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Original article

Effect of the timing of orchiectomy on survival in patients with metastatic germ cell tumors of testis

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Abstract

Objectives: Classically, orchiectomy (OE) is the first step of treatment in patients with metastatic germ cell tumors (mGCTs) of testis. However, some patients have severe symptoms of disease, which require immediate beginning of chemotherapy (CT) followed by OE. This retrospective analysis was performed to find the effect of time constraints of delayed OE on survival in patients with mGCT.

Methods and materials: We analyzed the data of 1,483 CT-naive patients with advanced mGCT of the testis treated in our Department from 1986 to 2009. Delayed OE was performed on 71 (4.8%) patients: seminoma in 8 patients (11.2%), nonseminomatous tumor in 50 patients (70.4%), and unknown tumor histology in 13 patients (18.4%). Twenty percent, 40%, and 40% of patients belonged to good, intermediate, and poor International Germ Cell Cancer Consensus Group prognostic groups, respectively. Median time from the beginning of the CT to OE was 18 (range, 1–250) days. OE was performed on 39 (55%), 21 (29.5%), and 11 (15.5%) patients during cycle 1, cycle 2 to completion of CT, and after the finishing of induction CT, respectively. Median follow-up time was 156 (range, 3–241) months. Etoposide and cisplatin-based CTs were received by 66 patients (93%).

Results: Three-year overall survival (OS) of all 1,483 patients was 75%. An excellent primary tumor response to CT was observed among the patients, who had delayed OE after completion of CT ($n = 11$): only mature teratoma ($n = 4$) and tumor necrosis ($n = 7$) were found. The 3-year OS in patients with delayed OE was 63%. OE performed after completion of CT was associated with better prognosis. The 3-year OS in patients with delayed OE performed during the cycle 1 (group 1) was 67%, cycle 2 to completion of CT (group 2) was 39%, and after finishing of CT (group 3) was 88% (groups 1 vs. 3: hazard ratio 3.7, 95% confidence interval 0.69–10.1, $P = 0.15$; groups 2 vs. 3: $P = 0.01$, hazard ratio 8.1, 95% confidence interval 1.32–18.,72). It seems that if OE had been performed during CT, the beginning of the successive cycle was delayed and dose intensity of CT was decreased.

Conclusions: In case of severe symptoms of disease, which require an immediate start of CT, performing OE simultaneously with other surgeries after completion of induction CT was associated with better OS, when compared with performing OE during induction CT.

Keywords: Germ cell tumors; Delayed orchiectomy; Chemotherapy

1. Introduction

Germ cell tumors are a rare group of tumors. However, these tumors rank first in cancer incidence among young men. In 85% of cases, the primary germ cell tumor is in the testis. In patients with stage I disease, orchiectomy (OE) is the most important part of treatment. In metastatic disease, it is common to perform OE at the first stage, followed by induction chemotherapy (iCT) and resection of residual tumor mass. This mode of treatment achieves cure in a majority of patients [1]. In addition, performing OE before iCT is justified by the presence of the hematotesticular barrier, which leads to poor penetration of chemotherapeutic agents in to the primary tumor [2–4].

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In everyday clinical practice, medical oncologists sometime deal with patients in poor condition caused by a massive tumor burden. These life-threatening cases require immediate start of iCT. In such complex situations, clinicians always face a dilemma whether to perform OE immediately during the cycle 1, or during the successive cycles, or postpone it to the completion of CT as a 1-stage surgery with the removal of residual tumor. In this study, we studied the effect of delayed OE on overall survival (OS) in patients with metastatic germ cell tumors (mGCTs) of testis.

2. Methods

2.1. Patients

It is a single institutional retrospective study. From 1986 to 2009, 1,483 patients were treated for mGCTs of the testis in the Department of Clinical Pharmacology and Chemotherapy, N. N. Blokhin Russian Cancer Research Center (Fig. 1). Eligibility criteria included male patients with primary germ cell tumor in the testis in whom a delayed OE was performed. In circumstances where urgent start of chemotherapy was needed, diagnosis was based on clinical presentation of disease with considerable elevation of serum alpha-fetoprotein (AFP) or human chorionic gonadotropin (hCG). In cases of negative tumor markers, a biopsy before initiation of treatment was obligatory. The study was approved by the institutional review board.

2.2. Pretreatment evaluation

Pretreatment evaluation included physical examination, computed tomography (CT) scanning or ultrasound of the abdomen, CT scanning of the chest or chest x-Ray, and measurement of serum AFP, hCG, and lactate dehydrogenase levels. A contrast-enhanced CT scan or a magnetic resonance imaging scan of the brain was performed in all patients presenting with central nervous system symptoms and in those with serum hCG levels $>$ 50,000 IU/l.

2.3. Treatment program

Treatment consisted of 4 to 6 cycles of BEP (bleomycin, 30 mg: days 1,3, and 5; cisplatin 20 mg/m^2: days 1–5; etoposide 100 mg/m^2: days 1–5, administered every 21 days), T-BEP (paclitaxel, 175 mg/m^2 as a 3-hour infusion: day 2; bleomycin, 30 mg: days 1,3, and 5; cisplatin, 20 mg/m^2: days 1–5; etoposide, 100 mg/m^2: days 1−5, administered every 21 days), or EP (cisplatin, 20 mg/m^2: days 1–5; etoposide, 100 mg/m^2: days 1–5, administered every 21 days). In the 1980s, 4 to 6 cycles of VAB-6 (vinblastine, 4 mg/m^2: day 1; cyclophosphamide, 600 mg/m^2: day 1; dactinomycin, 1,0 mg/m^2: day 1; bleomycin, 30-mg bolus: day 1; bleomycin, 20 mg/m^2 as a 72-hour IV infusion: days 1–3; cisplatin, 120 mg/m^2: day 4, every 28 days) were administered. Number of cycles depended on time to normalization of tumor markers, but never exceeded 6. In cases of slow marker decline, defined as elevated AFP or hCG levels after 3 or 4 cycles of therapy, a further 1 or 2 cycles of iCT were administered. The timing of the OE was classified as during cycle 1, from cycle 2 to completion of CT, or after completion of the iCT. Secondary resection of residual masses, if technically feasible, was planned for all patients who achieved a marker-negative or near marker-negative partial remission.

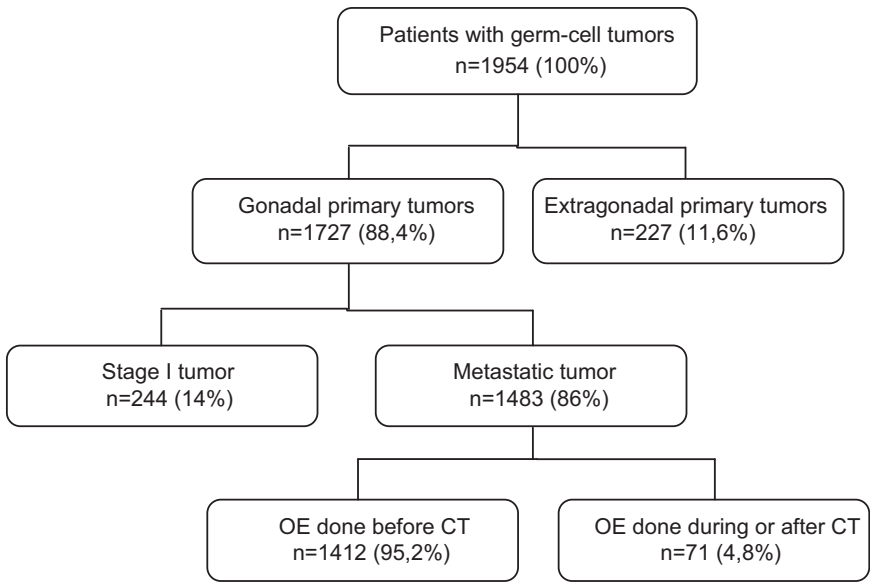

Fig. 1. Distribution of patients with germ cell tumors.