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Late relapse and fertility issues after testicular germ cell tumors treatment: a ten-year experience

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Background: Testicular germ cell tumors (GCT) can today be cured in the vast majority of patients, the main concerns of survivors being relapse and long term treatment side effects. Although late relapse is associated with a poor prognosis, reliable predictive factors are yet to be identified. Also, the most psychologically burdening treatment side effect (fertility impairment) often does not appear to have specific risk factors.
Methods: A retrospective study over 10 years' period was designed under uniform inclusion criteria for patients diagnosed with advanced (stage II-III) GCT. All patients were evaluated for history of undescended testis, age, treatment, cell types, lymphovascular/ local invasion, and marker levels. Patient's conserved fertility was defined (based on responses to a questionnaire) in terms of children born without any interventions after treatment for GCT.
Results: 114 patients with histologically confirmed GCT, aged 18−77 (median 31), were treated between 1997 and 2006 with cisplatin-etoposide-based CT. Conventional radiation therapy (RT) was performed in 10 patients (8.8%). All 36 (31.6%) patients with normalized tumor markers and retroperitoneal residual masses underwent nerve-sparing retroperitoneal lymph nodes resection (nsRPLND) – in 16 patients, necrosis only; in 20 patients, persistent carcinoma or teratoma, treated with an additional 3 to 4 cycles of BEP. 16 patients (12.9%) had late relapse (median DFS 31.3 months), 9 as distant metastases (3 liver, 6 lung) and 7 patients as lymph node enlargement, irrespective of initial treatment. Median OS is 84.7 months, 96% of the patients currently alive and disease-free. In our study, late relapse prognostic factors were: absence of teratoma in primary tumor, normal pre-CT LDH level and radiological partial response in lymph nodes after CT. 97 out of 114 patients (85%) responded to our fertility questionnaire. 50 tried to have a child and there were 28 children born without any interventions. There was no statistical difference in fertility by type of treatment: CT alone (17/55; 30.9%), CT plus nsRPLND (8/32; 25%) and CT plus RT (3/10; 30%) ($p > 0.1$).
Conclusions: We did not find treatment-related fertility issues, probably because RPLND was performed selectively. Although rare, late relapse justifies long-time clinical and radiological post-therapeutic surveillance of advanced GCT patients. The predictors identified may help to reach a therapeutic decision in selected cases.

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Upfront medical management of clinical stage (CS) I−IIA testicular cancer patients with embryonal carcinoma predominance and/or lymphovascular invasion

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Background: CS I, IIA testicular cancer with embryonal carcinoma predominance (ECP) and/or lymphovascular invasion (LVI) are considered at high risk of relapse. We retrospectively evaluated the outcome of these patients (pts) who were treated by upfront medical management followed by retroperitoneal lymph node dissection (RPLND) in selected cases.
Materials and Methods: Between 1993 and 2003, 188 pts with CSI-IIA non seminomatous germ-cell testicular cancer were treated in our institution. Of these, 110 had evidence of ECP and/or LVI. Seventy seven pts with CSI were managed by surveillance followed by chemotherapy (CT) and surgical exeresis of residual disease in case of relapse and 33 pts with CSIIA underwent upfront CT and RPLND in case of residual masses. Median follow up (MFU) was 54 months (1–131).

	Patients	RPLND	CT	MFU (mo)	% Alive
This series	110	23 (21%)	65 (59%)	54	109 (99%)
Stephenson et al. [1]	267	267 (100%)	82 (30%)	53	267 (100%)

Results: In CSI: 33/77 pts (43%) relapsed: 19 in the retroperitoneum only, 4 in the lung only, 6 in both localizations, 3 had biologic marker elevation only and 1 had relapse in the perineum. Treatment: 18 CT only, 13 both CT and RPLND, 1 CT followed by wedge resection of lung metastases; 1 was lost to follow-up. Median time to relapse was 4.8 months [1−41]. One patient died after RPLND.
In CSIIA: 10/33 pts (30%) required RPLND following CT. Two pts relapsed. One of them had growing teratoma. All pts are still alive with no evidence of disease.
Review of histological specimen at relapse for all pts showed 13 necrosis (54%), 9 teratoma (38%) and 2 residual embryonal carcinoma (8%).
The table summarizes treatment requirements and survival in our series compared to an upfront RPLND management and secondary CT in selected cases.
Conclusion: Upfront medical management is the preferred treatment option for CSI-IIA testicular cancer pts with ECP and/or LVI. Up to 79% of pts avoid RPLND.

References

[1] Stephenson A, Bosl G, Bajorin D, et al.: Retroperitoneal lymph node dissection in patients with low stage testicular cancer with embryonal carcinoma predominance and/or lymphovascular invasion. J Urol 174: 557–560, 2005.

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Immature teratoma in resected post-chemotherapy residual tumors: patient's outcome and prognostic factors

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Background: Unlike other viable malignant germ cell tumors, immature teratoma is characterized by a low proliferative potential and poor sensitivity to chemotherapy (CT). There are no data about prognosis and management of NSGCT pts with resected immature teratoma in post-CT residual masses. We performed this retrospective survey to study the natural history of pts with immature teratoma in resected post-CT residual masses.
Patients and Methods: From December 1987 to May 2006, 315 pts with advanced NSGCT, whose tumor markers were normalized after induction etoposide- and cisplatin-based CT (EP, BEP, C-BOP-3BEP or T-BEP regimens), underwent resection of residual tumor masses in our center. The morphology of resected residual masses was classified according to the worst histological findings presented: carcinoma (n = 58), immature teratoma (n = 15), mature teratoma (n = 97), or necrosis (n =145).
Results: All 15 pts with immature teratoma had testicular primary tumor and initially belonged to good (n = 7), intermediate (n = 3) and poor (n = 5) IGCCCG prognostic groups. 10 post-CT retroperitoneal lymph node dissections, 5 pulmonary resections and 2 supraclavicular LN dissections were performed. 8 pts received 2 cycles of adjuvant CT (commonly VAB-6) after resection. 2 pts died due to massive intraoperative bleeding, which was a complication of retroperitoneal lymph node dissection and there were two other deaths due to disease progression (both pts received adjuvant CT). With median follow-up of 65 (range, 14–150) months, 5-year OS is 69%, which is comparable with OS of pts with resected viable tumor (62%), and lower than resected residual tumor, which contained mature teratoma (82%) only. 'No evidence of disease (NED)' status after surgery was the only prognostic factor: among 11 pts, who became NED, 10 (91%) pts are still alive, compared with 1 (25%) out of 4 pts with persistent residual tumor.
Conclusions: In general prognosis of pts with immature teratoma in resected residual tumor after induction chemotherapy is poor. Aggressive surgery, which attempts to resect all residual masses, can substantially improve the prognosis of pts.

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Individual treatment with stem cell rescue in patients with germ-cell tumours

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Background: Treatment with high dose chemotherapy and autologous stem cell rescue in pacients with poor risk germ cell tumors is still controversial. Results of multicentric randomized EBMT study IT 94 presented at ASCO 2002 show benefit in 1-year EFS in high dose arm