Management of Primary Mediastinal Yolk Sac Tumors: A Single Institution Experience with 10 Patients

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Research Article

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Abstract

Background: Primary mediastinal yolk sac tumors is a kind of primary mediastinal non-seminomatous germ cell tumor . The current treatment strategies in primary mediastinal non-seminomatous germ cell tumor is neoadjuvant chemotherapy followed by residual mass surgical resection . We reviewed our institutional 5 years' experience with Primary mediastinal yolk sac tumors who treated with platinum-based neoadjuvant chemotherapy and extended resection.

Methods: We experienced 10 cases of Primary mediastinal yolk sac tumors from October of 2014 to October of 2019. 7 patients received preoperative platinum-based chemotherapy followed by surgical resection of residual mediastinal mass. The other 3 patients were received initial surgical resection without preoperative chemotherapy.

Results: R0 resection was achieved in 8 patients (80%), and R2 resection

was in the other 2 patients (20%). All the 7 patients with neoadjuvant chemotherapy were R0 resections, however all of them had viable tumor in their surgical specimen. Morbidities after surgery occurred in 2 patients, including 2 pneumonias ,1 type I respiratory failure and 1 acute left heart failure, and They were died within 2 months after surgery. At the time of writing ,3 patients are alive without evidence of disease,7 patients died , of which 5 patients have died of tumor-related causes and 2 died of postoperative complications. 8 patients were included in the follow-up. Among them 7patients experienced progressed within one year. 8 patients were included in the follow-up,mPFS and mOS in 8 patients were 3.7 months (2.6-41.3m) and 23.15 months (8.6-41.3m) , respectively. The 7 patients with neoadjuvant chemotherapy followed by surgical resection of residual diseases, 2-year survival rate was 57.1%,The 3-year survival rate was 28.6%

Conclusion: An aggressive, multidisciplinary treatment including neoadjuvant chemotherapy followed by residual mass surgical resection is the optimal treatment and can be associated with prolonged survival.

Introduction

Primary mediastinal yolk sac tumors (PMYST) is a kind of primary mediastinal non-seminomatous germ cell tumors (PMNSGCT) . It is rare. Germ cell tumors (GCTs) usually arising in the gonads, and extragonadal origin accounts for only 1% to 5% of GCTs (1) , nevertheless PMYSTs only account for 15% of all mediastinum GCTs(2).

Most patients are young men.(3)They often present with elevated alfa-fetoprotein （AFP）and/or beta-hCG(β-HCG）at diagnosis, (4)and a computed tomographic scan of the chest aways revealed a giant mediastinal mass.

PMYST carries a very poor prognosis. The optimal treatment for PMNSGCT is chemotherapy followed by radical resection for residual mass. (5,6)At some centers, surgery is considered even in cases of the first-line chemotherapy with non-responders, because of dismal results with second-line chemotherapy. (7,8)Despite aggressive treatment, the prognosis of these patients is still poor.(9)

Literatures on PMYST are rare. Here is a review of our single-center experience.

Material And Methods

A retrospective study of 10 patients with PMYST who underwent extended resection referred to the West China hospital,Sichuan University , from October of 2014 to October of 2019, were performed. Tumor response was assessed with the use of RECIST, version 1.1. The pathological diagnosis in the surgical specimen were registered by pathologist **(Figure 1 and Figure 2)** .

Statistics

Survival data was calculated from the date of diagnosis, until their last known follow-up day, or date of death. Actuarial survival curves were calculated according to the Kaplan-Meier method.

Result

Patient and Tumor Characteristics

A retrospective study of 10 patients with PMYST who underwent extended resection referred to the West China hospital,Sichuan University , from October of 2014 to October of 2019, were performed.Patients' characteristics are summarized in Table 1.

Radiographic and Pathologic Response to Preoperative Chemotherapy

7 patients experienced some degree of radiographic tumor shrinkage from the preoperative chemotherapy. 6 patients met the criterion for PR(**Figure 3**)and 1 patients had SD. 8 of the 10 patients (80%) underwent an R0 resection and 2 (20%) an R2 resection. All the 7 patients with neoadjuvant chemotherapy were R0 resections, however All patients had viable tumor cells in their surgical specimen.

Operation and Surgical Complications

Details of surgery and complications are outlined in Table 2. Morbidities after surgery occurred in 2 patients, including a postoperative pneumonia and type I respiratory failure in 1 patient, and pneumonia,a persistent sinus tachycardia and acute left heart failure in the other one. They were died within 2 months after surgery.

Recurrence and Survival

At the time of writing, 3 patients are alive without evidence of disease,7 patients died, Of which 5 patients have died of tumor-related causes and 2 died of postoperative complications.

8 patients were included in the follow-up, among them 7patients experienced progressed. 6 patients progressed mainly in the form of metastasis, such as lung, brain, liver, bone, 1 had experienced anterior mediastinum recurrence which was due to R2 excision. mPFS and mOS in 8 patients were 3.7 months (2.6-8.6m) and 23.15 months (8.6-41.3m) , respectively . The 7 patients with neoadjuvant chemotherapy followed by surgical resection of residual diseases, 2-year survival rate was 57.1%,the 3-year survival rate was 28.6%.

Discussion

The majority of Germ cell tumors (GCT) originates from gonad, whereas only 1% to 5% of all GCT may occur in the extragonadal places.(10)Extragonadal germ cell tumors can occur in the mid-line of the body from the retroperitoneum ,anterior mediastinum and in other areas such as the pineal gland or the coccyx .(11)The mediastinum represents the most common site of extragonadal primaries (50% to 70%). (3)Primary malignant mediastinal germ cell tumors(PMMGCT) are divided into two broad groups, primary mediastinal seminomatous germ cell tumors (PMSGCT)and primary mediastinal nonseminomatous germ cell tumors (PMNSGCT). (12) PMNSGCT includes choriocarcinoma, teratoma,embryonic carcinoma, and yolk sac tumor(13). Primary mediastinal yolk sac tumors(PMYST) of the mediastinum is rather rare.

PMYST carries a very poor prognosis.Prognostic data of patients with neoadjuvant followed by radical resection for residual mass are more reported for PMNSGCT. Walsh et al.(5) reported 20 cases of PMNSGCT from 1993 to 1998, 9 of them were PMYST , and the overall survival at 2 years was 58%. Kesler et al. (6)Reported 158 cases of PMNSGCT, from 1981 to 1998, 76 cases of PMYST with 2-year overall survival of 56% .Sarkaria et al. (8)Reported from 1980 to 2008. 57 cases of PMNSGCT, 16 of them were PMYST . The median OS from time of chemotherapy were 31.5 months. OS at 2 years were 56%. In our series, the 2-year OS of PMYST was 57.1%, the 3-year survival rate was 28.6% which was very similar to prognosis of PMNSGCT reported previously. The median overall survival was 25.5 months.

Elevated AFP and β-HCG at diagnosis is seen in 90% of nonseminomatous germ cell tumor patients. (11) Serum AFP levels are useful for the diagnosis and may guide treatment. In our report, AFP information was available for 6 patients receiving neoadjuvant chemotherapy, which decreased after chemotherapy and elevated when the tumor recurred, but no one was approaching normal levels . All the 7 patients receiving neoadjuvant chemotherapy were R0 resection, however, the surgical specimen of these patients exhibited viable tumors.

Due to the rarity of PMYST , oncologists recommend treating this disease like testes NSGCT. Multiple clinical studies have proved that cisplatin based chemotherapy combined with surgical resection of residual diseases is one of the most successful modes of multidisciplinary therapy(3,6,8). Firstly, PMNSGCT always located in the anterior mediastinum close to important mediastinal anatomical structures such as the great vessels ,the lung and the heart and so on . It is often impossible to achieve complete excision by initial surgery. Moreover, PMNSGCT are sensitive to first-line chemotherapy, however, second-line salvage chemotherapy are ineffective, with only approximately 5%–10% of patients.(4,14). We recommend treat in a more aggressive way. Surgical resection was encouraged if resection was feasible after first-line chemotherapy, even if Tumor regression did not achieve partial response. Finally, After cisplatin-based chemotherapy for PMNSGCT, viable tumor cells were still found in their surgical specimen (6). In our study, 7 patients underwent surgical resection after preoperative chemotherapy , of which 6 patients reached partial response and one with stable disease . However active tumor cells was still detected in all postoperative pathological specimens. Therefore, our data also support the view of surgical resection of residual tumor mass after chemotherapy.

In conclusion, PMYST is rare, and the prognosis is poor. A multidisciplinary aggressive approach including neo-adjuvant chemotherapy followed by surgical resection is the optimal treatment, but overall survival is still not satisfactory. We need to accumulate more experience and explore new treatments for this rare malignancy.

Declarations

Ethics approval and consent to participate the Biomedical Ethics Committee of West China Hospital of Sichuan University approved the study.

Consent for publication Not applicable.

Availability of data and materials All data generated or analysed during this study are included in this published article.

Competing interests The authors declare that they have no competing interests

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Authors' contributions

Yang Yu	Mading contributions to the conception ,design of the work,interpretation of data,drafted the work
Yong Jiang	Mading contributions to interpretation of data
Xuanwei Zhang	Mading contributions to drafted the work
Feifei Na	Mading contributions to Analysis of data
Weigang Xiu	Mading contributions to interpretation of data
Meijuan Huang	Mading contributions to substantively revised it
You Lu	Mading contributions to substantively revised it
Youling Gong	Mading contributions to the conception,design of the work and substantively revised it

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Tables

Table 1. Clinical characteristics of ten patients

Case no.	Age	Symptom	AFP before Chemotherapy (ug/L)	Preoperative Chemotherapy(cycle/drug)	Course	Surgical (approach)	Resection	Major postoperative complications	Postoperative chemotherapy (cycle, drug)	RT
1	23	Cough Chest pain SVCS	ID	6,BEP	PR	Yes (MS	R0	None	ND	ND
2	25	Cough Dyspnea Fever	2114	3,BEP	PR	Yes (MS	R0	None	3,EP	Yes (50.
3	44	Cough SVCS hemoptysis	1210	1,EP 4,BEP	PR	Yes (MS	R0	None	ND	Yes (50(
4	17	Chest pain Fever	650	4,BEP	PR	Yes (RMSAT	R0	None	2,BEP	ND
5	32	Dyspnea Fever SVCS	1210	4,BEP	PR	Yes (MS	R0	None	ND	ND
6	20	Fever Chest pain	1210	2,EP 1,BEP	SD	Yes (MS	R0	None	4,EP	Yes (50(
7	23	Dyspnea Chest pain SVCS	1210	3,EP 2,BEP	PR	Yes (MS	R0	None	4,EP	ND
8	33	Dyspnea	ND	ND	None	Yes (MS	R2	Pneumonia, Heart failure	ND	ND
9	22	Dyspnea Chest pain	ND	ND	None	Yes (MS	R0	Pneumonia, Respiratory failure	ND	ND
10	23	Chest pain Night sweats	1210	ND	None	Yes (LMSAT	R2	None	6,BEP	Yes (61.

ND: not done; ID: information drop; NED: no evidence of disease;AD: alive with disease; BEP: bleomycin, etoposide, cisplatin; VIP: etoposide, ifosphamide, cisp
EC:etoposide and caboplatin;SVCS: superior vena cava syndrome;AFP:a-fetoprotein LMSAT:left muscle-sparing axillary thoracotomy; MS:median sternotomy
thoracotomy;RT:radiotherapy;PR:partial response;SD:stable disease;PD:Progressive disease ;RO :no residual tumor;R2: macroscopic residual tumor;

Table 2. Operation-related factors

	N=10
Surgical approach	
Median sternotomy	8
Muscle-sparing axillary thoracotomy	2
Site of combined resection	
Vascular prosthetic replacement	2
Venous sheath resection	5
Arterial sheath excision	3
Lung (type of resection)	
left total pneumonectomy	1
Partial resection	7
Right atrial appendage	1
Phrenic nerve	1
Lymph node dissection	3
Blood loss (ml)	733(100-2500ML)
Patients who received blood transfusion	4
Resection	
R0	8
R2	2
Postoperative complications	
pneumonia	2（case 8 and 9）
Respiratory failure	1（case 9）
heart failure	1（case 8）
R0 :no residual tumor;R2: macroscopic residual tumor.	

Figures

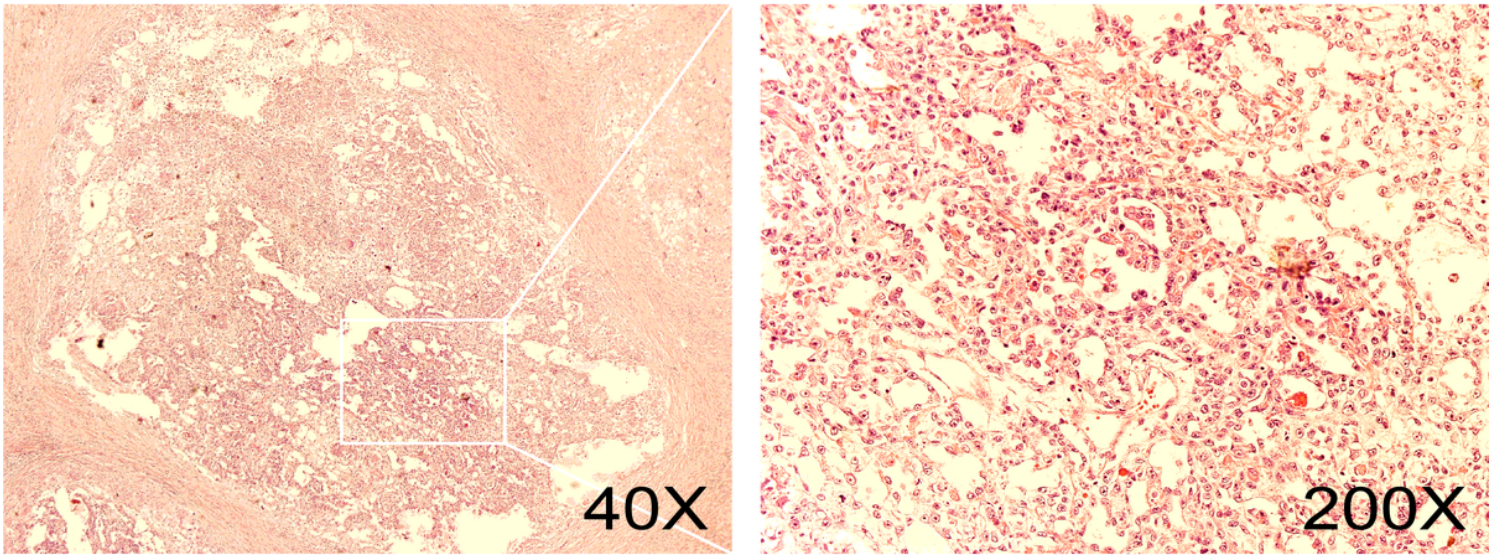

Figure 1

Histologic patterns of mediastinal yolk sac tumors (YST).

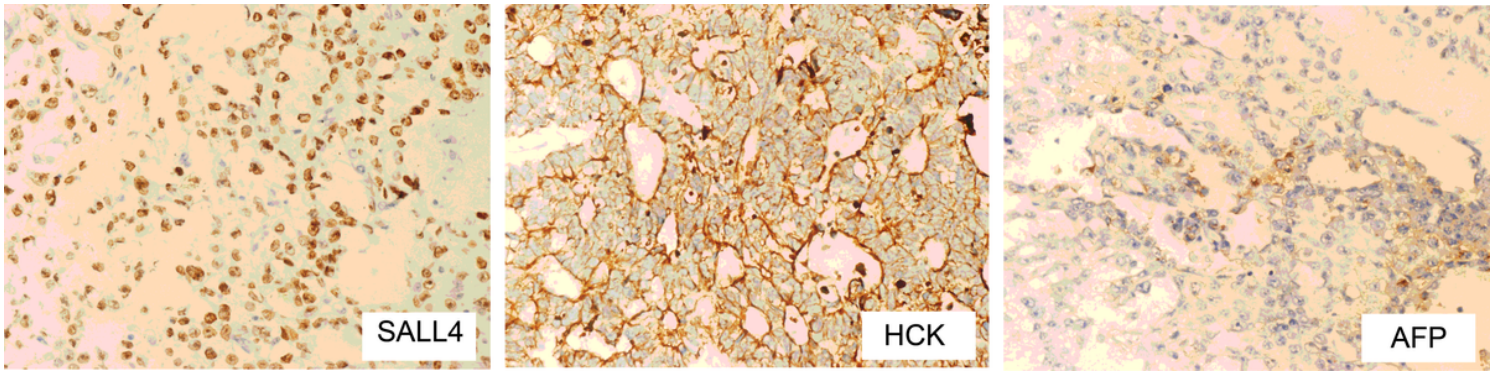

Figure 2

Characteristic staining pattern of mediastinal yolk sac tumors (YST). SALL4(+). HCK(+). AFP(+).

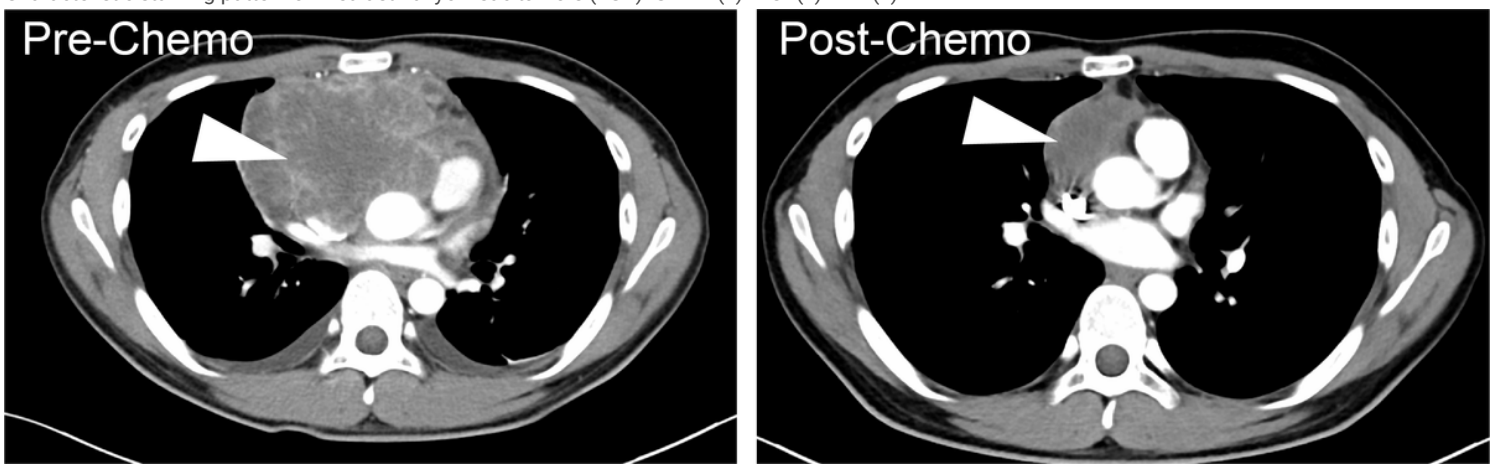

Figure 3

Contrast-enhanced computed tomography (CT) of case 2. CT scan of the chest before preoperative chemotherapy and CT scan of the chest after 3cycles preoperative chemotherapy.