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CASE REPORT

Successful radiotherapy in postoperative recurrence of a primary mediastinal yolk sac tumor: A case report

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Abstract

A woman in her 60s was evaluated for anterior chest pain. Computed tomography (CT) revealed a 50 mm mass with irregular contrast enhancement in the anterior mediastinum. α-fetoprotein (AFP) level was elevated to 1188 ng/mL. A germ cell tumor was diagnosed, mostly comprising of a yolk sac tumor (YST). Two courses of chemotherapy with cisplatin (CDDP) and etoposide (VP16) were administered and surgical tumor resection was then performed. The final diagnosis was YST. CDDP and VP16 were continued postoperatively; however, because the AFP level increased about six months after surgery, the chemotherapy regimen was altered to bleomycin and CPT-11. As the AFP again increased and a CT scan revealed tumor re-enlargement, recurrent YST was diagnosed and radiotherapy was administered. The patient received a total of 60 Gy (2 Gy per fraction). The tumor started to shrink during radiotherapy and AFP levels decreased. By one month post-radiotherapy, AFP levels had normalized and the tumor had disappeared. As of six years after radiotherapy, the patient remains alive without recurrence. Mediastinal YSTs are rare, and treatment usually includes surgery and preoperative and postoperative chemotherapy with cisplatin-based regimens. Successful treatment with radiotherapy has occasionally been reported. Our patient showed recurrence of a YST after surgery and chemotherapy, but achieved long-term survival after radiotherapy. Few patients with YST have undergone radiotherapy, but this approach was successful in our patient. In cases of postoperative recurrent YST resistant to chemotherapy, radiotherapy, together with salvage surgery, may offer a valuable option.

Introduction

A yolk sac tumor (YST) is a malignant germ cell tumor that was first described by Teilum in 1959.[1] Although it typically arises from the gonads, 10–15% of cases may arise from various midline extragonadal sites. Furthermore, primary mediastinal YST is a rare tumor, first reported by Teilmann *et al*. in 1976.[2] Treatment typically includes surgery with neoadjuvant and adjuvant cisplatin-based chemotherapy. Outcomes have improved since the introduction of cisplatin, but these tumors still have a poor prognosis. Successful treatment with radiotherapy has occasionally been reported.[3,4]

Herein we report the case of an elderly female with recurrent mediastinal YST who was successfully treated with radiotherapy after complete surgical resection and chemotherapy. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Case presentation

The patient, a woman in her 60s, had experienced left-sided chest pain for approximately one month before presenting to the hospital; her performance status scale score was 1. Computed tomography (CT) showed a 50 mm solid mass with irregular contrast enhancement in the anterior mediastinum (Fig 1a). Hemothorax occurred secondary to tumor rupture into the pleural cavity. No abnormalities were apparent at other sites. Blood count and biochemistry tests were generally normal, but the α-fetoprotein (AFP) level was elevated to 1188 ng/mL (normal range, 0–20 ng/mL). All other tumor markers were within normal ranges.

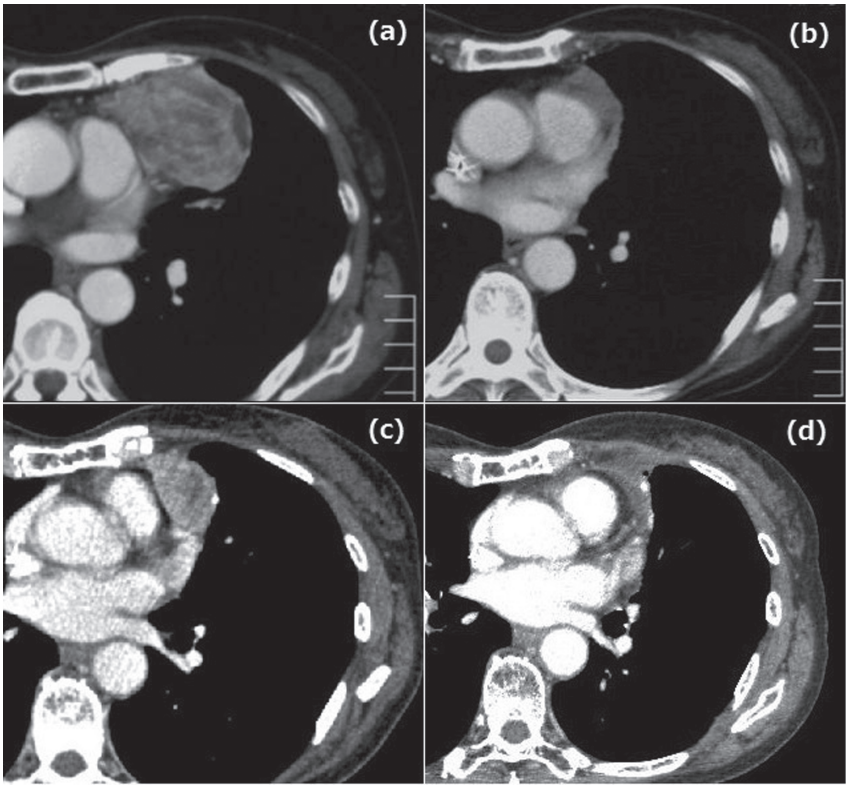

Figure 1 (**a**) Contrast-enhanced computed tomography (CT) at initial evaluation. An approximately 50 mm mass with irregular contrast enhancement is apparent in the anterior mediastinum. The border is relatively distinct. (**b**) After preoperative chemotherapy, the tumor has decreased in size. (**c**) CT at the time of recurrence. An approximate 25 mm tumor with contrast enhancement is seen at the resection site. (**d**) Post-radiotherapy CT. The tumor has disappeared. No serious radiation pneumonitis developed, and the patient has been stable for six years without tumor recurrence.

Suspecting a primary mediastinal germ cell tumor, CT-guided biopsy was performed. The histological diagnosis was germ cell tumor, majorly comprising YST. Two courses of chemotherapy with cisplatin (CDDP) and etoposide (VP16) were administered, after which AFP levels normalized and the tumor decreased in size (Fig 1b). Subsequently, complete surgical resection was performed and a 4.5 × 3 cm tumor was obtained; histopathology showed atypical cells with large irregular nuclei and Schiller–Duval body-like structure; there were no other germ cell components. Immunohistochemistry was positive for AFP and negative for placental alkaline phosphatase, confirming a diagnosis of YST (Fig 2a,b). The presence of thymoma was also confirmed (Masaoka classification: stage II).

Cisplatin and VP16 were continued postoperatively. However, the AFP level increased approximately six months after surgery; therefore, bleomycin was added to the treatment regimen. Because the AFP level did not decrease to within the normal range, the chemotherapeutic regimen was changed to bleomycin and irinotecan (CPT-11), to which the patient responded favorably.

However, approximately three months after bleomycin and CPT-11 administration, the AFP level increased once more, while the other tumor markers remained within the normal range. In addition, CT showed tumor enlargement (Fig 1c). Based on blood count and the overall condition of the patient, either CDDP alone or CPT-11 alone was continued. At this time, we considered recurrent YST because AFP level is a marker of chemotherapeutic efficacy and tumor recurrence. We commenced radiotherapy, which was performed using 10 megavolt photons and opposing two-port irradiation to intermittently deliver 2 Gy doses until a total of 60 Gy was administered (Fig 3). The tumor began shrinking during radiotherapy and the AFP level decreased. One month post-radiotherapy, the AFP level had normalized and the tumor was not detectable (Fig 1d). Three courses of bleomycin were administered after radiotherapy. The patient has since shown recurrence-free survival for six years without either tumor enlargement or AFP level elevation which would necessitate further treatment.

Discussion

Non-seminomatous germ cell tumors (NSGCT) can be distinguished from seminomas through morphology and treatment response. NSGCT include embryonal carcinoma, YST,

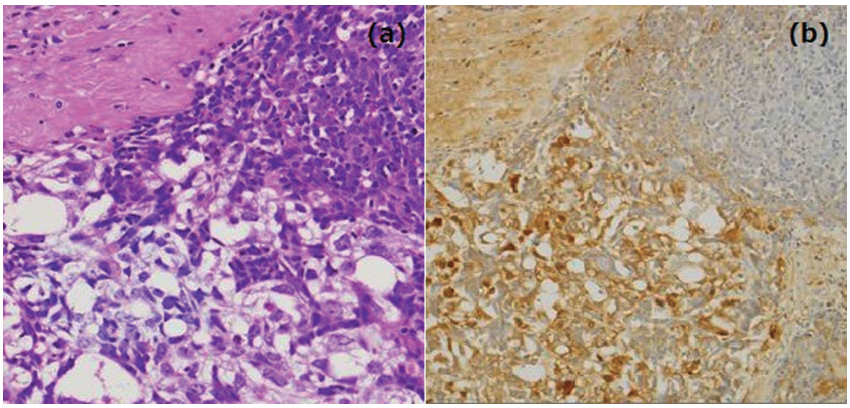

Figure 2 (**a**) Hematoxylin and eosin (HE) staining. A reticular structure or luminal structure is seen against a background of edematous interstitium and proliferating atypical cells with large irregular nuclei (HE × 200). (**b**) Immunohistochemical staining for α-fetoprotein (AFP). Tumor cells show positive immunohistochemical staining for AFP.

choriocarcinoma, and teratoma.[5] Most germ cell tumors in the mediastinum are teratomas, followed by seminomas; YST is the least common germ cell tumor in the mediastinum.[6–8]

Pure seminomas can effectively be treated by radiotherapy and have a relatively good prognosis. Conversely, YSTs respond poorly to surgery, radiotherapy, or chemotherapy. Since the introduction of cisplatin-based chemotherapy, the outcome for patients with a YST has markedly improved.[4,5,9] Concomitant use of other anticancer drugs has occasionally been reported; however, the data is inconsistent. With respect to pediatric mediastinal YST, Gooncratne *et al*. first reported a case of a female infant who survived for a long duration after surgery and adjuvant CDDP-based chemotherapy.[10] Hawkins et al. reported upon two survivors who underwent surgery and PVB (CDDP + vinblastine + bleomycin).[11] Rossi et al. reported three cycles of BEP (bleomycin, VP-16, and cisplatin) as adjuvant therapy for YST.[3]

A determination of the number of cycles of neoadjuvant chemotherapy and the timing of surgery is based on AFP level and the reduction of tumor size. In many patients, YST stage is already advanced at diagnosis and, thus, the tumor cannot be completely resected, in which case prognosis is often poor, even after chemotherapy and surgery. The five-year overall survival rate for patients with mediastinal NSGCT is only 40%.[12] Kesler et al. reported that 76% of resected specimens retained viable tumor cells even after chemotherapy for

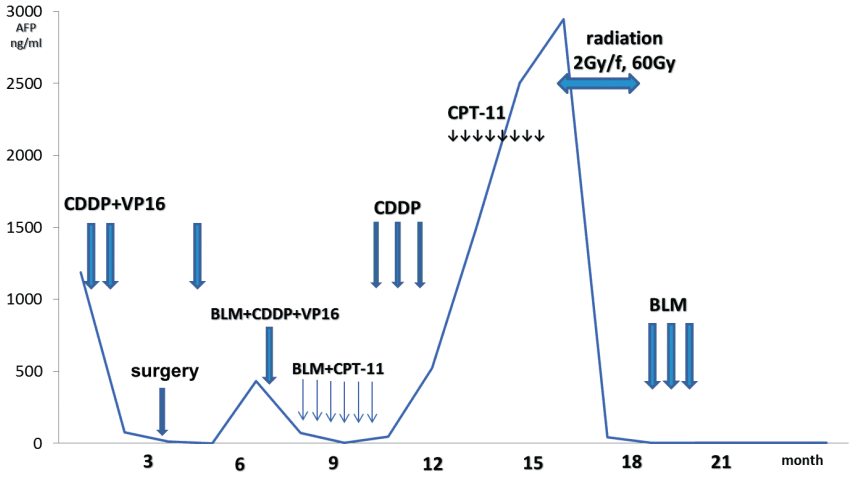

Figure 3 Treatment course. α-fetoprotein (AFP) level decreased with preoperative chemotherapy, but increased again after surgery, indicating recurrence of the yolk sac tumor YST. No improvement was seen despite administration of multiple anticancer drugs, so radiotherapy was commenced. After radiotherapy, three courses of bleomycin were administered, and the AFP level decreased. AFP level has not shown any subsequent increases, despite the absence of further treatment.BLM, bleomycin; CDDP, cisplatin; CPT-11, irinotecan; VP16, etoposide.

residual disease.[13] The majority of deaths or recurrences occur two years after treatment; patients who survive longer are often those who have undergone complete resection.

Germ cell tumors grow rapidly, highlighting the importance of early diagnosis and the initiation of appropriate treatment. Our case presented with left-sided chest pain secondary to hemothorax. We considered that tumor enlargement may have resulted in ischemia, necrosis, and then, rupture. This enabled early discovery, chemotherapy initiation, and complete resection. Similar to previous reports, a chemotherapeutic regimen comprising CDDP, VP16, and bleomycin was effective in our case. We deemed that resection after neoadjuvant chemotherapy was crucial. A diagnosis was established after repeat surgery, and although continuing a three-drug combination incurred side effects, the therapeutic response was favorable. In many cases, where difficulty in continuation of full-dose chemotherapy occurs, combination therapy using three drugs is proposed. In our case, bleomycin was used depending on the patient's general condition after surgery. The AFP level decreased during radiotherapy and by one month post-radiotherapy, the AFP level had normalized. This result indicates that radiotherapy was most effective for our YST patient. If chemotherapy is no longer effective, changing to early radiotherapy is recommended. In our patient, although there was postoperative recurrence, early radiotherapy proved effective and resulted in long-term survival. However, only a few reports regarding successful radiotherapy for YST have been reported.

Apoptotic death was reported to be an important factor for tumor sensitivity to radiotherapy or chemotherapy. p53 is suspected to function as a control checkpoint for response to DNA damage and plays a role in the induction of apoptosis.[14] Cells with no p53 function, which is induced by the loss of p53 gene mutation, fail to recognize DNA damage and initiate apoptosis. Investigation of rat YSTs, including wild-type and radiation-resistant cell lines, demonstrated that p53 gene status influenced differences in apoptosis and radiosensitivity of both cell lines.[15] VP16 has also been reported to increase radiation-induced apoptosis in radiation-resistant cell lines.[16] In addition, CDDP in combination with early radiation has been reported to have an additive effect in both cell lines.[17] Based on such findings, the success of radiotherapy in our patient suggested YST with insignificant p53 mutation. Resistance may have been acquired after repeated chemotherapy. We also concluded that the anticancer drugs may have either increased the radiosensitivity of the tumor or killed all radioresistant tumor cells. Because of inconsistent reports on actual clinical cases of YST, the recommended radiation dose and schedule are yet to be determined. However, considering the radiation doses tolerable to surrounding organs, the general condition of the patient, and the degree of tumor shrinkage during radiotherapy, the radiation dose that we used for this patient may be appropriate. Further studies on a large number of cases will be necessary to validate the utility of radiotherapy for YST.

Conclusion

Radiotherapy may be a valuable option for postoperative recurrent YSTs that are resistant to chemotherapy.

Disclosure

No authors report any conflict of interest.

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