

E-JCRT Correspondence

Late relapse of testicular cancer: Recurrence after 24 years and treatment with chemotherapy alone

ABSTRACT

Late relapse of testicular cancer, defined as >2 years interval between initial treatment and recurrence, is a rare disease with the incidence rate of 2.6%. Due to its chemoresistant features, treatment options of late relapses are controversial while surgical approach and cisplatin-based chemotherapies can be considered. We report here a patient with nonseminomatous germ cell tumor who experienced relapse 24 years after his first diagnosis. After detecting left supraclavicular lymphadenopathy and absence of any other malignant lesion in positron emission tomography-computerized tomography, patient was treated with three cycles of VeIP regimen (vinblastine/ifosfamide/cisplatin). Second complete response to this treatment was achieved with chemotherapy alone.

KEY WORDS: Late relapse, nonseminoma, salvage chemotherapy, seminoma, testicular cancer

INTRODUCTION

Late relapse of testicular cancer (LRTC) is a rare event with the incidence rate of 2.6%.^[1] Late relapse is commonly defined as recurrences beyond 2 years after achieving complete response to initial treatment.^[2,3] Testicular cancer is known as responds well to chemotherapy, while late relapses are characterized by presentation with chemoresistance feature.^[4] Treatment modalities of LRTC are dependent on histologic subtypes. Cisplatin-based chemotherapies are more likely the treatment of choice in seminoma patients. Surgical approach is considered the most important part of previously chemotherapy-treated nonseminoma patients.^[1]

We report here a patient with nonseminomatous germ cell tumor who experienced relapse 24 years after his first diagnosis and who achieved a second complete response with chemotherapy alone.

CASE REPORT

This was a case report of a 32-old-male patient presented with a solid mass in his left testis, in 1988. Computerized tomography (CT) scan revealed a 3 cm lymph node in the retroperitoneal area. Laboratory evaluations were beta human chorionic gonadotropin (bHCG) 650 IU/l, alpha fetoprotein (AFP) 25 ng/ml and lactate dehydrogenase 250 U/l. Patient underwent a left orchiectomy and pathological examination revealed

nonseminomatous germ cell tumor and was treated according to the BEP regimen (bleomycin/etoposide/cisplatin) with three cycles. After the treatment, tumor markers of patient reduced to the normal levels. Retroperitoneal lymph node dissection (RPLND) was performed due to detection of 1 cm paraaortic lymph node and pathologic examination confirmed the lesion as necrotic tissue. Patient was under-control with the status of no evidence of disease until March 2012. After 24 years from his original diagnosis, left supraclavicular lymphadenopathy developed and his AFP level increased to 98 ng/ml. Tru-cut biopsy demonstrated adenocarcinoma infiltration and it was unsuccessful to specify the primary malignancy. F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET-CT) was performed due to determine the primary lesion. PET-CT showed a left supraclavicular hypermetabolic lymph node (SUVmax: 16.3), which measured 4.0 cm × 3.8 cm and no other abnormalities or lesions [Figure 1]. Testicular ultrasonography revealed atrophy in remained right testis with no sign of mass. Given his clinical history of testicular cancer and absence of primary malignant lesion, patient was treated as relapsed testicular cancer with three cycles of VeIP regimen (vinblastine/ifosfamide/cisplatin). After this treatment, the mass disappeared and his AFP levels reduced to 0.4 ng/ml [Graph 1]. Patient remains with no evidence of disease 14 months after the treatment that was concluded with complete response.

Emre Akar,
Deniz Tural¹,
Deniz Arslan²,
Cumhur İbrahim
Başsorgun³,
Özcan Yıldız⁴

Cerrahpasa Medical Faculty, Istanbul University, Istanbul, Departments of ¹Medical Oncology, and ³Pathology, School of Medicine, Akdeniz University, Antalya, Departments of Medical Oncology, ²Erzurum Research and Education Hospital, Erzurum, ⁴School of Medicine, Istanbul Medipol University, Istanbul, Turkey

For correspondence:

Dr. Emre Akar,
Medical Student,
Cerrahpasa Medical Faculty, Istanbul University, TR-34098 Istanbul, Turkey.
E-mail: emrevonakar@gmail.com

Access this article online

Website: www.cancerjournal.net

DOI: 10.4103/0973-1482.137915

Quick Response Code:



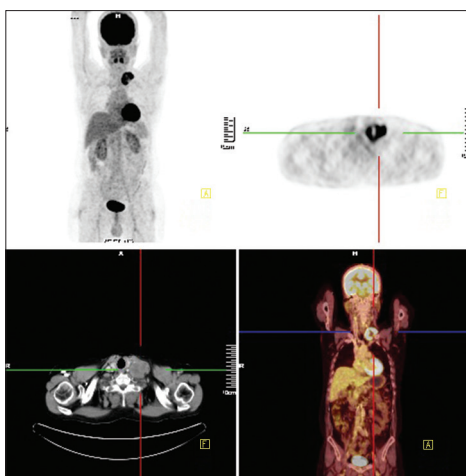


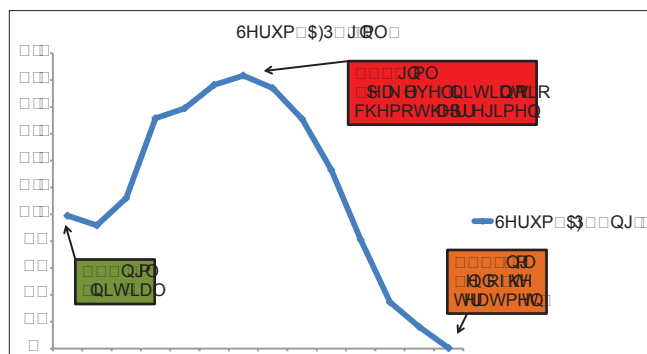
Figure 1: Positron emission tomography PET-computerized tomography images of the patient

DISCUSSION

About 10-30% of initially treated testicular cancer patients experience recurrence despite highly curable feature of these tumors. Recurrences commonly occur in the first 2 years after treatment.^[5] LRTC, defined as >2 years interval between initial treatment and recurrence, is not a completely understood event because of the wide variety of patient and tumor characteristics. Exact definition of LRTC, inclusion and exclusion criteria for late relapsing patients, prior treatments and initial chemotherapy regimens are different, which make it difficult to arrive at common conclusion. Withal, a few numbers of studies have been published to determine a consensus. A pooled analysis of 5880 patients with testicular cancer revealed late relapse in 119 of 3704 (3.2%) and in 31 of 2176 (1.4%) patients with nonseminoma and seminoma, respectively.^[1]

The most frequent site of late relapses in both seminoma and nonseminoma patients are the retroperitoneal space followed by the chest (lung and mediastinum). Neck and supraclavicular area are the third common recurrence site accounting for 6.5% and 14.5% with nonseminoma and seminoma, respectively. Moreover of the symptoms aroused from recurrence area (back pain or palpable mass), elevated AFP or human chorionic gonadotropin are signs for detection of LRTC.^[1] AFP plays a predominant role for to detect asymptomatic patients in annual follow-up evaluations.^[6] In our patient, AFP was useful for verification of diagnosis that was adenocarcinoma, confusingly. Decrease in levels of AFP also confirmed the response to treatment.

Treatment options in LRTC depend on histologic subtype of recurrence tumor and prior treatments. Teratoma may be found in both initial seminoma and nonseminoma and a cure is achieved only by a complete resection in these patients.^[7] In seminoma, radiotherapy and cisplatin-based chemotherapy are the treatment options. Relapses after single-agent carboplatin



Graph 1: Serum alpha fetoprotein AFP levels of the patient

are mostly salvaged by cisplatin-based chemotherapy or by radiotherapy. Relapse after cisplatin-based chemotherapy is very rare. VeIP regimen has been shown efficient in these patients. Surgery might be considered in selected patients, but it seems to be less often applied than in nonseminoma.^[1,8] In nonseminoma, chemoresistance features of late relapses restrict the success of chemotherapy-based approaches. Hence, complete surgical resection seems to be more appropriate prospect for a cure in patients with localized LRTC.^[9] Nevertheless, VeIP regimen achieved a continuously disease-free status, but in a minority of patients (15-24%).^[1] In consideration of these treatment options, best approach to obtain cure is a multi-disciplinary decision that should be made in experienced centers. In current patient; surgery wasn't performed due to patient's request. However, the result obtained from chemotherapy shows that evidence-based regimens are noteworthy in case of patients unwillingness to have surgery.

F-18 FDG-PET is very specific for staging in testicular cancer. Although PET is not generally used in the routine staging, it can be useful in detecting disease that is not evident on CT. PET-CT should be considered as the initial diagnostic test to identify and locate the site of recurrence in patients who are found to have high tumor marker levels alone at follow-up.^[10] On the other hand, Pfannenber *et al.* found the high percentage of lesions have a false-negative PET results with the low sensitivity of 62% and the low negative predictive value of %48 in a prospective study, which evaluated PET after high-dose chemotherapy in patients with metastatic non-seminomatous germ cell tumors.^[11] In our patient, PET-CT was performed due to, reveal whether there is second primary malignancy. However, there was no other PET-avid lesion and supraclavicular lymphadenopathy was thought to be adenocarcinoma component of testicular cancer recurrence with elevated AFP levels.

Indeed, 24 years is very long time interval for relapse of cancer that was agreed on as "cured disease." There are some publications regarding very long time periods between initial diagnosis and late relapse in testicular cancer. Reports from Kohei *et al.* (21 years), Kalaitzis *et al.* (23 years), Pavic *et al.* (32 years) and Mukhtar *et al.* (42 years) emphasize the importance of long-term follow-up that is necessary for early-detection of recurrences.^[12-15]

REFERENCES

1. Oldenburg J, Martin JM, Fosså SD. Late relapses of germ cell malignancies: Incidence, management, and prognosis. *J Clin Oncol* 2006;24:5503-11.
2. Sharp DS, Carver BS, Eggener SE, Kondagunta GV, Motzer RJ, Bosl GJ, *et al.* Clinical outcome and predictors of survival in late relapse of germ cell tumor. *J Clin Oncol* 2008;26:5524-9.
3. Ehrlich Y, Baniel J. Late relapse of testis cancer. *Urol Clin North Am* 2007;34:253-8.
4. Lipphardt ME, Albers P. Late relapse of testicular cancer. *World J Urol* 2004;22:47-54.
5. Shahidi M, Norman AR, Dearnaley DP, Nicholls J, Horwich A, Huddart RA. Late recurrence in 1263 men with testicular germ cell tumors. Multivariate analysis of risk factors and implications for management. *Cancer* 2002;95:520-30.
6. Gerl A, Clemm C, Schmeller N, Hentrich M, Lamerz R, Wilmanns W. Late relapse of germ cell tumors after cisplatin-based chemotherapy. *Ann Oncol* 1997;8:41-7.
7. Baniel J, Foster RS, Gonin R, Messemer JE, Donohue JP, Einhorn LH. Late relapse of testicular cancer. *J Clin Oncol* 1995;13:1170-6.
8. Miller KD, Loehrer PJ, Gonin R, Einhorn LH. Salvage chemotherapy with vinblastine, ifosfamide, and cisplatin in recurrent seminoma. *J Clin Oncol* 1997;15:1427-31.
9. Geldart TR, Gale J, McKendrick J, Kirby J, Mead G. Late relapse of metastatic testicular nonseminomatous germ cell cancer: Surgery is needed for cure. *BJU Int* 2006;98:353-8.
10. Rutherford EE, Ferguson JL, Geldart TR, Mead GM, Smart JM, Tung KT. Late relapse of metastatic non-seminomatous testicular germ cell tumours. *Clin Radiol* 2006;61:907-15.
11. Pfannenber AC, Oechsle K, Bokemeyer C, Kollmannsberger C, Dohmen BM, Bares R, *et al.* The role of [(18) F] FDG-PET, CT/MRI and tumor marker kinetics in the evaluation of post chemotherapy residual masses in metastatic germ cell tumors – Prospects for management. *World J Urol* 2004;22:132-9.
12. Kohei N, Kinoshita H, Kamoto T, Terai A, Kakehi Y, Ogawa O. Late relapse of testicular cancer 21 years after first complete remission: A case report. *Hinyokika Kiyo* 2008;54:39-42.
13. Kalaitzis C, Bantis A, Tsakalidis G, Giannakopoulos S, Sivridis E, Touloupidis S. Osteolytic bone destruction resulting from relapse of a testicular tumour 23 years after inguinal orchiectomy and adjuvant chemotherapy: A case report. *J Med Case Rep* 2009;3:8702.
14. Pavic M, Meeus P, Treilleux I, Droz JP. Malignant teratoma 32 years after treatment of germ cell tumor confined to testis. *Urology* 2006;67:846.e11-3.
15. Mukhtar S, Beatty J, Agrawal S, Christmas TJ, Jameson C, Huddart RA. Germ cell tumour: Late recurrence after 43 years. *Ann R Coll Surg Engl* 2011;93:e24-6.

Cite this article as: Akar E, Tural D, Arslan D, Bassorgun CI, Yildiz O. Late relapse of testicular cancer: Recurrence after 24 years and treatment with chemotherapy alone. *J Can Res Ther* 2015;11:661.

Source of Support: Nil, **Conflict of Interest:** None declared.

