Testicular Cancer in Soetomo Hospital Surabaya Retrospective Study

by Ade Indra Mukti

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TESTICULAR CANCER IN SOETOMO HOSPITAL SURABAYA : RETROSPECTIVE STUDY

[1]Ade Indra Mukti, [1]Sunaryo Hardjowijoto, [1]Wahjoe Djatisoesanto, [1]Lukman Hakim.

[1]Department of Urology, Faculty of Medicine/Universitas Airlangga, Soetomo General Hospital, Surabaya.

ABSTRACT

Objective: *The aim of this study was to determine the characteristics of the testicular cancer that were managed in Soetomo Hospital.* ***Materials & Methods:*** *This was a retrospective descriptive study. We reviewed the medical records of patient with testicular tumor admitted in Soetomo Teaching Hospital Surabaya, from January 2008 until December 2013. The data regarding demographic characteristics, clinical presentation, grading and staging based on pathological examination result, and the management of the cancer. Data was presented in tabular and narrative in order to know the number and percentage of testicular cancer in Surabaya.* ***Results:*** *There were 46 patients with testicular cancer with mean age of 27.1 ± 7.9 years. Peak incidence was 15–35 years old (54%). Testicular mass was the most frequent clinical presentation in 42 patients (91%), abdominal mass and other complaints in 4 patients (9%). Most of the patients live outside Surabaya in 34 patients (72%). Location of the tumor was more frequently in scrotum, which occured in 42 patients (91%). A total of 4 patients (9%) were found to have a history of UDT. Based on the TNM staging, patients with stage pT3 were as many as 20 patients (43%), pT4 11 patients (24%), pT2 7 patients (15%) and pT1 4 patients (9%). In regional lymph nodes staging (N) N3 were as many as 26 patients (57%), N0 9 patients (20%), N2 5 patients (11%) and N1 2 patients (4%). Metastase staging (M) M0 was found in 27 patients (58%) and M1 tumor was found 42%. The major pathological finding was seminoma in 37 patients (80%), Yolk sac tumor in 4 patients (9%), Embryonal Ca in 1 patient (2%), Teratoma in 1 patient (2%) and mixed germ cell tumor in 3 patients (7%). The most widely theraphy was underwent orchidectomy followed by PEB chemotheraphy in 29 patients (64%), 3 patients (6%) underwent EBRT and PEB chemotheraphy, 5 patients (11%) underwent PEB chemotheraphy, There were 9 patients (19%) underwent orchidectomy alone. Group of seminoma tumor show normal limit of tumor marker α-FP and β-HCG and increased in non seminoma.* ***Conclusion:*** *Testicular cancer mostly appears in younger males. Most of testicular cancer was seminoma, diagnosed in advanced stage with metastase 42% of the patient. Most of the patients received orchidectomy followed by PEB chemotheraphy.*

Keywords: *Germ cell tumor, testicular cancer, radical orchidectomy.*

ABSTRAK

Tujuan: *Tujuan penelitian ini adalah untuk menentukan karakteristik kanker testis yang dirawat di RSUD Dr. Soetomo Surabaya.* ***Bahan & cara:*** *Penelitian ini adalah penelitian deskriptif retrospektif. Kami mereview rekam medis pasien dengan tumor testis yang datang ke RSUD Dr. Soetomo Surabaya, dari bulan Januari 2008 sampai Desember 2013. Data-datanya termasuk karakteristik demografi, presentasi klinis, grade dan stage berdasarkan hasil penilaian patologi, dan perawatan kanker. Data ditampilkan dalam tabel dan narasi untuk mengetahui angka dan persentase kanker testis di Surabaya.* ***Hasil:*** *Terdapat 46 pasien kanker testis dengan rerata usia 27.1 ± 7.9 tahun. Puncak kejadian adalah antara 15–35 tahun (54%). Massa testis adalah yang paling sering muncul pada 42 pasien (91%), massa abdominal dan keluhan lain pada 4 pasien (9%). Sebagian besar pasien tinggal di luar Surabaya 34 pasien (72%). Lokasi tumor lebih sering pada skrotum, yang muncul pada 42 pasien (91%). Sebanyak 4 pasien (9%) memiliki riwayat UDT. Berdasarkan stage TNM, pasien dengan stage pT3 sebanyak 20 pasien (43%), pT4 11 pasien (24%), pT2 7 pasien (15%) and pT1 4 pasien (9%). Pada daerah stage getah bening (N) N3 sebanyak 26 pasien (57%), N0 9 pasien (20%), N2 5 pasien (11%) dan N1 2 pasien (4%). Stage metastase (M) M0 ditemukan pada 27 pasien (58%) dan tumor M1 ditemukan sebanyak 42%. Temuan patologi yang utama adalah seminoma pada 37 pasien (80%), tumor Yolk sac pada 4 pasien (9%), kanker embrional pada 1 pasien (2%), teratoma pada 1 pasien (2%) dan sel tumor gabungan pada 3 pasien (7%). Terapi yang paling banyak digunakan adalah orkidektomi disertai dengan kemoterapi PEB pada 29 pasien (64%), 3 pasien (6%) menjalani EBRT dan kemoterapi PEB, 5 pasien (11%) menjalani kemoterapi PEB, terdapat 9 pasien (19%) menjalani hanya orkidektomi. Kelompok tumor seminoma menunjukkan batas normal tumor marker α-FP dan β-HCG dan meningkatkan non seminoma.* ***Simpulan:*** *Kanker testis lebih banyak muncul pada laki-laki muda. Sebagian besar kanker testis adalah seminoma, didiagnosa stadium lanjut dengan metastase pasien 42%. Sebagian besar pasien mendapatkan orkidektomi disertai dengan kemoterapi PEB.*

Kata kunci: *Tumor sel kuman, kanker testis, radikal orkidektomi.*

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Correspondence: Ade Indra Mukti, c/o: Department of Urology, Faculty of Medicine/Universitas Airlangga, Soetomo General Hospital. Jl. Mayjend. Prof. Dr. Moestopo 6-8, Surabaya 60286. Phone: +62 31 5501318; Fax: +62 31 5024971. Mobile phone: 0811636809. Email: indra2885@gmail.com.

INTRODUCTION

Testicular cancer is relatively rare. In many countries, however, it is the most common cancer among men aged 15 to 40 years.[1] Testicular cancer is an uncommon malignancy, accounting for 1–2% of all tumours in men and 5% of all urogenital tumors.[2] The incidence of testicular cancer has been increasing over the last 30–40 years.[1] However, it is important because its incidence is increasing worldwide, particularly in white Caucasian populations, it occurs most commonly in young males, and is curable in most instances.[2]

There has been an increase in the incidence of testicular cancer in many Western countries over the past 40 years and the global incidence of testicular cancer has doubled over the past three decades.[1,2] The age-standardized incidence rate is a summary measure of a rate that a population would have if it had a standard age structure. Age-standardized incidence rates are used to compare incidence rates of disease between populations with different age distributions, as is the case with testicular cancer. The age standardized incidence rate is expressed as the number of new cases per 100.000 person years, and is calculated first by estimating the age-specific rates and then applying these rates to the reference population. The most frequently used reference population is the world standard population. There is marked geographical variation in the age standardized incidence rate for testicular cancer, ranging from as low as 0.5/100.000 in Egypt to as high as 9.2/100.000 in Denmark.[2]

Ninety four percent of testicular tumors are Germ Cell Tumors (GCT). The incidence of testicular seminoma is increasing compared to that of non-seminoma GCT. GCT can be categorized as seminoma and nonseminoma (NSGCT) based on its pathology and treatment.[3] In United States of America about 8400 people had Testicular Cancer and 380 people died because of it.[4] Germ Cell Tumor incidence is increasing around the world. In United States of America, its prevalence rate among patient with age 15 until 49 years old increased from 2.9 per 100.000 in 1975 became 5.1 per 100.000 in 2004. The incidence rate of Seminoma is higher than NSGCT. Prevalence rate of Testicular Tumor tend to increase, 55% in 1973 became 73% in 2001. About 10% until 30% of the cases will come with far metastasis.[4] The data from Surveillance Epidemiology and End Result (SIER) Program (1973-1998) shows that the risk of having Seminoma among Caucasian men in United States of America is increasing.[5,6] Based on a study about testicular cancer at Soetomo General Hospital in 2008 until 2013, there were 37 testicular seminoma cases (80%), 4 yolk sac tumor cases (9%), 1 embryonal tumor case (2%), 1 teratoma case (2%), and 3 mixed germ cell tumor cases (3%).

OBJECTIVE

The aim of this study was to determine the characteristics of the patients, age, history of undescencus testes, tomor marker, pathological result and kind of treatment that were managed in our department.

MATERIAL & METHODS

This was a retrospective descriptive study. Data on age, location of tumor, staging, serum levels of the tumor marker place of living, history of undescencus testes and variety of treatment were obtained from medical records of patient with testicular tumor and has been managed in Soetomo Teaching Hospital Surabaya from January 2008 to December 2013, and analyzed using SPSS 17.0.

Patients diagnosed with testicular tumor based on the histopathology of the specimen taken from the surgery. We record identity of patient, age, history operation and tumor marker. Staging of patient also describe with TNM classification. Treatment was record base on each patient, from kind of surgery and kind of chemotheraphy. No special treatment in this study.

Data were analyzed by descriptive statistic and presented in table and graphic to describe variety of the data patient of testicular cancer in our clinic.

RESULTS

There were 46 patients with testicular cancer with mean age of 27.1 ± 7.9 years old in

Soetomo Teaching Hospital from January 2008 – December 2013. In Soetomo Teaching Hospital the age distribution peak incidence was 15–35 years old (54%), most of them was live outside Surabaya and referred to Surabaya because of limited treatment (Table 1).

Table 1. Characteristic based on age & residence.

Characteristic	N	(%)
Age (years)		
< 15	10	22
15–35	25	54
> 35	11	24
Residence		
Surabaya	12	28
Outside	34	72

Patient who came to Soetomo hospital mostly complaint with lumps in scrotum area and feel discomfort with the condition, in about 42 patient (91%). Undescencus testes were found only 4 patient (9%) because they reliazed after fell mass intraabdomen with abscent one of the testis (Table 2).

Table 2. Characteristic based on location of tumor.

Characteristic	N	(%)
Location		
Scrotum	42	91
Intraabdomen	4	9
History UDT		
With	4	9
Without	42	91

Tumor marker was one of diagnostic tools in soetomo hospital for testicular cancer, every suspicious of testicular mass after palpate in physical examination, we check serum tumor marker, after operation we evaluate tumor marker with pathological result to confirm and the possibility of residual tumor. Most of testicular cancer in our hospital was seminoma, about 37 patients (80%) with increase of serum tumor marker alpha fetoprotein (AFP) 10 patient (21%) and beta-human chorionic gonadotropin (β-HCG) 11 patients (24%) from all testicular patient. Non seminoma pathological result after operation about 20 % from all tumor. There are 4 patient (9%) with yolc sac tumor with increased of serum tumor marker AFP 3 patient (7%) and β-HCG 1 patient (2%). There is only 1 patient with embryonal cancer pathology result (2%) with no increase of serum tumor marker. For teratoma pathology there is also only 1 patient (2%) with no increase of tumor marker. The other were mixed pathological result about 3 patients (7%) with increased of serum tumor marker AFP 2 patients (4%) and β-HCG for 1 patient (3%) (Table 3).

Table 3. Characteristic based on pathological & tumor marker.

Characteristic	N	(%)
Seminoma	37	80
AFP	10	21
B-HCG	11	24
Yolk sac	4	9
AFP	3	7
β-HCG	1	2
Embryonal Ca	1	2
AFP	0	0
β-HCG	0	0
Teratoma	1	2
AFP	0	0
β-HCG	0	0
Mixed	3	7
AFP	2	4
β HCG	1	3

Tabel 4. Characteristic based on stage.

Characteristic	N	(%)
Tumor		
T1	4	9
T2	7	15
T3	20	43
T4	11	24
Nodes		
N0	9	20
N1	2	4
N2	5	11
N3	26	57
Metastase		
M0	27	58
M1a	8	18
M1b	11	24

Testicular cancer was classified based on TNM staging after perform MSCT abdomen and operation, patient came to our hospital was more frequently in late stadium after the mass getting bigger and disturb their activity. Most of tumor (T)

Tabel 5. Characteristic based on treatment.

Characteristic	N	(%)
Treatment		
Radical orchidectomy	9	19
Chemotheraphy	5	11
Radical orchidectomy + Chemotheraphy	29	64
Radical orchidectomy + Chemotheraphy + EBRT	3	6

stage was T3 about 20 patients (43%), followed by T4 for 11 patients (24%), T2 for 7 patients (15%) and T1 for 4 patients (9%). Beside of tumor mass, patient mostly came to our hospital because of abdominal mass and breathless after node getting bigger in the abdomen and compliate to other organ. In regional lymph nodes, most of node (N) was N3 about 26 patients (57%), followed by N0 for 9 patients (20%), N2 for 5 patients (11%) and N1 for 2 patients (4%).

Incidence testicular cancer for metastase (M) in our hospital for M0 was 27 patients (58%), followed by M1b for 11 patients (24%) and M1a for 8 patients (18%) (Tabel 4).

A total of 46 patients with testicular cancer in Soetomo Hospital discussed for the most suitable for the patients. Before treatment we educate and informed about the risk and complication in the future.

DISCUSSION

Testicular cancer is the most common cancer found in men age 15–35 years old. The incidence was rare at the age under 15 years old or more than 60 years old. Overall was 1-2% of malignant cancer in man, and also one of tumor that have good quality of life if treated exactly. Testicular seminoma often happen in the 4th decade of live, while nonseminoma often happen in the 3rd decade of live. Incidence among children only 0.5–2.0 per 100.000 population, the age distribution in children also different than in adult.[7] Based on study result, there are 25 testicular cancer patients with average age is 27.1 ± 30.9 years old.

Most of the patient lived outside Surabaya, because of limited trearment from their origin, patients who came to Surabaya also referred because there still limited of urologist from outskirt hospital. Chemotheraphy and external radiation also only available in big city like Surabaya as a result most of patient with testicular cancer reffered and gathered in Surabaya. In this study as many as 34 patients (72%) came from outside Surabaya.

The most important factor that considered having correlation with testicular cancer is cryptorchidismus history on the testis. About 7–10% testicular cancer patients have cryptorchidismus history, seminoma is the common testicular cancer that happen among this kind of patients. Cryptorchidismus raises the cance of having testicular cancer 4 until 6 times higher. The risk is higher in testis located intra abdominal (1 in 20 cases), and significantly lower in testis located in inguinal (1 in 80 cases)[4] Based on study result, tumor located in scrotum as many as 42 patients (91%), than intra abdomen, 4 patients (9%). History of UDT presences in 4 patients (9%).

Although fetal AFP serum level is high, after 1 year old, it becomes very low.[4] AFP will not increase in pure seminoma or choriocarcinoma.[3] Increasing level of Beta-hCG is not happened in pure embryonal cell carcinoma, this cancer cell doesn't contain syncytiotrophoblast, increasing level of AFP in pure embryonal cell carcinoma is rare and if it is happened, it usually accompanied by yolk sac tumor.[8] There are many combination of mixed tumor, usually it consists of embryonal cell carcinoma, seminoma, yolk sac, teratoma or synctiotrophoblast. Based on the type of base cells, AFP level usually increases in yolk sac tumor, and Beta hCG level increases if the element of syncytiotrophoblas exists.[8] Tumor marker serum is an important value for diagnosis (before orchiectomy) also for prognosis (after orchiectomy). AFP and β-hCG are increasing in 50-70% and 40-60% patients with nonseminomatous germinal cell tumor (NSGCT). The increasing of one or two tumor markers is happened in almost 90% NSGCT. β-hCG increases in almost 30% of seminoma patients during the progression of the disease. LDH is a non specific tumor marker, its concentration increasing equal to tumor volume. β-hCG usually increases in 80% testicular cancer patient with older age. Placenta

Alkali Fosfatase (PLAP) is a tumor marker that can be checked in patient with pure seminoma, but it is not recommended for smoker.[8] Based on study result, 37 patient were diagnose with seminoma from pathological result with 10 patients (21%) are with increasing concentration of AFP, β-hCG concentration is increasing in 11 patients (24%).

Seminoma is highly sensitive to platinum-containing chemotherapy. The present data show that moderate elevation of serum β-hCG levels is common in metastatic seminoma and appears not to influence the results of combination chemotherapy. It's clear that residual masses are common after completion of chemotherapy for advanced seminoma, particulary if disease is bulky initially. These masses resolve slowly over months, and in some instances, years. Seminoma is a highly chemo-responsive tumour in which the influence of tumour volume on the outcome chemotherapy appears to be less obvious tham is the cases for non-seminomas although residual masses are commonly present one month after completion of chemotherapy.[9]

Non seminoma tumor also obtained in this study, yolk sac tumor increase serum tumor marker for the most part of the case, around > 90% was occurred, more than 85% was diagnosed limited to the testis and not yet spread to other organs, and most of them managed with radical orchidectomu alone. Based on this study there are 4 patients (9%) histologically show yolk sac tumor with increasing of AFP 3 patients (7%) and the other show increase of β-HCG. In embrional carcinoma there is no increase of β-HCG serum marker, these cells was not contain of *syncytiotrophoblast,* serum marker AFP rarely increase in pure embrional carcinoma. Some condition which increase serum marker generally coincided with yolk sac tumor, in this study only 1 patient (2%) histologically show embrional ca which no increase of serum tumor marker.

Mixed tumor happen with a lot of combination of variety pathology testicular tumor, such as seminoma, yolk sac, teratoma, etc. All combination depend on composer of the cell type, increase of serum tumor marker AFP ussualy accured if cell type based on yolk sac tumor, the other hand increased of β-HCG happend if there is element of *syncytiothropoblast*.[8] In this study we found 3 patient (7%) with mixed tumor where 2 patient (4%) was increased of serum marker AFP and 1 patient with increased of serum marker βHCG.

Tumor stadium was determined based on TNM system from EAU Guideline as a standart of clinical stadium, in this study we obtain most of tumor (T) stage was T3 about 20 patients (43%), followed by T4 for 11 patients (24%), T2 for 7 patients (15%) and T1 for 4 patients (9%). For lymfe node regional we found most of node (N) was N3 about 26 patients (57%), followed by N0 for 9 patients (20%), N2 for 5 patients (11%) and N1 for 2 patients (4%). And for metastasis disease who spread to non regional lymfe node or lungs, we found metastase (M) for M0 was 27 patients (58%), followed by M1b for 11 patients (24%) and M1a for 8 patients (18%). Testicular cancer in our hospital mostly not yet spread to other organ, some of them have spread to other organ like lungs and bones.

Most of the treatment were perform radical orchidectomy followed by chemotheraphy BEP because of spreading to the lymph node, there are as many as 29 patients (64%), for patient with localized tumor we successfully only performed radical orchidectomy without chemotheraphy, there were about 9 patients (19%). Some patient unfit to performed radical orchidectomy because of condition of the tumor as a result we only performed chemotheraphy BEP without resection of the tumor, there were as much as 5 patients (11%). And the last we performed combination of surgery followed by chemotheraphy and external radiation as many as 3 patients (6%) (Tabel 5).

The gold standart treatment for testicular cancer was radical orchidectomy, this procedure performed by clamp funiculus spermaticus in ingunal area before resection of the testis completely. Seminoma testis was sensitive to external radiation, more than 95% stasium I seminoma only performed radical orchidectomy followed with radiation at retriperitoneal region. Advanced stage of seminoma with increase of serum marker AFP, the first choised treatment was chemotheraphy platinum based, 90% patients with testicular cancer in advanced stage have good result treatment with chemotheraphy.[8,10,11]

For Non Seminoma germ cell tumor (NSGCT) with early stadim, *retroperitoneal lymph node dissection* (RPLND) after radical orchidectomy was therapeutic option. Advanced stage non seminoma with large mass in retroperitoneal or has spreaded, treated with chemotheraphy platinum base combine after radical orchidectomy. If serum tumor marker show normal limit and from radiology CT scan show residual mass after chemotheraphy, then the residual mass must be taken because there was risk to grow into tumor for 20% and 40% become teratom or fibrosis. In this study patient who performed radical orchidectomy only was 9 patients (19%), 5 patients (11%) only perform chemo-

theraphy, 3 patients (6%) performed chemotheraphy with radiation, and most of the patients (64%) performed radical orchidectomy followed by chemotheraphy platinum base such as BEP in Soetomo General Hospital Surabaya.

CONCLUSION

Testicular cancer mostly appears in younger males, who live outside of Surabaya. Largely they come to the hospital in advanced stadium, with total patients 46 patients in 5 years. Testicular seminoma is the most frequently testicular cancer obtained in Surabaya. Radical orchidectomy follow with chemotheraphy were most widely treatment which is conducted.

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