcinoma; in particular, OCT3/4 is useful for confirmative diagnoses because of its especially high sensitivity and specificity¹⁾. For patients in whom dumb-bell tumors are recognized during adolescence to late middle age, it is important to perform additional staining procedures as described above, taking into account the possibility of a germ cell tumor. In addition, not only pathological examination findings, but also the levels of serum tumor markers such as AFP and β -HCG have been reported to be reliable markers for the diagnosis of germ cell tumors. Rivera *et al.*⁷⁾ reported that having an AFP level higher than 1000 IU and a β -HCG level higher than 5000 IU are helpful for confirming the diagnosis of a non-seminomatous germ cell tumor. Unfortunately, these serum tumor markers were not measured during the treatment of our patient.

Two important factors that determine the vital prognosis in the treatment of mediastinum germ cell tumors are the degree of tumor progression (whether it is localized or has infiltrated or metastasized to surrounding organs) and its responsiveness to chemotherapy⁵⁾. Complete tumor resection by integrative therapy, including chemotherapy and surgery, would dramatically improve the vital prognosis³⁾.

Since we did not suspect a germ cell tumor in the above-described case, we chose a chemotherapy regimen that had been applied to malignant soft tissue tumors in our institution. This resulted in tumor shrinkage and disappearance of the lesions that showed a high SUV in the subclavicular lymph node, considered to accompany the primary tumor. CDDP and VP-16, which are included in the standard regimen at our institution, are also included in the chemotherapy regimen for germ cell tumors, as proposed by the National Comprehensive Cancer Network⁶⁾. We speculate that our chemotherapy was effective because of these inclusions.

We considered that 2 factors, intrathoracic dissemination and epidural dissemination, would determine whether marginal resection after chemotherapy could be achieved. We first performed the thoracoscopic evaluation to confirm the former; then we could confirm the absence of intrathoracic dissemination. We decided to evaluate epidural dissemination according to the intraoperative findings, because there was no preoperative observation method that would carry a lower risk of tumor contamination. Fortunately, we could confirm the absence of tumor cells by intraoperative rapid pathological diagnosis of the epidural tissue. This case is valuable because the margins were negative for tumor cells on postoperative pathological evaluation, and the thoracic wall, vertebral body, and tumor could be resected en bloc. Furthermore, 18 months after the surgery, there is no sign of recurrence. Therefore, a long-term vital prognosis can be expected for this patient.

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The authors report no conflict of interest concerning the materials or the methods used in this study or the findings specified in this paper.

CONFLICTS OF INTEREST/DISCLOSURE

No benefits in any form have been or will be received from a commercial entity related directly or indirectly to the subject of this manuscript.

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