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BRIEF REPORT

Primary mediastinal yolk sac tumor treated with platinum-based chemotherapy and extended resection: Report of seven cases

Bing Liu, Gang Lin, Jingwei Liu, Haibo Liu, Xueqian Shang & Jian Li

Department of Thoracic Surgery, Peking University First Hospital, Peking University, Peking, China

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Correspondence
Jian Li, Department of Thoracic Surgery, Peking University First Hospital, Peking University, Xi Shiku Road 8th, XiCheng District, Peking 100034, China.
Tel: +86 135 0123 5625
Fax: +86 10 8357 2417
Email: pkufts@163.com

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Abstract

Background: Primary mediastinal yolk sac tumor, which is also known as endodermal sinus tumor, is a rare but lethal neoplasm, and it is a kind of mediastinal nonseminomatous germ cell tumor. The current standard treatment in mediastinal nonseminomatous germ cell tumors is chemotherapy combined with postchemotherapy residual mass resection. We report on seven cases of primary mediastinal yolk sac tumor treated with platinum-based chemotherapy and extended resection.

Methods: We experienced seven cases of primary mediastinal yolk sac tumor between August 2014 and August 2017. All cases had markedly raised α-fetoprotein and normal β-human chorion gonadotropin. Computed tomography scan revealed an anterior mediastinal tumor in all cases. Five patients underwent needle core biopsy, which showed a mediastinal yolk sac tumor. They received preoperative platinum-based chemotherapy and then underwent extended resection, and four of them received postoperative platinum-based chemotherapy. Two other patients did not receive preoperative biopsy, and they underwent surgical extended resection and then received postoperative platinum-based chemotherapy.

Results: Two patients (29%) experienced a postoperative complication, including one pneumonia and one atelectasis. There were no operative deaths. R0 resection was achieved in six patients (86%), and R2 resection was achieved in the other patient. Three patients experienced pulmonary metastases within one year, and two of them soon died. Four other patients were alive without recurrence at the time of writing.

Conclusion: Primary mediastinal yolk sac tumor is rare, and the prognosis is poor. A multimodality aggressive approach including adjuvant chemotherapy followed by surgical resection is the optimal treatment and may lead to long-term survival.

Introduction

Common germ cell tumors (GCT) of the mediastinum are seminoma, choriocarcinoma, teratoma, embryonic carcinoma, and yolk sac tumor (also known as endodermal sinus tumor).[1] Yolk sac tumor is the most frequent primary germ cell tumor of a non-teratomatous and non-seminomatous type that occurs in the mediastinum.[2] It is in pure form or in combination with other forms of GCT.

Most patients are young men.[3] They often present with a history of cough, shortness of breath, and chest pain. Some patients may present with fever, hemoptysis, superior vena cava syndrome[4] and night sweats. Most patients have markedly raised α-fetoprotein (AFP), and some also have elevated serum β-human chorion gonadotropin.

The optimal treatment for yolk sac tumor is chemotherapy combined with postchemotherapy residual mass excision, but the prognosis remains poor. We prefer this approach when possible.

In the literature, there are some small series and cases reports about mediastinal yolk sac tumors. We retrospectively reviewed our single-center experience.

Methods

Between August 2014 and August 2017, there were seven cases with a mediastinal yolk sac tumor who underwent extended resection in the thoracic surgery ward of Peking University First Hospital.

Before surgery, five patients were histologically diagnosed with yolk sac tumor by needle core biopsy, then they received preoperative platinum-based chemotherapy and then underwent extended resection, and four of them received postoperative platinum-based chemotherapy. Two patients did not undergo biopsy and preoperative chemotherapy. They were histologically diagnosed with yolk sac tumor after surgery, and then underwent chemotherapy.

All patients underwent extended resection, and resection status was determined from the operative notes and the pathology reports.

Results

Clinical characteristics

Seven consecutive patients were treated for primary mediastinal yolk sac tumor from August 2014 to August 2017 (Table 1). All patients were young men, and the mean age was 23 years (range 14–35 years). Five patients presented with chest distress or chest pain. Two of them meanwhile presented with intermittent fever, and one also presented superior vena cava syndrome. One of the other two patients presented with cough. One presented with a markedly raised AFP without any symptom. All patients had no medical problems in the past, except case 5, who presented with Klinefelter syndrome (47,XY,+X).

All patients had a markedly raised AFP (mean 14 276 ng/mL, range 285.5–42 034 ng/mL) and normal serum β-human chorion gonadotropin. Computed tomography scan revealed an anterior mediastinal tumor in all cases. Five patients underwent needle core biopsy, which showed a mediastinal yolk sac tumor. They received preoperative platinum-based chemotherapy, and one patient also underwent radiotherapy (40 Gy). All of them presented a partial response to chemotherapy (Fig 1). We did not consider that the other two patients (case 3 and 6) could have mediastinal yolk sac tumor according to the computed tomography scan (Fig 2). Therefore, they did not receive preoperative biopsy and preoperative chemotherapy. They were histologically diagnosed with yolk sac tumor after surgery.

Surgical management

Muscle-sparing axillary thoracotomy was used in four patients, two on the left and two on the right according to tumor location. Median sternotomy was used in the other three patients, because the tumor invaded their lungs or great vessels.

All patients underwent extended resection. Case 1 underwent tumor resection, partial pericardiotomy, and phrenic nerve resection. Case 2 underwent tumor resection, partial pericardiotomy, and pulmonary wedge resection. Case 3 underwent tumor resection and partial pericardiotomy. Case 5 underwent tumor resection and extended thymectomy. Case 6 underwent tumor resection and phrenic nerve resection. Case 4 and 7 underwent tumor resection, partial pericardiotomy, pulmonary wedge resection, and partial superior vena cava resection, but case 4 did not undergo superior vena cava reconstruction because of complete obstruction of the superior vena cava. They also underwent mediastinal lymphadenectomy, but there was no lymph node metastasis.

Table 1 Clinical characteristics of seven patients

Case	Age (years)	Symptom	AFP before chemotherapy (ng/mL)	Preoperative chemotherapy (cycle, drug)	AFP after chemotherapy (ng/mL)	Surgical approach	Resection	Major postoperative complications	Postoperative chemotherapy (cycle, drug)	Recurrence location	Status	Survival (months)
1	16	Chest distress fever	9545.00	4, PEB	4.84	LMSAT	R0	None	2, PEB	None	Alive	38
2	17	Chest distress chest pain	285.50	4, PE	13.31	MS	R0	Pneumonia	2, PEB	Pulmonary	Alive	29
3	32	None	2697.00	None	None	RMSAT	R0	None	4, PEB	Pulmonary	Dead	11
4	35	Chest distress SVC syndrome	12 045.00	6, PEB	1117.00	MS	R2	Atelectasis	None	Pulmonary	Dead	5
5	14	Chest pain fever	32 105.00	6, PEB	10.91	RMSAT	R0	None	2, PEB	None	Alive	13
6	22	Cough	1210.00	None	None	LMSAT	R0	None	4, PE	None	Alive	5
7	22	Chest pain Cough	42 034.00	2, PEB	261.60	MS	R0	None	4, PEB	None	Alive	3

LMSAT, left muscle-sparing axillary thoracotomy; MS, median sternotomy; PE, cisplatin and etoposide; PEB, cisplatin, etoposide, and bleomycin; RMSAT, right muscle-sparing axillary thoracotomy.

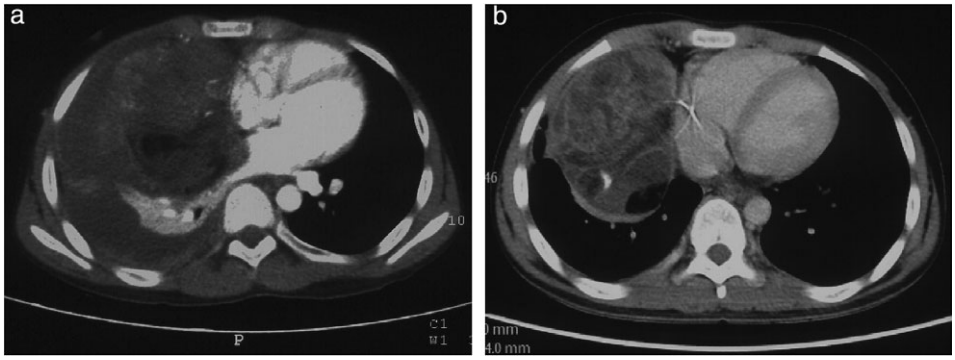

Figure 1 Computed tomography scan of case 5. (**a**) Computed tomography scan of the thorax before preoperative chemotherapy. (**b**) Computed tomography scan of the thorax after preoperative chemotherapy.

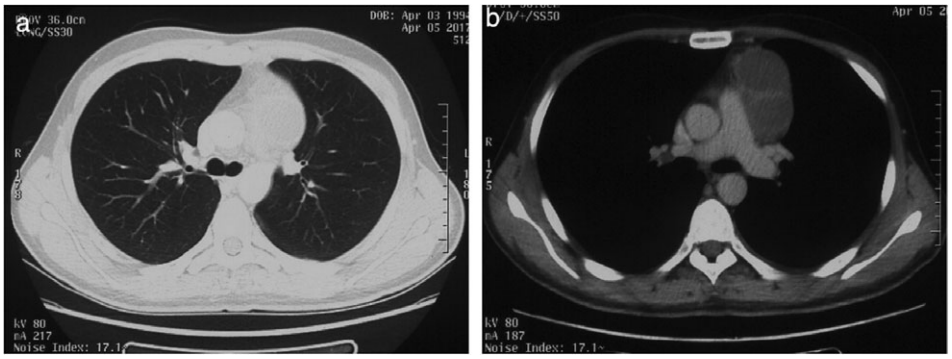

Figure 2 Computed tomography scan of case 6 before surgery. (**a**) Computed tomography of the lung. (**b**) Computed tomography of the thorax.

R0 resection was achieved in all patients except case 4, who underwent R2 resection. There was no perioperative death, and two patients (29%) experienced a postoperative complication, including one pneumonia and one atelectasis.

Histology reports revealed that there were yolk sac tumors in five patients, and there was no residual yolk sac tumor in case 1. In case 5, there was no residual yolk sac tumor and remaining teratoma after preoperative chemotherapy, so it was a hybrid GCT that consisted of a yolk sac tumor and teratoma.

Postoperative treatment

Four of the patients who received preoperative chemotherapy received postoperative platinum-based chemotherapy and one of them (case 4) did not receive postoperative chemotherapy because of poor physical condition. An adjuvant platinum-based chemotherapy was given to the other two patients (case 3 and 6), who did not receive preoperative chemotherapy.

Patient survival

Recurrence with pulmonary metastasis occurred in three patients at three months (case 4), five months (case 2), and seven months (case 3) after surgery (Table 1). Case 3 and case 4 died soon after recurrence. Case 2 received chemotherapy and immunotherapy after recurrence, and he was alive at the time of writing. Four other patients are alive without recurrence to now.

Discussion

Extragonadal GCTs account for 1–5% of all germ cell tumors.[5] They typically arise in midline locations, and the most common sites are the anterior mediastinum, the retroperitoneum, and the pineal and suprasellar regions in adults. GCTs account for 15% of primary anterior mediastinal tumors in adults. Mediastinum GCTs are classified as seminomas GCTs, non-seminomatous GCTs, mature teratomas, and immature teratomas based on histology. Yolk sac tumor is a kind of non-seminomatous GCT, and it accounts for 15% of all mediastinum GCTs.

Primary mediastinal yolk sac tumor is rare, but highly malignant, and it carries a very poor prognosis. Several causes of this unfavorable prognosis have been suggested, one of which is the bulky presentation that makes complete surgical resection impossible in patients with advanced stages of the disease[5] and another is its rapid growth and early metastasis, often to the lung, brain, liver, and bone.[6] The current standard treatment for non-seminomatous GCTs is chemotherapy combined with postchemotherapy residual mass excision to achieve long-term survival. Walsh *et al.* reported from 1993 to 1998, 20 cases of non-seminomatous GCTs, nine of them were

primary mediastinal yolk sac tumors.[7] All patients were treated with chemotherapy followed by radical resection for residual mass, and the overall survival at 2 years was 58%. Kesler *et al.* reported, from 1981 to 1998, 40 cases of yolk sac tumors with overall survival of 61% after an average follow-up of 48 months.[8] Three variables affect long-term survival: (i) AFP level after preoperative chemotherapy; (ii) residual mass pathological status; and (iii) lung metastasis.[8] Complete resection after chemotherapy for a residual tumor is very difficult and demands high surgical skills, because tumors often have dense fibrotic adhesions to the adjacent organs, such as the pericardium, great vessels, and so on.

We experienced seven cases of primary mediastinal yolk sac tumor between August 2014 and August 2017. The AFP levels of the patients who received preoperative chemotherapy had decreased obviously, particularly for case 1 who had survived for 38 months without recurrence. Case 4, who received R2 resection, recurred at 3 months after surgery and died soon after.

Platinum-based chemotherapy is suggested as the initial therapy for patients with yolk sac tumor.[9] Some recommend four cycles of VIP (cisplatin, etoposide, and ifosfamide), and PEB (cisplatin, etoposide, and bleomycin) is an alternative. If viable malignancy is identified, two additional cycles of chemotherapy should be given. We choose PEB or PE (cisplatin, etoposide, and blemycin), and adjust the cycle according to the general condition of patients. Two patients did not receive preoperative chemotherapy because they did not undergo preoperative biopsy. Therefore, the preoperative biopsy is important when we experience anterior mediastinal tumor. The administration of further chemotherapy for patients with mediastinal yolk sac tumor who recur after chemotherapy and surgery has been minimally effective.[10,11] Immunotherapy might be feasible, such as case 2 who received immunotherapy after recurrence at the MD Anderson center.

Mediastinal non-seminomatous GCTs are associated with Klinefelter syndrome[12] and the frequent development of a hematological malignancy.[13] This is different from gonadal non-seminomatous GCTs. Case 5 of our cases presented with Klinefelter syndrome (47,XY,+X).

Primary mediastinal yolk sac tumor is rare but highly malignant, and the prognosis is poor. A multimodality aggressive approach including adjuvant chemotherapy followed by surgical resection is the optimal treatment, and may lead to long-term survival. As more experience is gathered with this rare malignancy, more specific guidelines can become available.

Disclosure

No authors report any conflict interest.

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