

Relapse of testicular cancer after 15 years

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ABSTRACT

The introduction of cisplatin-based chemotherapy into clinical practice has resulted in a substantial improvement of relapse-free and long-term survival of patients with testicular germ cell tumors. Late relapse (LR) of testicular cancer has recently been described as a unique entity. It is currently defined as tumor recurrence more than 2 years after complete remission following primary treatment, including chemotherapy. The incidence ranges from 2 to 6%, with a median relapse-free interval of 5.4-7.1 years from the initial treatment. Authors report a case of non-seminomatous germ cell tumor of the testis that recurred 15 years after the completion of first-line therapy. Though a few such late relapses have been observed, this condition remains extremely rare. Although the majority of recurrences are encountered in the first 2 years after treatment and later recurrences are rare, their time-course and pattern have implications for long-term follow-up. [Turk J Cancer 2008;38(4):190-193]

KEY WORDS:

Testicular cancer, late relapse, chemotherapy, surgery

INTRODUCTION

Testicular germ cell tumors are highly curable malignancies and only 10-30% of patients have recurrences after initial treatment. The majority of recurrences occur in the first 2 years following treatment. Late relapses are relatively rare; however, time-course and pattern have implications for long-term follow-up. The frequency of late relapses after cisplatin-based chemotherapy of germ cell tumors is 4.3%, and appears to be associated with high initial tumor burden (1). Median relapse-free interval is 5.4-7.1 years from the initial treatment and relapses after 10 years is extremely rare (2-4). Here we report a patient with germ cell tumor experiencing relapse 15 years after the initial diagnosis.

CASE REPORT

A 44-year-old male presented with headache, insomnia and alterations in consciousness. Magnetic resonance imaging (MRI) of the brain showed a mass of 4x5x7 cm in the right occipital lobe, which resulted in edema and shift of the adjacent structures (Figure 1). Prophylactic anticonvulsants and antiedema therapy with dexamethasone were initiated. He had a past history of embryonal carcinoma of the right testis and had undergone orchiectomy and cisplatin chemotherapy 15 years ago. He was in remission, however, he had not have any follow-

up visits since at least 10 years. Physical examination and ultrasonography of left testis was normal and right testis was absent. Laboratory tests revealed increased lactate dehydrogenase (LDH) 846 U/L (N: 230-460) and alpha-fetoprotein (AFP) was over 1000 IU/ml (N: 0-5.8). Blood counts were normal. Computed tomography (CT) of the thorax and abdomen revealed multiple metastases, the largest of which was 12x8x5 cm in pericaval and peripancreatic region resembling to conglomerated lymphadenopathies. He also had visceral metastases, the largest being 3 cm in the lung. Urgent subtotal excision of the cranial lesion was performed and histopathological examination revealed embryonal cell carcinoma. His neurological examinations became normal after surgery. He was treated with whole-brain radiotherapy after metastasectomy.

We decided that these new lesions represented a recurrence of his earlier malignancy. He had remained in remission for 15 years following orchiectomy and single agent cisplatin therapy. We decided to give bleomycin, etoposide and cisplatin combination (BEP), which is considered the current standard of care. After one cycle, he developed deep vein thrombosis in the right popliteal vein and imaging studies showed progression of the intraabdominal conglomerated lymphadenopathies. AFP and LDH increased to 250000 IU/ml and 941 U/L, respectively. Treatment was switched to high dose etoposide at a dose of 1800 mg/m² followed by G-CSF support. He tolerated the therapy well and after the 2nd cycle evaluation a partial response could be achieved, with an AFP of 92000 IU/ml. Then we plan to give high dose chemotherapy with autologous stem cell rescue as a subsequent salvage treatment.

DISCUSSION

It has been postulated that late recurring disease (arbitrarily defined as later than 2 years) has a different natural history when compared to newly diagnosed primary tumors. It is characterized by slow growth, production of AFP, chemoresistance, and poor prognosis (1).

Patients whose late recurrences consisted of teratoma only had the most favorable outcomes. Patients whose late

recurrences consisted of pure “nongerml cell malignant tumor” or pure germ cell tumor (yolk sac tumor or other types) had a much worse prognosis: Patients with two different types of nonteratomatous malignancies in their late recurrences had a dismal clinical course: Furthermore, late recurrence is not likely to respond to chemotherapy and is best treated by surgical excision when possible (5).

Teratoma was the most common type of neoplasm in late recurrences (60%) and teratoma was the only element in 22% these patients. Excluding teratoma coexisting with other types of neoplasms, yolk sac tumor was the most frequent type of tumor in patients with late recurrence. It occurred in 47% of patients either alone or with teratoma. Twenty percent of patients with late recurrence had a nonteratomatous germ cell tumor other than yolk sac tumor, either alone, with yolk sac tumor, or with a “nongerml cell malignant tumor.” Most of these nonteratomatous germ cell tumors other than yolk sac tumor were embryonal carcinoma, like our patients although rarely seminoma and choriocarcinoma were encountered. “Nongerml cell malignant tumors,” including both sarcomas and carcinomas of various types, occurred in 23% of late-recurrence patients, either alone or with a nonteratomatous germ cell tumor (5).

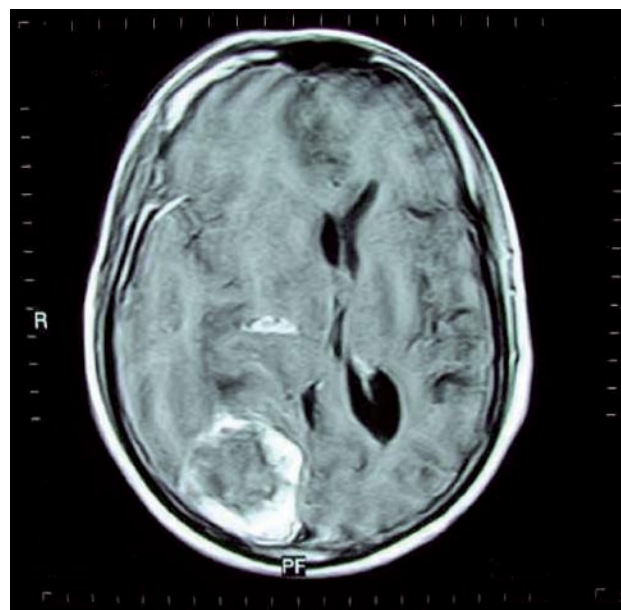


Fig 1. Magnetic resonance images of the brain showing the metastatic mass

The possible explanations for late recurrence of germ cell neoplasms include the following: 1.) malignant degeneration of mature teratoma to germ cell malignancy; 2.) growth of an occult testicular tumor not eliminated by chemotherapy due to the presence of a blood-testicular barrier; 3.) development of a second primary germ cell neoplasm; or 4.) late relapse due to persistent microscopic viable tumor with an atypical less aggressive biologic behavior (6). The last explanation appears to be the most plausible for our patient, as he had had orchiectomy and apparently no residual lesions after chemotherapy.

Shahidi et al. (1) have identified that positive markers at presentation of disease and the presence of differentiated teratomas in post-chemotherapy surgical specimens are significant predictors for risk of recurrence after 2 years.

Risk estimates for synchronous and metachronous contralateral testicular cancers vary widely. Fossa et al. (7) studied that for 29,515 testicular cancer cases and they found that a total of 175 men presented with synchronous contralateral testicular cancer; 287 men developed metachronous contralateral testicular cancer (O/E=12.4, 95% CI=11.0-13.9; 15-year cumulative risk=1.9%, 95% CI=1.7%-2.1%).

Second malignancies in patients with pure testicular seminoma were studied in order to look for adverse late effects of treatment and to study the significance of second malignancies during follow-up. 758 patients received radiotherapy, 76 underwent chemotherapy, 5 had surveillance only. Twenty-two second cancers (13 contralateral testicular tumors, 9 extratesticular malignancies) were recorded. The overall risk of having a second cancer was RR=4.8 (95% CI=3.0-7.3). The risk of having a subsequent testicular tumor is RR=44.8 (95% CI=23.9-76.7). 1.1% of the patients developed a nontesticular second tumor. The risk of having a

nontesticular second cancer is RR=2.1 (95% CI=1.0-4.0). A significantly increased risk was observed for renal cell cancer as well (RR=12.5; 95% CI=1.5-45.1). Increased RR without reaching statistical significance were found for rectal cancer (RR=5.0; 95% CI=0.1-27.9) and non-Hodgkin lymphoma (RR=6.7; 95% CI=0.2-37.1). None of the second cancers were directly located within the radiation field; 5 neoplasms arose at the border of the radiation field. This study confirmed the increased risk of having a second testicular germ cell cancer. There is also a small but definitely increased overall risk of having a nontesticular second cancer (8).

These studies confirmed the increased risk of having a second testicular germ cell cancer. There is also a small but definitely increased overall risk of having a nontesticular second cancer. Second cancer is a real hazard following treatment of testicular cancers and should always be considered during follow-up.

Our patient presented with a life-threatening metastasis and was resistant to BEP regimen. He was then given salvage chemotherapy with high-dose etoposide, a regimen with high activity against resistant and recurrent NSGCT. With this treatment, a partial remission could be obtained and we planned to give high dose chemotherapy with autologous stem cell rescue subsequent salvage treatment (9-12).

Although the majority of recurrences are encountered in the first 2 years after treatment and later recurrences are rare, their time-course and pattern have implications for long-term follow-up. Currently, there is no consensus on the long-term follow-up policy of these patients. We believe that annual follow-up evaluations can allow detecting the majority of late relapses at an asymptomatic stage and should be extended throughout the patient's life.

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