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TREATMENT RESULTS OF STAGE III GERMINAL TESTICULAR TUMORS*

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After Li et al[1] introduced combined drug therapy in 1960, great progress has been made in the treatment of testicular tumors. The complete remission rates have been greatly influenced by the introduction of the VAB regime by the Memorial-Sloan Kettering Cancer Center and other institutions[2]. The development of cis platinum combined regimes brought about a potential cure rate of 45% - 60% in advanced disease[3]. Our experience in stage III germinal testicular tumors is presented.

Material and Methods

Twenty-eight patients with stage III disease treated in the Hacettepe University Department of Urology between 1979 and 1983 are included. Eighty-four percent of our patients had their orchidectomy elsewhere. Their ages ranged between 16 and 40, with a mean age of 27.4 years. Nine out of the 28 patients had seminoma, and their ages ranged between 16 and 40 with a mean age of 32 years. The 19 with non-seminomatous tumors were aged between 19 and 38, with a mean age of 25.3 years. The histopathological distribution of the tumors is presented in Table I. The average follow-up was 20.5 months.

TABLE I

The Histopathological Distribution of Stage III Germinal Testicular Tumors

Histopathological diagnosis	Number of patients		(%)
Seminoma	9		32
Nonseminomatous tumors	19		68
Embryonal carcinoma	6	21	
Choriocarcinoma	1	4	
Mixed type	12	43	
Total	28		100

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Staging

All patients underwent the usual diagnostic investigations for clinical staging of the tumor. These included hemoglobin, WBC, chest X-ray, liver function tests, excretory urography, whole-lung tomography, bipedal lymphangiography, abdominal ultrasonography, CT scanning and tumor markers, i.e. alphafetoprotein (AFP) and beta subunit of human chorionic gonadotropin (β HCG).

Metastatic disease beyond the retroperitoneum, and/or palpable abdominal mass or metastasis in abdominal organs were accepted as stage III. The criteria for clinical staging of the patients are presented in Table II.

TABLE II

The Criteria for Clinical Staging of Patients with Stage III Testicular Tumors

Histopathological type	Abdominal lump		Distant organ metastasis		Abdominal lump + distant organ metastasis		Elevated markers		Total
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.
Seminoma	8	(89%)	1	(11%)	0	(0%)	–	–	9
Nonseminomatous tumors	7	(37)	5	(26%)	6	(32%)	1	(5%)	19
Total	15	(54%)	6	(21%)	6	(21%)	1	(4%)	28

Chemotherapy Regimens

All patients were treated by a chemotherapy regimen consisting of cis platinum + vinblastine + bleomycin once in 3 weeks for 4 cycles. The dosage and administration of the drugs are summarized in Table III. After 4 cycles of this treatment the patients were reassessed for clinical response. Response to treatment was considered to be complete remission (CR) when all measurable disease disappeared and partial remission when there was a measurable decrease in metastatic disease.

After 4 cycles of chemotherapy patients with CR were followed up with monthly examinations. All other patients were considered non-responders and treated with cis platinum + Vepesid® (Table III).

Results

The clinical response after 4 cycles of PVB chemotherapy is summarized in Table IV. A complete response rate of 45% was achieved in stage III seminoma. The CR rate of nonseminomatous tumors was 21% highest (25%) in the group with a mixed type of histopathology. Progression after 4 cycles of PVB was noted to be 11% for seminoma and 26% for nonseminomatous tumors. It is clear that the most malignant tumor is choriocarcinoma (Table IV).

TABLE III

Chemotherapy Regimens used in the Treatment of Stage III Germinal Tumors

A. Regimen 1.			
Cis platinum	(P) : 20 mg/m^2	IV 1st-5th days	Repeat cycles every 3 weeks.
Vinblastine	(V) : 0.15 mg/kg	IV 1st and 2 nd days	
Bleomycin	(B) : 30 mg	IV 2nd day	Weekly for 12 weeks.
B. Regimen 2.			
Cis platinum	: 20 mg/m^2	IV 1st-5th days	Repeat cycles every 3 weeks.
Vepesid	: 100 mg/m^2	IV 1st, 3rd, 5th days	

TABLE IV

The Clinical Response after 4 Cycles of PVB Chemotherapy

No. of evaluable patients	Complete remission		Partial remission		No change		Progression	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
9	4	(45%)	3	(33%)	1	(11%)	1	(11%)
19	4	(21%)	9	(48%)	1	(5%)	5	(26%)
6	1	(17%)	2	(33%)	1	(17%)	2	(33%)
1	0	(0%)	0	(0%)	0	(0%)	1	(100%)
12	3	(25%)	7	(58%)	0	(0%)	2	(17%)
28	8	(29%)	12	(43%)	2	(7%)	6	(21%)

Seminoma

Nonseminomatous tumors

Embryonal carcinoma

Choriocarcinoma

Mixed type

Total

Table V summarizes the prognosis of patients with different histopathological diagnoses during the follow-up period. A disease-free survival of 33% was achieved in patients with seminoma during a mean duration of follow-up of 26.9 months. Twenty-one percent of the patients with nonseminomatous tumors were disease-free after 17.7 months. Patients with mixed types of tumors which responded quite well to 4 cycles of PVB chemotherapy had a high rate of mortality (67%).

TABLE V

The Prognosis of Stage III Testicular Tumors Treated by Various Regimens of Chemotherapy

No. of evaluable patients	Patients surviving disease-free		Patients surviving with disease		Deaths		Mean duration of survival till death (in months)	Mean duration of follow-up (in months)
	No.	(%)	No.	(%)	No.	(%)		
9	3	(33%)	4	(45%)	2	(22%)	16	26.9
19	4	(21%)	2	(11%)	13	(68%)	17.1	17.7
6	1	(17%)	1	(17%)	4	(66%)	25	20
1	0	(0%)	0	(0%)	1	(100%)	19	19
12*	3	(25%)	1	(8%)	8	(67%)	15.9	16.5
28	7	(25%)	6	(21%)	15	(54%)	16.9	20.5

Seminoma

Nonseminomatous tumors

Embryonal carcinoma

Choriocarcinoma

Mixed type

Total

* One patient had a lumpectomy of the abdominal mass after chemotherapy when he had negative markers.

Among patients with nonseminomatous tumors who had only distant organ metastasis, two patients out of 5 are still alive without evidence of disease and one patient is living with disease. Three out of 7 patients who had a lump in the abdomen in their first assessment are still alive. One patient is disease-free, one patient is living with disease and the third patient had a lumpectomy after chemotherapy and is now alive without evidence of disease.

The patients who had a lump in the abdomen plus distant organ metastasis and the patient who had elevated levels of markers are all dead. All patients with seminoma had normal levels of tumor markers, whereas all patients with nonseminomatous tumors had elevated levels after orchidectomy.

Serious complications of chemotherapy were sepsis, angioneurotic edema, deep vein thrombosis, anemia and leucopenia (Table VI).

TABLE VI

Complications of Chemotherapy

Complication	No. of patients
Sepsis, bone marrow depression	1
Angioneurotic edema, deep vein thrombosis	1
Anemia (fall in Hb level≥3 gm)	1
Leucopenia (<3000)	1
Sepsis	1
Total	**5**

Discussion

The progress which has been made in the chemotherapy of this particular malignancy is due to the availability of new drugs which were tested by clinical observations. Various combinations of chemotherapeutic drugs achieved a complete response rate ranging from 51% to 74%[4]. Einhorn and Donohue[5] reported a complete response rate of 74% using cis platinum + vinblastine + bleomycin.

Paschal et al[6] used modified PVB and despite a 90% complete response among patients with minimal disease, none of their patients with advanced abdominal disease responded to this particular modality. Einhorn and Williams[7], however, obtained a 50% complete remission in patients with advanced abdominal disease. Green et al[8] stated that 4 cycles of PVB is not as effective in the patients who have bulky disease as in the low volume disease. Even using a modified Einhorn schedule, others did not achieve any complete remission in patients who had bulky disease in the abdomen[9].

As in our series and the above mentioned ones, survival of patients with high volume metastasis is lower than of those with pulmonary metastasis only.

Vepesid can be used in combination with cis platinum as the first line combination chemotherapy in this particular group of patients in order to achieve better results.

Initially high dose cyclophosphamide was used as a single drug regime for the patients who had advanced stage seminoma, but a cis platinum + vinblastine + bleomycin regime is as effective in patients with seminoma as for nonseminomatous tumors[10]. A complete response rate of 63% has been reported[10].

Although drug toxicity still remains a problem in treating these patients, complications of our patients did not necessitate either any major dosage modifications or termination of treatment.

Summary

Twenty-eight patients with stage III germinal testicular tumor were treated between 1979 and 1983 with an average follow-up of 20.5 months. Chemotherapy consisting of cis platinum + vinblastine + bleomycin was given once in three weeks for 4 cycles. The patients with complete remission were followed up at monthly examinations, while all other patients were treated with cis platinum + Vepesid® . One patient with a mixed testicular tumor who had a lump in the abdomen and negative markers was treated surgically.

After 4 cycles of chemotherapy, complete remission was obtained in 45% of the patients with seminoma and in 21% of the patients with nonseminomatous tumors. The progression rate was 11% and 26%, respectively.

Serious complications of chemotherapy were sepsis, angioneurotic edema, deep vein thrombosis, anemia and leucopenia.

High volume metastasis and increased levels of tumor markers were the worst prognostic features.

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