Teratoma identified after postchemotherapy retroperitoneal lymphadenectomy

Argirovic M. Djordje [1], Argirovic Dj. Aleksandar [2]
[1]Clinic of Urology, CCS, Outpatient Clinic „Argirović“, Urology, Belgrade, Serbia
[2]Clinical Hospital Center Zemun-Belgrade, Department of Urology, Zemun, Serbia

Abstract

The histologic finding of teratoma occures in aproximately 40% of all postchemotherapy retroperitoneal lymphadenectomy (PC-RPLA) for disseminated nonseminomatous testicular tumors (NSTT). We evaluated patients undergoing PC-RPLA for teratoma to determine risk factors for recurrence and clinical outcome. Among a survey of 193 patients submitted to PC-RPLA due to metastatic NSTT from 1980-2005, we identified 82 patients (42%) who were found to have only teratoma in the retroperitoneum. Sixty-seven patients (82%) received only induction cisplatin-based chemotherapy, and 15 (18%) required 2nd line chemotherapy. PC-RPLA histology revealed mature teratoma (MT) in 86%, immature teratoma (IMT) in 12% and teratoma with malignant transformation (TMT) in 2%. Sixteen patients (19%) relapsed within median free interval of 22 months. Among 13 patients submitted to redo-RPLA, discordant histology occurred in 6 patients (46%) (2 TMT, 4 viable germ cell tumors [GCT]), all with worst histology in comparison to primary RPLA. One relapsing patient with only elevated serum tumor markers (STMs) achieved complete response with chemotherapy alone. Two patients relapsed at 21 and 74 months with widespread metastasis and died despite salvage chemotherapy. Seven of 13 patients (54%) who were rendered free of disease (FOD) with redo-RPLA, relapsed again. All but one died despite salvage treatment (2 of chemotherapy related toxicity) within mean survival time (MST) of 86.7+/-26.1 (95% confidence interval [CI], 98.79-149.21). At mean follow-up (MFU) of 135+/-62.6 months (95% CI, 98.79-149.21), alive and free of disease (AFD) are 90% patients. The probability of being reccurence-free at 5- and 10- year was 87% and 81%, respectively. The 5- and 10- year probability of disease speciphic survival (DSS) were 98% and

Teratom identifikovan posle posthemiterapijske retroperitonealne limfadenektomija kod pacijenata sa diseminovanim neseminomskim tumorima testisa

Argirović M. Đorđe[1], Argirović Đ. Aleksandar[2]
[1]Urološka Klinika, KCS, Poliklinika „Argirović“, Urologija, Beograd, Srbija
[2]Služba urologije, Kliničko Bolnički Centar Zemun-Beograd, Srbija

Apstrakt

Histološki nalaz teratoma postoji kod oko 40% od ukupnog broja posthemioterapijskih retroperitonealnih limfadenektomija (PH-RPLA) zbog metastatskog neseminomskog tumora testisa (NSTT). Evaluacija pacijenata podvrgnutih PH-RPLA je imala za cilj da odredi faktore rizika za pojavu recidiva i klinički ishod. Od 193 pacijenata podvgnutih PH-RPLA zbog metastatskog NSTT u periodu između 1980-2005, identifikovali smo 82 pacijenta (42%) kod kojih je nađeno samo prisustvo teratoma u retroperitoneumu. Šestdeset i sedam pacijenata (87%) je primilo samo indukcionu hemioterapiju na bazi cisplatine, dok je 15 (18%) iziskivalo hemioterapiju druge linije. Histologija na PH-RPLA je pokazala prisustvo zrelog teratoma u 86%, nezrelog teratoma u 12% i teratoma sa malignom transformacijom u 2%. Šesnaest pacijenata (19%) je imalo recidiv unutar srednjeg vremenskog intervala od 22 meseca. Od 13 pacijenata podvrgnutih ponovnoj RPLA, različita histologija je nađena kod 6 pacijenata (46%) (2 teratom sa malignom transformacijom, 4 vitalni karcinom), svi sa lošom histologijom u poređenju sa primarnom RPLA. Jedan pacijent je imao recidiv u vidu samo povišenih vrednosti tumorskih markera i preveden je u kompletnu remisiju pomoću samo hemioterapije. Dva pacijenta su imala recidiv posle 21 i 74 meseci sa diseminiranim metastazama i umrli su uprkos salvage hemioterapije. Sedam od 13 pacijenata (54%) koji su prevedeni u ponovnu remisiju sa ponovljenom RPLA, su imali novi recidiv. Svi sem jednog su umrli uprkos salvage tretmana (2 od toksiciteta hemioterapije) sa srednjim vremenom preživljavanja od 86.7+/-26.1 meseci (95% interval poverenja [IP],66.1+/-107.1). Živo i bez znakova tumora je 90% pacijenata pri srednjem praćenju od 135+/-62.6 meseci (95% IP, 98.79+/-149.21). Mogućnost preživljavanja bez recidiva posle 5 i 10 godina je bila 87% i 81%, respektivno. Mogućnost preživljavanja na 5 i 10 godina je bila 98% i 89%, respektivno.

89%, respectively. On multivariate analysis residual mass size (p<0.005) and worse IGCCCG risk group (p=0.01) predicted disease recurrence. Patients with residual teratoma after PC-RPLA continue to exibit a 19% risk of recurrence even 10 years after RPLA, with 46% recurrence being with worse histology. These data support that these patients should undergo long-term surveillance of their retroperitoneum in the setting of a large residual mass or elevated IGCCCG classification risk.

Keywords: teratoma, postchemotherapy, retroperitoneal lymphadenectomy, predictors, outcome.

Na multivarijantnoj analizi veličina rezidualne mase (<0.005) i loša IGCCCG rizična grupa (p=0.01) su bili prediktori za nastanak recidiva. Pacijent sa rezidualnim teratomom na PH-RPLA imaju mogućnost reda veličine 19% za nastanak recidiva čak i 10 godina posle RPLA, sa tim da je bilo 46% recidiva sa lošom histologijom. Ovi podaci podržavaju potrebu za dugotrajnim praćenjem retroperitonealnog prostora kod ovih pacijenata, pogotovu kod onih sa velikom rezidualnom masom ili visokim IGCCCG klasifikacionim rizikom.

Ključne reči: teratom, posthemioterapija, retroperitonealna limfadenektomija, prediktori, ishod.

Introduction

The histologic finding of teratoma occurs in approximately 40% pf all PC-RPLA. The histological potential of teratoma remains unpredictable, with a capacity for local growth or transformation into somatic malignancies such as sarcoma or carcinoma, therefore identifying its presence in the retroperitoneum remains important. However, patients who undergo PC-RPLA may harbor micrometastasis that are undectable with current diagnostic modalities. The incidence of malignant transformation is approximately 3% to 6% in men undergoing PC-RPLA after induction chemotherapy, but increases to 12% and 18% in men undergoing redo-RPLA and in men experiencing late relapse[1-3]. Recurrence rates for patients with teratoma histology at PC-RPLA ranged from 6% to 39%[4,5]. Late recurrences with MT/IMT and TMT have been reported and account approximately 25% and 14% of all late relapse[6,7]. An inadequately controlled retroperitoneum is the most common site of late relapse, and it has been reported that late recurrences of teratoma may be related to the completness of the initial PC-RPLA.

We evaluated patients undergoing initial PC-RLA after induction or 2nd line chemotherapy who where found to have teratoma in the retroperitoneum to determine their clinical outcome. Additionally, we investigated clinical variables to determine predictors for disease recurrence.

Material and methods

Among a survey of 193 patients submitted to PC-RPLA due to metastatic NSTT from 1980 to 2005, we identified 82 patients (42%) who were found to have only teratoma in the retroperitoneum. Teratoma was identified as the presence of MT, IMT and TMT. Patients undergoing extraretroperitoneal surgery were not included in this study, because previous analysis demonstrated that these patients may be at higher risk of relapse and progression independent of tumor histology at surgery[8]. Therefore, 163 fully available patients managed with cytoreductive chemotherapy are included in this study, with occurrence of teratoma in 50% patients.

Clinical and pathologic information was obtained from our prospective database. The IGCCCG risk classification was asigned before induction chemotherapy[9]. Patterns of relapse and subsequent therapies are reported during follow-up according to IGCCCG risk classification and RP histology. Retroperitoneal nodal size before and after chemotherapy was determined by the transverse diameter of the largest mass on computed tomography (CT) imaging. Long-term clinical outcome is reported using the Kaplan-Meier method for disease recurrence and DSS. Differences in survival probabilities were assessed using the long-rank test. Cox proportional hazards regression was used for univariately evaluate variables that may predict for disease recurrence. Variables that were significant at the p=0.05 level in univariare analyses entered in a multivariate Cox regression model. P<0.05 was considered statistically significant, and hazard ratios with 95% CIs were reported for our Cox regression model.

Results

Among 82 patients with only teratomatous elements at PC-RPLA, only 15 (18%) required salvage chemotherapy for persistently elevated STMs, following induction chemotherapy. The majority of patients (56%) presented with advanced stage initially and 16 (74%) had teratoma compound in the primary orchiectomy specimen. Patients were classified based on IGCCCG risk criteria, with good, intermediate-and poor-risk disease in 55 patients (67%), 26 patients (32%) and 1 patient (1%). Pre-RPLA patients characteristics are listed in Table 1.

CHARACTERISTICS	NO. OF PATIENTS (%)
Mean age, ± SD (range)	28.8 ± 3.6 (16-59)
Histology at initial diagnosis	
With teratoma compound	61 (74)
Initial clinical stage	
A (I /IS)	10 (12)
B1/B2 (IIA/IIB)	26 (32)
B3 (IIC)	34 (41)
C (III)	12 (15)
IGCCCG classification	
Low risk	55 (67)
Intermediate risk	26 (32)
Poor risk	1 (1)
Second line chemotherapy	15 (18)

Table 1. PRE-RPLA Characteristics of patients found to have teratoma only at PC-RPLA

The vaste majority of patients with postchemotherapy retroperitoneal nodal size measuring >5cm (63%). The median pre-and postchemotherapy nodal size were 4.0 cm and 3.0 cm, respectively. At PC-RPLA all patients had normal values of STMs. Histology at PC-RPLA revealed MT (86%), IMT (12%) and TMT (2%). Complete PC-RPLA was performed in 80 patients (98%) (Table 2.).

CHARACTERISTICS	NO. OF PATIENTS (%)
PC RP nodal size, cm	
< 5	30 (37)
> 5	52 (63)
Median Pre-C RP nodal size, cm (range)	4.0 (2.5-7.0)
Median Post-C RP nodal size, cm (range)	3.0 (1.5-5.3)
Serum tumor markers at PC-RPLA	
Normal	82 (100)
Histology at PC-RPLA	
Mature teratoma (MT)	70 (86)
Immature teratoma (IMT)	10 (12)
Teratoma With Malignant Transformation (TMT)	2 (2)
PC-RPLA completeness	
Complete	80 (98)

Table 2. PRE-RPLA Characteristics of patients found to have teratoma only at PC-RPLA

Sixteen patients (19%) relapsed within median free interval of 22 months. Among 13 patients submitted to redo-RPLA, discordant histology occurred in 6 patient (46%) (2 TMT, 4 viable GCT), all with worst histology in comparison to primary RPLA. One relapsing patient with only elevated STMs achieved complete response with chemotherapy alone. Two patients relapsed at 21 and 74 months with widespread metastases, and died despite salvage chemotherapy. Seven of 13 patients (54%) who were rendered free of disease with redo-RPLA, relapsed again. All but one died despite salvage treatment (2 of chemotherapy related toxicity) within MST of 86.7+/-26.1 months (95% CI, 66.1-107.1). Overall, at MFU of 135+/-62.6 months (95% CI, 98.79-149.21), AFD are 74 patients (90%) (Table 3. and 4.).

CHARACTERISTICS	NO. OF PATIENTS (%)
	82
Relapses	16 (19)
MFI to relapse, months (range)	22 (2-119) [9 (60%) within 1st 2 years]
Elevated STM only (C)	1 (6)
RP LN (redo-RPLA)	13 (82)
Widespread metastasis (C)	2 (12)
Rendered grossly free of disease	14 (87)
New relapse following CR	7 (54)
DOD/DOC	8 (10)
AFD	74 (90)
MFU, months	135±62.6 (95%CI, 98.79-149.21)

Table 3. Fate and survival following PC-RPLA in patients with residual teratoma

CHARACTERISTICS	NO. OF PATIENTS (%)
	13
Histology	7 (54) MT, 2 (15) TMT, 4 (31) viable GCT
New relapse	7 (54)
Localization of relapse	Metachronous GCT (1)
	RPLN + lung (1)
	RPLN (1)
	Persistently elevated STM (2)
	RP + cervical LN (1)
	Lung + brain (1)
CR to salvage treatment in new relapse	1 (14)
DOD/DOC	6 (46)
AFD	7 (54)
MFU, months	86.7±26.1(90%CI, 66.1-107.1)

Table 4. Fate and survival following REDO-RPLA in patients with residual teratoma

Overall, the 5-and 10-year probabilities of DSS were 97.56% (95% CI, 95.86-99.26) and 88.54% (95% CI, 53.10-94.04), respectively. The probability of being relapse-free after 5-and 10-year was 87.5% (95% CI, 79.2-95.7) and 81.2% (95% CI, 71.4-83.9), respectively.

Patients with unfavorable IGCCG risk classification at initial RPLA are at significantly higher risk for relapse (33% vs. 7%) ($p<0.0001$). Patients with favorable histology at primary RPLA are at significantly lower risk of having worse histology at relapse compared to those with worse histology initially (60% vs. 100%)($p<0.0005$) (Table 5.).

IGCCCG RISK CLASSIFICATION AND INITIAL HISTOLOGY	NO. OF PATIENTS WITH RECURRENCE (%)	MT/IMT NO. PTS. (%)	TMT NO. PTS (%)	VIABLE GCT NO. PTS (%)
IGCCCG risk classification				
Good risk (n=55)	4 (7)	2 (50)	1 (25)	1 (25)
Intermediate/poor risk (n=27)	9 (33)	5 (55)	1 (11)	3 (34)
PC-RPLA histology				
MT/IMT (n=80)	12(15)	7 (60)	1 (8)	4 (32)
TMT (n=2)	1(50)	0	1 (100)	0

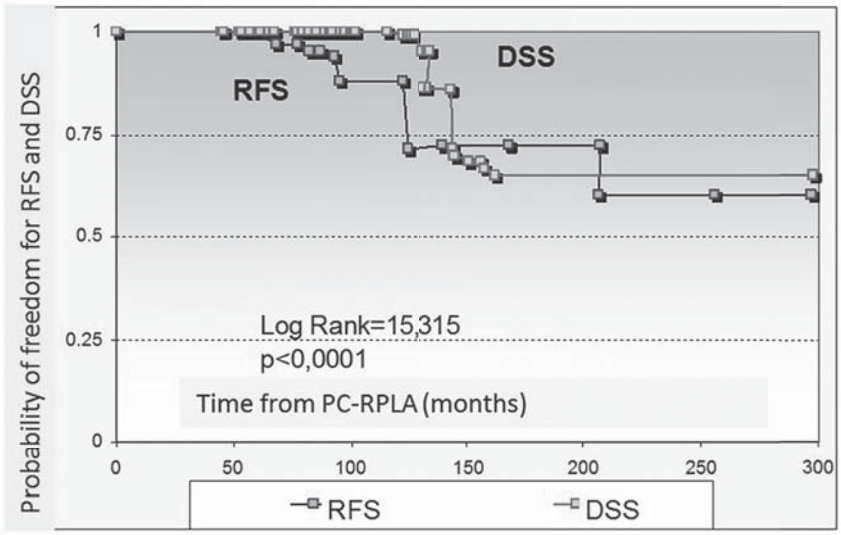
Table 5. Histology of relapses according to the initial IGCCCG risk classificatio and retroperitoneal histology

Worse (TMT/viable GCT) vs. favorable (MT) histology on redo-RPLA predicted unfavorable survival in 1 of 6 patients (17%) vs. 6 of 7 patients (86%) ($p<0.0001$) (Table 6.).

HISTOLOGY	NO. OF PATIENTS	DIED NO. PTS (%)	ALIVE, FREE OF DISEASE NO. PTS (%)
Mature teratoma (MT)	7	1 (14)	6 (86)
Teratoma with malignant transformation (TMT)	2	1 (50)	1 (50)
Viable GCT	4	4 (100)	-
TOTAL	**13**	**6 (46)**	**7 (54)**

Table 6. Clinical outcome in relation to histopathologic analysis on REDO-RPLA

At MFU of 155+/-62.08 and 97.33+/-13.95 months, DSS and RFS are achieved in 90.2% and 80.5%, respectively (Figure 1.)



	TIME (YRS)			
	5 yrs	95% CI	10 yrs	95%CI
DSS	97.56 %	(95.86-99.26)	88.54%	(57.67-66.23)
RFS	87.5 %	(79.2-95.7)	81.2%	(71.4-89.9)

Figure 1. DSS and RFS in patients with finding of teratoma at PC-RPLA

The probabilities of freedom for recurrence were statistically significant between retroperitoneal histology (86% vs. 54%)(p00.01), IGCCCG risk classification (87% vs. 67%)(p=0.02) and nodal size (94% vs. 59%) (p<0.0005)(Table 7.)

CHARACTERISTICS	95 % CI	p
IGCCCG risk classification		
Good risk (n=55)	87 % (76-88)	= 0.01
Intermediate/Poor risk (n=28)	67 % (38-79)	
PC RP RM size, diameter,cm		
< 2 (n=9)	94 % (76-99)	< 0.0005
2-5 (n=21)	91% (82-96)	
> 5 (n=52)	59 % (42-72)	
RP histology at PC-RPLA		
TMT (n=2)	54 % (25-77)	= 0.001
MT/IMT (n=80)	86 % (78-90)	

Table 7. Probabilities of freedom for recurrence according to IGCCCG risk classification, size of PC RP RM size and histology at PC-RPLA

On univariate analysis, higher pre- and postchemotherapy retroperitoneal nodal size (p<0.0005), intermediate/poor IGCCCG risk classification (p=0.02) and the presence of TMT (p00.002), were significant predictors of disease recurrence. In multivariate analysis, retroperitoneal residual mass size (p<0.005) and unfavorable IGCCCG risk group (p=0.01) predicted disease recurrence (Table 8.).

VARIABLES	HAZARD RATIO	95% CI	p
Univariate analysis			
Pre-chemotherapy RP nodal size	1.16	1.08-1.24	< 0.0005
IGCCCG classification			0.02
Good vs intermediate risk	2.86	1.2-6.83	
Good vs poor risk	3.09	1.29-7.39	
2nd line chemotherapy	0.65	0.15-2.75	0.6
Post-chemotherapy RP nodal size	1.15	1.09-1.22	< 0.0005
Histology, MT/IMT vs TMT	4.17	1.69-10.72	0.002
Multivariable analysis			
Post-chemotherapy RP nodal size	1.15	1.07-1.23	< 0.0005
IGCCCG risk, low vs intermediate/poor	3.46	1.63-7.33	0.001
Histology, MT/IMT vs TMT	2.35	0.88-6.28	0.09

Table 8. Cox proportional hazards model evaluating clinical variables predicting for desease recurrence in patients with teratoma after PC-RPLA for methastatic NSTT

Discussion

Our study confirmed that teratomatous elements are present in the retroperitoneum in approximately 40% of patients submitted to PC-RPLA for metastatic NSTT[10]. Despite the histologically benign nature of teratoma, there are significant advantages to complete resection. Unresected teratoma may grow, obstructed, or invade adjecent structures. Additionally, there is the risk of malignant transformation to non-germ cell malignant elements such as sarcoma, adenocarcinoma and primitive neuroectodermal elements. In our series, TMT was present in 2% of patients overall. Patients with teratomatous histology on PC-RPLA have variable clinical course that depends on a complete surgical resection and the presence of unrecognized viable GCT outside the retroperitoneum. At a median follow-up of >11 years, this series provides outcomes for patients with longest follow-up duration published to date. Disease recurrence was identified in 16 of 82 patients (19%), including 4 recurrences with viable GCT and 2 recurrences with TMT. The corresponding 10- year probability of freedom for disease recurrence was 81.2%.

The finding of residual teratoma at PC-RPLA have been assumed to be a favorable prognostic factor. However, several series reported a high frequency of recurrences. Loehrer et al. 4 identified 51 patients with teratoma at PC-RPLA and reported disease recurrence in 20 (30%). The histology of recurrence was distributed evenly between teratoma and viable GCT. Sonneveld et a.l[5] reported disease recurrence in 9 of 51 patients (9.8%), including 5 recurrences with MT, 3 with non-GCT, and 1 with viable GCT. Carver et al.[11] observed disease recurrence in 30 of 310 patients (14%) who had teratoma at PC-RPLA. Ten of those 30 patients (14%) who had developed disease recurrence with MT/IMT, 5 (17%) with TMT, and 15 (50%) had viable GCT. Svatek et al.[12] identified disease recurrence in 21 of 97 patients (22%), including 8 recurrences with viable GCT.

Disease recurrence for patients with finding of teratoma at PC-RPLA is caused by incomplete sugical resection or by unrecognized metastatic disease at the time of surgery. Similar to other series[11,12,] we observed that most recurrences on redo-operation occurred in extraretroperitoneal sites. Wood et al.[13] demonstrated an 8% incidence of contralateral spread of disease among 113 patients with bulky retroperitoneal disease at PC-RPLA. However, many series have shown that bilateral dissection is not necessary in all cases[14-16]. Rabani et al.[17] reported low incidence of teratoma outside the bounderies of a modified template of dissection. To minimize ejaculatory dysfunction, Aprikian et al.[18] removed the mass initially and performed either bilateral or limited RPLA according to results of intraoperative frozen section analysis. All teratomas and viable GCT were located within the macroscopic residual masses. Modified template surgery may be suggested for patients with unilateral localized tumor <5 cm or no palpable residual disease, left-sided primaries, and right-sided testis cancer with absence of MT/IMT or viable GCT in the residual mass.

The possibility of unrecognized disease metastases at the time of surgery must be considered when following patients after PC-RPLA. Viable GCT on redo-RPLA developed in 32% patients despite normal STMs an MT at the time of PC-RPLA.

In an effort to establish appropriate clinical follow-up protocols, some investigators have evaluated variables oredicting for disease recurrence in men after chemotherapy for metastatic NSTT, Loehrer et al.[4] identified the initial tumor burden, the presence of IMT, and mediastinal disease site as significant predictors of disease recurrence on multivariate analysis. Svatek et al.[12] reported that patiens with mediastinal site at presentation or an elevated serum AFP before PC-RPLA were at higher risk for disease recurrence. Our study demonstrated that patients with worse IGCCCG risk classification and those with larger retroperitoneal residual mass (>5cm) are at higher risk of relapse (probability of freedom for recurrence were 87%, 67% and 94%, 91% and 59%, respectively). Although the histologic finding of TMT was not a significant predictor of disease recurrence in our multivariate analysis, these patients have a guarded prognosis, with a probability of freedom for recurrence of 54%. However, our high in-field recurrence rate highlits the importance of complete surgical resection for patients submitted to PC-RPLA for residual teratoma. Therefore, every effort should be made to control the retroperitoneum at PC-RPLA. Furthermore, clinical follow-up should be guided according to the risk of relapse after PC-RPLA for teratoma, such that patients with a high risk of disease relapse should undergo more frequently surveillance with physical examination, determination of STMs, and periodic abdominopelvic and lung imaging. We currently recommend CT imaging once yearly, combined with ultrasound examination af the abdomen and minor pelvis, including a remained testicle, on every check-up visit, although we are currently evaluating wheter this should be performed more frequently in patients at an increased risk for recurrence.

Six of 82 patients (7.3%) in our study died from testis cancer. Similarly, 9 of 97 patients (9.3%) in the Svatek et al.[12] series died of disease. Loehrer et al.[4] also observed that 8 of 51 patients (15.7%) with teratoma at PC-RPLA died. Others reported lower proportion of cancer-related death among their patients. Sonneveld et al.[5] reported incidence of death in 2%, while Carver et al.[11] observed death from disease in 4.7% of their 210 patients. For men relapsed after PC-RPLA with solitary site of metastasis and and normal STMs, redo-resection is the optimal mode of treatment. Patients with widespread metastases and elevated STMs, should receive appropriate salvage chemotherapy followed by surgical resection of any residual metastasis. Patients experiencing recurrence with TMT continue to have a guardeed prognosis, and in our series, one of these is alive.

Our study have several implications for the management and follow-upo of patients who were submitted to PC-RPLA or teratoma. It is the third study which incorporated the IGCCCG risk calssification and postchemotherapy retroperitoneal nodal size measuring >5cm in diameter are adverse predictors of disease relapse. After PC-RPLA, the 10-year DSS and RFS are 88.54% and 81.2%, respectively, highlighting importance of continued follow-up, particularly in patients with adverse prognostic factors. Most relapses at redo-surgery occurred outside the retroperitoneum, indicating the need for meticulous surgery and for careful monitoring of extraretroperitoneal sites. Futhermore, 9 patients (11%) with teratoma had residual lymph node metastasis measuring <2cm in diameter, demonstrating that the retroperitoneum remains difficult to stage clinically. We reported an remarkable outcome in patients submitted to PC-RPLA due to RM <2cm (5-year probability of freedom from relapse, 94%), justifying an aggressive surgical approach for all patients with metastatic NSTT and normal values of STMs following chemotherapy.

In conclusion, patients with residual teratoma after PC-RPLA are at significant risk of progression because of unpredictable nature of teratoma and the presence of unrecognized viable GCT outside the retroperitoneum. Therefore, 19% of patients are at risk of progression even 10 years following completion of primary treatment, with 46% recurrence being with worse histology. These data suggest that these patients should undergo long-term surveillance in the setting of large residual mass and elevated IGCCCG classification risk. Although the indentification of these two risk factors help predict which patients suffer from recurrence, these variables are not sufficiently accurate to be used as the bases for surveillance modification or treatment decisions. Therefore, until improved diagnostic modalities are available to identify patients who harbor micrometastases, patients with teratoma at PC-RPLA should undergo close surveillance and prompt salvage therapy as indicated.

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Literature

1. Sheinfeld J. The rola of adjunctive postchemotherapy surgery for nonseminomatous germ-cell tumors: current concept and contraversies. Semin Clin Oncol 2002;20:262-71.
2. Argirovic D. Late reccurences of germ cell testicular tumours. A population based experience over 23 years. Eur Urol Meet 2007;2(5):38.
3. Argirovic D. Late relapse of germ cell testicular tumors following cisplatin-based chemotherapy. Eur Urol Meet 2007; 8(7):138.
4. Loehrer PJ sr, Hui S, Clarck S, Seal M, Einhorn LH, Williams SD, et al. Teratoma following cisplatin-based combination chemotherapy for nonseminomatous germ cell tumors: a clinicopathologic consideration. J Urol 1986;135:1183-89.
5. Sonneveld DJ, Sleijfer DT, Koops HS, Keemers-Gels ME, Molenaar WM, Hoeckstra HJ. Mature teratoma identified after postchemotherapy surgery in patients with disseminated nonseminomatous testicular germ cell tumors: a plea for an agressive surgical approach. Cancer 1998;82:1343-51.
6. Baniel J, Foster RS, Gonin r, Messemer JE, Donohue JP, Einhorn LH. Late relapse of testicular cancer. J clin Oncol 1995;13:1170-6.
7. Lipphardt ME, Albers P. Late relapse of testicular cancer. World J Urol 2004;22:47-54.
8. Argirovic D, Stanic V, Argirovic A. The impact of residual extra-retroperitoneal masses in patients with advanced nonseminomatous testicular tumors. Eur Urol Meet 2009;8 (8):625.
9. International Germ Cell Cancer Colaboration Group. International Germ Cell Consensus Classification. A prognostic factor-based staging system for metastatic germ cell cancer. J Clin Oncol 1987; 15:594-603.
10. Toner GC, Panicek DM, Heelan RT, Galler NL, Lin S-Y, Bajorin D, et al. Adjunctive surgery after chemotherapy for nonseminomatous germ cell tumors: recommendations for patient selection. J Clin Oncol 1990;8:1683-94.ž
11. Carver BS, Shayegan B, Sergio A, Motzer RJ, Bosl GJ, Sheinfeld J. Long-term clinical outcome after postchemotherapy retroperitoneal lymph node dissection in men with residual teratoma. J Clin Oncol 2007;25:1033-7.
12. Svatek RS, Spiess PE, Sundi D, Tu SM, Tannir NM, Brown GA, et al. Long-term outcome for men with teratoma found at postchemotherapy retroperitoneal lymph node dissection. Cancer 2009;115:1310-7.
13. Wood DP, Herr HW, Heller G, et al. Distribution of retroperitoneal metastases after chemotherapy in patients with nonseminomatous germ cell tumors. J Urol 1992;148:1812-5.
14. Steiner H, Peschel R, Bartsch G. Retroperitoneal lymph node dissection after chemotherapy for germ cell tumours: is a full bilateral template always necessary? BJU Int 2008;19:262-71.
15. Heidenreich A, Pfister D, Wittluhn R, Thuer D, Albers P. Postchemotherapy retroperitoneal lymph node dissection in advanced testicular cancer: radical or modified template resection. Eur Urol 2009; 55: 217-24.
16. Pettus JA, Carver BJ, Masterson T, Stasi J, Sheifeld J. Preservation of ejaculation in patients undergoing nerve-sparing postchemotherapy retroperitoneal lymph node dissection for metastatic testicular cancer. Urology 2009; 73: 328-31.
17. Rabbani F, Goldenberg SL, Gleave ME, Paterson RF, Murray N, Sullivan LD. Retroperitoneal lymphadenectomy for postchemotherapy residual masses: is a modified dissection and resection of residual masses sufficient? Br J Urol 1998; 81:295-300.
18. Aprikian AG, Herr HW, Bajorin DF, Bosl GJ. Resection of postchemotherapy residual masses and limited retroperitoneal lymphadenectomy in patients with metastatic germ cell tumors. Cancer 1994; 74:1329-34.