CARCINOMA TESTIS PROFILE IN TERTIARY HOSPITAL

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ABSTRACT

Objective: *This study was undertaken to estimate the epidemiological characteristics, histological types, and subtypes of testicular neoplasm according to the WHO classification in our patient group.* ***Material & Methods:*** *This was a retrospective study done over a period of ten years from January 2010 - December 2020 in our institution. Histopathological slides were retrieved and reviewed for tumour. Testicular Neoplasm patients who underwent orchidectomy and chemotherapy clinical data including the patient's age, tumor location, tumor side, pathological finding, tumor marker, chemotherapy regiment, prognosis, chemotherapy response, and side effect were observed. All the data were analyzed descriptively and using SPSS 17.0.* ***Results:*** *A total of 31 cases of testicular and paratesticular neoplasm were encountered in our study with a mean age of 32.5 years. The highest incidence was 15-35 years old (48.3). Scrotum mass was the most frequent clinical presentation (70.96%) and left side became the predominant area (52%). Most of the patients come in late stage T3 (51.61%) and N3 (67.74%) with no metastatic process (70.96). The major pathological finding was Seminoma (64.51%), Teratoma (16.12), Yolk Sac (12.9%), Embryonal, and Mixed (3.22%). AFP, B-HCG, and LDH were elevated in some Seminoma, Teratoma, and Yolk Sac groups. The most wide chemotherapy used was 4 series BEP (87.09%). Patient prognosis highest incidence were Intermediate (70.96%). Most of the patients showed complete response (67.74) of chemotherapy. Nausea, vomiting, alopecia, and mucositis were observed as chemotherapy side effect in all patients.* ***Conclusion:*** *Testicular neoplasm peak incidence appears in young male. Most patients come to health care service in late stage. Seminoma become the highest testicular neoplasm incidence in our study. Elevated tumor markers were found in some patients. Four cycle BEP chemotherapy regiment showed great outcome for these patients.*

Keywords: *Epidemiological, histological, testicular neoplasm.*

ABSTRAK

Tujuan: *Penelitian ini dilakukan untuk memperkirakan karakteristik epidemiologi, tipe histologis dan subtipe neoplasma testis menurut klasifikasi WHO pada kelompok pasien kami.* ***Bahan & Cara:*** *Studi retrospektif dilakukan selama sepuluh tahun dari Januari 2010 - Desember 2020 di institusi kami. Slide histopatologi diambil dan ditinjau untuk tumor. Pasien Neoplasma testis yang menjalani orkidektomi dan kemoterapi data klinis termasuk usia pasien, lokasi tumor, sisi tumor, temuan patologis, penanda tumor, regimen kemoterapi, prognosis, respon kemoterapi dan efek samping diamati. Semua data dianalisis secara deskriptif dan menggunakan SPSS 17.0.* ***Hasil:*** *Sebanyak 31 kasus neoplasma testis dan paratestikular ditemukan dalam penelitian kami dengan usia rata-rata 32.5 ± 16.2 tahun. Insiden tertinggi pada usia 15-35 tahun (48.3).Massa skrotum merupakan gambaran klinis yang paling sering (70.96%) dan sisi kiri menjadi area yang dominan (52%). Sebagian besar pasien datang pada stadium akhir T3 (51.61%), N3 (67.74%) tanpa proses metastasis (70.96). Temuan patologis utama adalah Seminoma (64.51%), Teratoma (16.12), Yolk Sac (12.9%), Embrional dan Campuran (3.22%). AFP, B-HCG dan LDH meningkat pada beberapa kelompok Seminoma, Teratoma, Yolk Sac. Kemoterapi yang paling banyak digunakan adalah BEP 4 seri (87.09%). Prognosis pasien dengan insidensi tertinggi adalah Intermediate (70.96%). Sebagian besar pasien menunjukkan respon lengkap (67.74) dari kemoterapi. Mual, muntah, alopecia, mukositis diamati sebagai efek samping kemoterapi pada semua pasien.* ***Simpulan:*** *Insiden puncak neoplasma testis muncul pada pria muda. Sebagian besar pasien datang ke pelayanan kesehatan pada stadium lanjut. Seminoma menjadi insiden neoplasma testis tertinggi dalam penelitian kami. Penanda tumor yang meningkat ditemukan pada beberapa pasien. Resimen kemoterapi BEP empat siklus menunjukkan hasil yang bagus untuk pasien ini.*

Kata kunci: *Epidemiologi, histologis, neoplasma testis.*

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INTRODUCTION

Testicular neoplasm consists of different types, depending on the cell of origin and the typical age at presentation, but germ cell-derived tumours account for the vast majority of cases. Germ cell tumours can be diagnosed in any age group, but more than 90% of cases occur in young men. These tumours, consisting of seminomas and nonseminomas, originate from germ cell neoplasia in situ (GCNIS).

The pathogenesis of testicular tumours associated with GCNIS partially overlaps with another developmental disorder of the male reproductive system, in testicular dysgenesis syndrome (TDS). Testicular somatic cell tumours, known as sex cord-stromal neoplasms, are rare but can have endocrine manifestations, such as precocious puberty or gynecomastia. In addition to its malignant characteristics, testicular neoplasm is a developmental, endocrine and reproductive problem.[1-2]

Testicular germ cell tumour (GCT) represents a malignancy with many unusual features: It is a rare disease with only 8-10 per 100 thousand men per year in northern European countries. In contrast to most other malignancies, this neoplasm has a peak incidence in young men aged 20-45 years, and most notably, more than 90% of cases are curable. GCT can involve a complex spectrum of characteristics with multiple histology and clinical and pathological stages (pT), with all of these features relevant to therapeutic decision-making.

Clinically, the most relevant characteristics consisted of histology, clinical stage and pT, primary tumour size, age, and serum biomarkers of beta-human chorionic gonadotropin (β-HCG), alpha-fetoprotein (α-AFP) and lactate dehydrogenase (LDH). Although these characteristics are fundamentally well recognized, the possible interrelationships between the various parameters are still poorly understood.[3-4]

Indonesia has ethnic variations and different geographical distributions, but data on the clinical presentation of testicular tumours and their management are still underreported. This study aimed to determine the clinical profile, treatment modalities, and survival of testicular tumours in the Indonesian population, especially Malang.

OBJECTIVE

The aim of this retrospective study to determine carcinoma of the testis characteristics of patients, age, tumor location, tumor side, pathological finding, tumor marker, chemotherapy regiment, prognosis, chemotherapy response and side effect.

MATERIAL & METHODS

This research was conducted at our institution and carried out from December 2020 to January 2021. This research is retrospective, using a medical record database in the study period 2010 to 2020. Inclusion criteria were patients diagnosed testicular neoplasm based on histopathology of the specimen. All the patients underwent orchidectomy and followed by chemotherapy treatment.

Thirty-one patients were included in this research. We record patients age, tumor location, tumor side, pathological finding, tumor marker, chemotherapy regiment, prognosis, chemotherapy response and side effect. TNM classification for testicular cancer was used to describe tumor stage.5 All the data were analyzed descriptively and using SPSS 17.0.

RESULTS

A total of 31 cases of testicular and paratesticular neoplasms were found in our study, with a mean age of 32.5 years.The age distribution peak incidence was 15-35 years group with 15 patients (48.3%) followed by >35 years group 12 patients (38.8%) and <15 years group 4 patients (12.9%). The location of neoplasm mostly in scrotum with 70.9% and left side become predominant area (Table 1).

NCCT of the abdomen and operation procedure were performed to evaluate the neoplasm staging. The testicular neoplasm was classified based on TNM staging. Our hospital data showed us, most of the patient seeking medical treatment in the late stage. Tumor (T) size, T3 become the highest incidence of testicular neoplasm with 16 patients (51.61%) followed by T2 with 7 patients (22.58), T4 with 6 patients (19.35%), and T1 with 2 patients (6.45%).

Nodus (N) involvement in occur in 27 patients while 4 patients (12.9%) come without

nodus involvement, N3 with 21 patients (67.74%) followed by N2 with 4 patients (12.9%), N1 with 2 patients (6.45%). Incidence of metastasis (M) in our hospital describe for M0 with 22 patients (70.96%) followed by M1a and M1b 5 patients (16.12%) 4 patients (12.9%) respectively (Table 2).

Table 1. Characteristics based data.

Characteristics	N	%
Age (years)		
<15	4	12.9
15-35	15	48.3
>35	12	38.8
Location		
Scrotum	22	70.96
Intraabdominal	8	25.80
Inguinal	1	3.22
Side		
Right	15	48
Left	16	52

Table 2. Tumor Staging.

Characteristics	N	%
Tumor		
T1	2	6.45
T2	7	22.58
T3	16	51.61
T4	6	19.35
Nodes		
N0	4	12.9
N1	2	6.45
N2	4	12.9
N3	21	67.74
Metastasis		
M0	22	70.96
M1a	5	16.12
M1b	4	12.9

Tumor marker become standard protocol for suspicious tumor disease for diagnostic tools. This study checked the tumor marker serum before and after surgery followed by chemotherapy with or without radiation therapy. There were three tumor serum marker that we analyze in our hospital, AFP, B-HCG, and LDH. The increasing result serum marker result measure from the cut off value of all the tumor marker based on EAU Guideline on Testicular Cancer.[6]

Histological assessment of all the patients showed us, most of the testicular neoplasm was seminoma 20 patients (64.51%) with increased AFP 9 patients (29.03%), B-HCG 8 patients (25.8%), LDH 1 patient (3.22%). Followed by Yolk Sac 4 patients (12.9%) with increased AFP 3 patients (9.67%), B-HCG 1 patient (3.22%), and LDH 1patient (3.22%). Teratoma 5 patients (16.12%) with increased AFP 1 patients (3.22%), B-HCG 1 patient (3.22%), LDH 1 patient (3.22%). Both Embryonal and Mixed pathological result only 1 patient with no elevated tumor marker serum (Table 3).

Table 3. Pathological and Tumor Marker.

Characteristics	N	%
Seminoma	20	64.51
AFP	9	29.03
B-HCG	8	25.8
LDH	1	3.22
Yolk Sac	4	12.9
AFP	3	9.67
B-HCG	1	3.22
LDH	1	3.22
Embryonal	1	3.22
AFP	0	0
B-HCG	0	0
LDH	0	0
Teratoma	5	16.12
AFP	1	3.22
B-HCG	1	3.22
LDH	1	3.22
Mixed	1	3.22
AFP	0	0
B-HCG	0	0
LDH	0	0

There are several chemotherapy regiments that we used in our hospital for treated testis carcinoma. Carboplatin and Four series of Bleomycin, Etoposide, Platinum (BEP) and Paclitaxel, Ifosfamide, and Platinum (TIP) were used as chemotherapy regiment. BEP regiment become the most chemotherapy treatment used with 27 patients (87.09), followed by TIP 3 patients (9.67%) and Carboplatin 1 patient (3.22%). Patient prognosis was classified according to the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification.[6] The incidence of intermediate prognosis group was 22 patients (70.96%), followed by Poor prognosis group 6 patients (19.35) and Good prognosis group 3 patients (9.67%) (Table. 4).

Patient chemotherapy response divide into three groups consist of, Complete, Partial, Stable

Disease, and Progressive. Complete response become the highest chemotherapy outcome with 21 patients (67.74%) followed by progressive 5 patients (16.12%), partial 3 patients (9.67%), and stable desease 2 patients (6.45%) respectively. Chemotherapy side effect were observed in all chemotherapy regiment. Nausea, vomiting, alopecia, and mucositis were found in all patients, but no lung fibrotic was observed in this study.

Table 4. Chemotherapy and Prognosis.

Characteristics	N	%
Chemotherapy		
BEP 4 Series	27	87.09
TIP 4 Series	3	9.67
Carboplatin	1	3.22
Prognosis		
Good	3	9.67
Intermediate	22	70.96
Poor	6	19.35

Table 5. Chemotherapy Response and Side Effect.

Characteristics	N	%
Chemotherapy Response		
Complete	21	67.74
Partial	3	9.67
Stable Disease	2	6.45
Progressive	5	16.12
Chemotherapy Side Effect		
Nausea, Vomiting	31	100
Alopecia	31	100
Mucositis	31	100
Lung Fibrotic	0	0

DISCUSSION

Testicular neoplasm is the most common malignancy in young adult men (aged 15–40 years).[7] Testicular neoplasm incidence has been increasing over the last 30 to 40 years.[8] Incidence rates among young white men in Nordic countries are more than 10 times higher than those observed among black and Asian men.[9] In this research finding the highest age group incidence was 15-35 years old with average age 32.5±16.2.

The testicular neoplasm was classified based on TNM staging. Our hospital data showed us, most of the patient seeking medical treatment in the late stage. Tumor (T) size, T3 become the highest incidence of testicular neoplasm with 16 patients (51.61%) followed by T2 with 7 patients (22.58), T4 with 6 patients (19.35%), and T1 with 2 patients (6.45%). Nodus (N) involvement in occur in 27 patients while 4 patients (12.9%) come without nodus involvement, N3 with 21 patients (67.74%) followed by N2 with 4 patients (12.9%), N1 with 2 patients (6.45%). Incidence of metastasis (M) in our hospital describe for M0 with 22 patients (70.96%) followed by M1a and M1b 5 patients (16.12%) 4 patients (12.9%) respectively. Stage 3 was the most common stage at presentation for all tumor variants.[11-13]

Testicular Neoplasms are classified based on their cell of origin: seminomatous, non-seminomatous, Leydig, Sertoli, choriocarcinoma, embryonal, teratoma, and yolk-sac derivatives.[14] Seminomas were the most common cases in the 10-year study conducted at the RSSA. This study data showed the major pathological finding was Seminoma (64.51%), Teratoma (16,12), Yolk Sac (12.9%), Embryonal and Mixed (3.22%). Cools et al (2011) in an epidemiological study of germ cell tumors showed that seminomas are the most common testicular Neoplasm in most countries with tumor registers.

Serum tumour markers AFP, B-HCG, and LDH represent valuable tools for the clinical management of GCTs.[15] AFP is a 70 kDa glycoprotein produced by cells of the yolk sac tumour and rarely by embryonal carcinoma.[16] B-HCG is a 38 kDa glycoprotein produced by syncytio-trophoblastic giant cells mainly in chorionic carcinoma.[17] LDH is a glycolytic enzyme that is present in all cells of the human body and that is released from cells upon cell death. Due to its unspecific origin, the clinical usefulness of LDH is less than that of the other two markers.[17]

Based on the biological diversity of GCTs, it was early recognized that not all GCTs have elevations of these markers and that the frequencies of elevation correlate with histology and tumour burden.[18] A recent meta-analysis revealed a prevalence rate of LDH in 40-60% of all GCT cases.[19] AFP is exclusively found to be elevated in 10-60% of non-seminomatous GCTs. BHCG is elevated in 10-40% of nonseminomas and 15-20% of seminomas while prevalence rates depend on clinical stages.[20]

The present data from our hospital showed us, most of the testicular Neoplasm was seminoma

20 patients (64.51%) with increased AFP 9 patients (29.03%), B-HCG 8 patients (25.8%), LDH 1 patient (3.22%). Followed by Yolk Sac 4 patients (12.9%) with increased AFP 3 patients (9.67%), B-HCG 1 patient (3.22%), and LDH 1 patient (3.22%). Teratoma 5 patients (16.12%) with increased AFP 1 patients (3.22%), B-HCG 1 patient (3.22%), and LDH 1 patient (3.22%). Both Embryonal and Mixed pathological result only 1 patient with no elevated tumor marker serum.

The standard of care in testicular neoplasm is mainly based on the integration between primary surgery and platinum-based chemotherapy.[22] Chemotherapy results in excellent cure rates in TC due to chemosensitivity to Cisplatin-based regimens.[23] In stage IIa and IIb seminomas, radiotherapy or 3 cycles of BEP chemotherapy may be offered for these patients.[24]

BEP regiment become the most chemotherapy treatment used in our study with 27 patients (87.09) followed TIP 3 patients (9.67%) and Carboplatin 1 patient (3.22%). Patient prognosis was classified according to the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification.[10] The incidence of intermediate prognosis group was 22 patients (70.96%), followed by Poor prognosis group 6 patients (19.35) and Good prognosis group 3 patients.

The chemotherapy side effect data showed us all the patients experience nausea, vomiting, alopecia, and mucositis but no lung fibrotic was observed in this study. With respect to quality of life, in the comparison of three versus four cycles, there were significant differences in favor of three cycles for physical functioning, role functioning, cognitive functioning, fatigue, nausea and vomiting, appetite loss, and overall quality of life.[25] Perhaps using 4 cycle BEP chemotherapy regiment increase the side effect incidence for these patients.

There are some limitations of this research. Short patient follow-up and thus long-term survival for the study population remains to be answered. There is incomplete preoperative clinical information because most of the patients present after orchiectomy elsewhere. In patients presenting after orchiectomy, tumour marker levels are unavailable or unreliable. This study involved a large sample size considering the low incidence of testicular carcinoma. To the author's knowledge, this study is the first study reported from Malang, Indonesia.

CONCLUSION

Testicular neoplasm peak incidence appears in young male. Most of patients come to health care service in late stage. Seminoma become the highest testicular neoplasm incidence in our study. Elevated tumor markers were found in some patients. Four cycle BEP chemotherapy regiment showed great outcome for these patients.

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