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Recent Developments in Research and Treatment of Testicular Cancer: Highlights from Oncologic Congresses in 2009

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Abstract

Objectives: This paper summarizes new findings on testicular cancer presented at the European Society for Medical Oncology and American Society of Clinical Oncology annual meetings in 2009.
Methods: Data were discussed during the seventh meeting of the European Association of Urology Section of Oncological Urology in January 2010. Selection of data was based on expert experience.
Results: An important molecular study on metastasized and nonmetastasized seminoma tissues showed that presence of metastases can be predicted with 100% specificity based on an 85-gene expression signature. Invasion of the rete testis and age (<30 yr) represented high-risk factors for patients with clinical stage I testicular seminoma, independent from the treatment selected. Long-term results (8 yr) of standard bleomycin (B), etoposide (E), and cisplatin (P) therapy for good prognosis germ cell tumors (GCTs) concluded a continuing survival benefit, with $_3B_{90}E_{500}P$ proving itself as the standard of care. A new individualized treatment protocol based on tumor marker decline in metastatic nonseminomatous germ cell testicular cancer is highly encouraging in all risk groups. But a phase 3 randomized trial with administration of front-line high-dose chemotherapy in poor-prognosis GCTs did not improve treatment outcome. The 20-yr experience with two cycles of PEB showed that late toxicity is rare; the two principal effects of the treatment were higher triglyceride and lower testosterone levels in this group of patients.

Two important studies investigated surgery versus surveillance for postchemotherapy residual masses in patients with metastatic nonseminomatous GCTs (NSGCTs). They both concluded that residual masses <15 mm after primary chemotherapy for metastatic NSGCT may be managed without surgery; no clear conclusions are drawn for larger masses, and further studies are needed. Retrospective analysis of complications of postchemotherapy residual tumor resection showed that full bilateral resection is not necessary in all cases and resection field should be adapted to the localization of disease and size of the mass to minimize complications.

The popular question of whether to use open or laparoscopic surgery for retroperitoneal masses remained unanswered. The results of a short follow-up study (15 mo) favored open surgery for better operating time and lower complication rate and laparoscopic surgery for shorter hospital stay. There was no difference in the rate of distant metastases.
Conclusions: New data presented at these meetings may contribute to improved management of testicular cancer.

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1. Introduction

Testicular cancer represents 1–1.5% of male cancers and 5% of all urologic tumors, with 3–6 new cases occurring per 100 000 males per year in Western society [1]. Testicular cancer usually affects men in the 15–35 yr age group. The histologic type varies, but there is a predominance of germ cell tumors (GCTs) (90–95%). Peak incidence is in the third decade of life for nonseminoma and in the fourth decade for pure seminoma [2]. Testicular cancer is one of the most curable forms of solid neoplasms. With the availability of effective treatment, even for patients with advanced disease, physicians have turned their attention to reduction of morbidity and increased quality of life by altering therapeutic protocols in selected subsets of patients. Surveillance Epidemiology and End Results data show that the 5-yr relative survival rate for all men with this cancer is 95.7%. If the cancer is confined to the testicle, the 5-yr relative survival rate is 99.5%. Even when the cancer has spread to the regional lymph nodes, the 5-yr relative survival rate is 96.3%. If the cancer has spread beyond the lymph nodes, the 5-yr relative survival rate is 70.1% [3].

Interesting data on testicular cancer were presented at the annual meetings of the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO). This paper focuses on the most relevant data presented at these congresses. A selection of abstracts on testicular cancer presented at these congresses was discussed at the seventh meeting of the European Association of Urology (EAU) Section of Oncological Urology (ESOU) in Vienna, Austria, during January 2010.

2. Methods

The selection of the abstracts was made based on expert experience, and no specific selection criteria were used. The data presented in this paper are derived from the published abstracts of the ESMO and ASCO congresses.

3. Diagnosis

3.1. Gene issues

In a preliminary study, Port et al [4] investigated possible gene targets to distinguish metastasized from nonmetastasized seminoma. Total RNA was isolated from metastasized seminoma ($n = 10$), nonmetastasized seminoma ($n = 21$), and corresponding normal tissues. The RNAs were screened on whole genome microarrays and 92 selected gene candidates were quantitatively examined using reverse-transcription quantitative polymerase chain reaction (RTQ-PCR). When $\geq$2-fold differences in gene expression were considered as the threshold value, whole genome microarrays identified 1912 upregulated and 2179 downregulated genes in metastasized seminoma as compared to nonmetastasized seminoma. RTQ-PCR results showed that mean gene expression values of the 92 genes in general were significantly reduced in metastasized seminoma. From these preliminary results, it was concluded that presence of metastases could be completely (100% specificity) predicted based on a selected 85-gene expression signature.

3.2. Patient selection

The Spanish Germ Cell Cancer Group designed a study to investigate high-risk factors for patients with clinical stage I testis seminoma to improve patient selection for risk-adapted therapies [5]. In a prospective study design, 588 patients with a median age of 33 yr and tumor size of 45 mm were enrolled. Three hundred and four patients (51.7%) with risk factors received two courses of adjuvant carboplatin; 284 patients (48.3%) without risk factors were managed by surveillance. After a median follow-up of 48 mo, relapses were less frequent after carboplatin treatment. Independent predictors of relapse were (1) rete testis invasion and (2) age (<30 yr) in the whole series (Table 1). Tumor size, histologic subtype (anaplastic), and serum preoperative beta human chorionic gonadotrophin (β-HCG) levels were not associated with prognosis. The conclusion of this prospective study was that invasion of the rete testis and age (<30 yr) represent high-risk factors for patients with clinical stage I testis seminoma, independent of the treatment selected. This finding may improve patient selection for risk-adapted therapies.

4. Treatment

4.1. Systemic therapy

4.1.1. Long-term results of standard bleomycin, etoposide, and cisplatin therapies for good-prognosis germ cell tumors

The Australia and New Zealand Germ Cell Trials Group reported on long-term outcomes and patterns of relapse in a multicenter randomized trial for good-prognosis GCTs of two

Table 1 – Invasion of the rete testis and age (<30 yr) represent high-risk factors for patients with clinical stage I testis seminoma

	Two courses of carboplatin	Surveillance
Patients, No. (%)	304 (51.7)	284 (48.3)
Relapse rate, %*	3	12
Independent predictors of relapse**	Age <30 yr Rete testis invasion	Age <30 yr Invasion beyond tunica albuginea Microvessel neoplastic invasion

* $p < 0.0001$.
** Cox regression.