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Clinicopathological Profile of Patients with Bladder Lesions in Sanglah Hospital during the Period 2013-2017

Perfil clinicopatológico de los pacientes con lesiones vesicales en el hospital Sanglah durante el período 2013-2017

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SUMMARY

Urinary bladder carcinoma is the ninth most common malignancy in the world. Various bladder lesions may show similar symptoms, so pathological examination is highly required to get a definitive diagnosis. This study aims to describe the clinicopathological features of patients with bladder lesions in Sanglah Hospital which can be used as baseline data for further research. Data were collected from pathological archives during the period January 1, 2013 – December 31, 2017. There were 127 cases of bladder lesions examined from biopsy, transurethral resection and cystectomy specimens. They consisted of 97 (76.4 %) males and 30 (23.6 %) females with an age range from the second to the ninth decades. Neoplasm were found in 90 (70.9 %) cases, whereas non neoplasm (generally cystitis) was found in 37 (29.1 %) cases. Eight (8.9 %) cases were metastases, the rest were primary neoplasms. The most common primary neoplasm was Infiltrating Urothelial Carcinoma (58.9 % cases). Some rare malignancies were also noted, including Squamous Cell Carcinoma, Adenocarcinoma, and Sarcomatoid Carcinoma. A Chi-square test shows that malignancies were significantly more frequent in males. The peak age was in the seventh decade. In conclusion, this study reveals infiltrating urothelial carcinoma as the most common bladder malignancy, and that it is more common in males and old age.

Keywords: *Bladder lesions, clinicopathological profile, Human and health.*

RESUMEN

El carcinoma de vejiga urinaria es la novena neoplasia maligna más común en el mundo. Varias lesiones de la vejiga pueden mostrar síntomas similares, por lo que es muy necesario un examen patológico para obtener un diagnóstico definitivo. Este estudio tiene como objetivo describir las características clinicopatológicas de los pacientes con lesiones vesicales en el Hospital Sanglah que pueden usarse como datos de referencia para futuras investigaciones. Los datos se recopilaron de archivos patológicos durante el período del 1 de enero de 2013 al 31 de diciembre de 2017. Se examinaron 127 casos de lesiones vesicales a partir de muestras de biopsia, resección transuretral y cistectomía. Consistían en 97 (76,4 %) hombres y 30 (23,6 %) mujeres con un rango de edad de la segunda a la novena décadas. Se encontraron neoplasias en 90 (70,9 %) casos, mientras que no neoplasias (generalmente cistitis) se encontraron en 37 (29,1 %)

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casos. Ocho (8,9 %) casos fueron metástasis, el resto fueron neoplasias primarias. La neoplasia primaria más frecuente fue el Carcinoma Urotelial Infiltrante (58,9 % casos). También se observaron algunos tumores malignos raros, incluidos el carcinoma de células escamosas, el adenocarcinoma y el carcinoma sarcomatoide. Una prueba de Chi cuadrado muestra que los tumores malignos fueron significativamente más frecuentes en los hombres. La edad pico fue en la séptima década. En conclusión, este estudio revela que el carcinoma urotelial infiltrante es la neoplasia maligna vesical más común, y que es más frecuente en el sexo masculino y en la vejez.

Palabras clave: *Lesiones vesicales, perfil clinicopatológico, humano y salud.*

INTRODUCTION

Data for the WHO 2011 indicated that cancer currently causes more deaths than coronary heart disease and stroke. Bladder cancer is the ninth most common cancer, with 430 000 new cases being diagnosed and 165 000 deaths in 2012 in the world (1,2). Bladder cancer is mainly a degenerative disease. Its incidence and prevalence increase in the sixth decade of life, with a peak in the seventh to eighth decades. It is 3-4 times more frequent in men than women. Some of the risk factors that increase the risk of bladder cancer are age, sex, smoking, occupation, arsenic, medical history, radiation and genetic susceptibility (3-6). Urothelial carcinoma is the most common type, found in over 90 % of bladder cancers. Squamous cell carcinoma and adenocarcinoma are less common (5,7). Several studies have reported secondary carcinoma in the bladder, originating from the cervix, colon, uterus, ovary and prostate. In endemic areas with Schistosoma infection, the incidence of squamous cell carcinoma accounts for about 75 % of bladder cancer (5,8-10).

The main clinical symptom of bladder cancer is painless hematuria. This symptom is commonly accompanied by others, such as dysuria, urgency and frequent urination. Those symptoms were also found in other bladder disorders, such as cystitis. It is a clinical challenge for early detection and adequate follow-up of bladder cancer (3,11).

Infiltrating, high grade urothelial carcinoma has a worse prognosis compared with papilloma, papillary urothelial neoplasm with uncertain malignant potential and low grade papillary urothelial carcinoma which have a very good prognosis, with a 10-year survival rate of about 98 % (3,12,13).

Bladder cancer incidence is common in developing countries. However, data on bladder cancer in Indonesia, especially in Bali, is very limited. For this reason, this study was conducted. This study aims to describe the clinicopathological features of patients with bladder lesions at Sanglah Hospital from 2013-2017. The study results can be used as the basic data for further research.

METHODS

This study is an analytical descriptive study with a cross-sectional design. Data were collected from the pathology examination archives from January 1, 2013 - December 31, 2017. Several clinicopathological parameters were collected, including: age, sex, clinical diagnosis, specimen collection method, and histopathologic conclusions (the type of lesions). The analysis was performed descriptively to calculate the frequency of each clinicopathological parameter. Correlation between parameters was analyzed using Chi-square test with a significance level (α) set at $p < 0.05$.

RESULTS

There were 127 cases of bladder lesions examined pathologically from 2013-2017. Most patients (97 cases/76.4 %) were male, and only 30 patients (23.6 %) were female. According to age distribution, most patients were in their fifth to eighth decades, in which the highest was found in the seventh decade (28.3 %), followed by the sixth (22 %), fifth (18.9 %) and eighth (17.3 %) decades, respectively. Specimen collection methods included biopsy (42.5 %), transurethral resection (37.8 %) and radical cystectomy (19.7 %). Microscopic features showed 90 (70.9 %) neoplastic lesions and 37 (29.1 %) non-

neoplastic lesions. Data are presented in Table 1.

In the neoplastic lesions group, urothelial neoplasms were the most frequent diagnosis. Among urothelial neoplasms, most were infiltrating urothelial carcinoma. This carcinoma counted for as much as 58.9 % of all neoplastic lesions and 78 % of all invasive bladder cancers. Other malignant neoplasms were metastatic cancer 8 (8.9 %), non-invasive papillary urothelial carcinoma 7 (7.8 %), squamous cell carcinoma 8 (8.9 %), and adenocarcinoma 7 (7.8 %) cases. In the non-neoplastic lesion group, the most frequent diagnosis was chronic cystitis with its variants. The histologic types of neoplastic and non-neoplastic lesions are shown in Tables 2 and 3.

Both neoplastic lesions and non-neoplastic lesions were more frequent in males than females. Patients with neoplastic lesions consisted of 78.9 % male and 21.1 % female. In contrast, patients with non-neoplastic lesions were 70.3 % male and 29.7 % female. This sex distribution was not statistically different between neoplastic lesion and non-neoplastic lesion ($p>0.05$).

Among the neoplastic lesions group, Table 4 shows that primary neoplastic lesions were more frequent in males than females. Metastatic cancer was found more frequently in females than males. By bivariate analysis these differences were statistically significant ($p <0.05$). Interestingly, all neoplastic lesions in females were invasive primary and metastatic cancer.

Table 1

Clinicopathological profile of bladder lesions

	Characteristic	N (%)
Years	2013	7 (5.5)
	2014	36 (28.3)
	2015	29 (22.8)
	2016	22 (17.3)
	2017	33 (26)
Sex	Female	30 (23.6)
	Male	97 (76.4)
Age	≤ 19	1 (0.8)
	20-29	2 (1.6)
	30-39	10 (7.9)
	40-49	24 (18.9)
	50-59	28 (22)
	60-69	36 (28.3)
	70-79	22 (17.3)
	80-89	4 (3.1)
Clinical	Malignancy	105 (82.7)
Diagnosis	Non-Malignancy	22 (17.3)
Sampling	TUR	48 (37.8)
Method	Biopsy	54 (42.5)
	Cystectomy	25 (19.7)
Histopathology	Neoplastic Lesion	90 (70.9)
Diagnosis	Non Neoplastic Lesion	29 (20.1)
Neoplastic	Malignant, Primary,	
Lesions	Invasive	69 (76.7)
	Dysplasia, In-situ/	
	Non-Invasive	9 (10)
	Uncertain Whether	
	Benign or Malignant	3 (3.3)
	Benign	1 (1.1)
	Metastatic Cancer	8 (8.9)

Table 2

Histology types of bladder neoplastic lesion

	Classification	n (%)
Invasive	Infiltrating urothelial carcinoma	53 (58.9)
	Squamous cell carcinoma	8 (8.9)
	Adenocarcinoma	7 (7.8)
	Sarcomatoid Carcinoma	1 (1,1)
Dysplasia,	Non invasive papillary	
In-situ/non-	urothelial carcinoma	7 (7.8)
invasive	Urothelial dysplasia	2 (2.2)
Uncertain	Papillary Urothelial Neoplasm	
	of Low Malignant Potential	
	(PUNLMP)	3 (3.3)
Benign	Urothelial papiloma	1 (1.1)
Metastatic cancer		8 (8.9)

Table 3

Histologic types of bladder non-neoplastic lesion

Classification	n (%)
Non-specific chronic cystitis	22 (81.5)
Chronic cystitis with squamous metaplasia	7 (25.9)
Cystitis glandularis	3 (11.1)
Polypoid cystitis	2 (7.4)
Bladder amyloidosis	1 (3.7)
Chronic suppurative cystitis	1(3.7)
Necrosis tissue	1(3.7)

Malignant lesions were found in patients aged 30 years old or older, while benign neoplastic lesions were found in only one case and found in old age. For invasive lesions, the peak was in the age range 60-69 years (29 %), followed by the range 50-59 years (24.6 %) and 70-79 years (21.7 %). The neoplastic lesions case distribution according to histologic types and age is shown in Table 5. Bivariate analysis revealed the difference was statistically significant ($p<0.05$).

Table 4

Distribution of Bladder Neoplastic Lesions Based on Sex and Histologic Types

Sex	Histologic Types					p
	Benign	Uncertain	In-situ, non-invasive	Malignant Primary invasive	Metastatic	
Female	0 (0 %)	0 (0 %)	0 (0 %)	12 (17.4 %)	7 (87.5 %)	<0.001
Male	1 (100 %)	3(100 %)	9(100 %)	57 (82.6 %)	1 (12.5 %)	

Table 5

Distribution of Bladder Neoplastic Lesions Based on Age and Histologic Types

Age (year)	Benign	Uncertain	*In-situ*, non-invasive	Malignant Primary invasive	Metastatic	p
30-39	0 (0 %)	0 (0 %)	0 (0 %)	6 (8.7 %)	2 (25 %)	0.007
40-49	0 (0 %)	1 (33.3 %)	2 (22.2 %)	9 (13 %)	2 (25 %)	
50-59	0 (0 %)	0 (0 %)	2 (22.2 %)	17 (24.6 %)	1 (12.5)	
60-69	0 (0 %)	1 (33.3 %)	4 (44.4 %)	20 (29 %)	3 (37.5 %)	
70-79	0 (0 %)	1 (33.3 %)	1 (11.1 %)	15 (21.7 %)	0 (0 %)	
80-89	1 (100 %)	0 (0 %)	0 (0 %)	2 (2.9 %)	0 (0 %)	

DISCUSSION

Bladder cancer is the ninth most common cancer in the world. There were an estimated 430 000 new cases by 2012, with 165 000 deaths due to bladder cancer. The incidence of bladder cancer is higher in developing countries. It is associated with the high rate of population growth and higher risk factors for bladder cancer, such as, smoking, obesity, alcohol consumption and red meat consumption (1,4,14).

The clinical symptoms of bladder cancer are painless hematuria, urgency, nocturia, and dysuria. These symptoms are also found in almost all types of acute and chronic cystitis. Dysuria is more commonly felt by women. Many cases of bladder cancer were delayed in definitive diagnosis because the symptoms will improve due to the treatment for suspected urinary tract infections (3,5). Early detection for bladder cancer should be carried out in patients with recurrent symptoms of bladder disorders. To establish a good diagnosis, a biopsy or tumor resection should be performed. In this study, 105 of 127 cases (82.7 %) were diagnosed as suspected malignancy clinically, but histology revealed only 90 (70.8 %) were neoplastic lesions.

Urothelial carcinoma, also known as transitional cell carcinoma, is the most common type of bladder neoplasm, estimated at 90 % in developing countries and 80 % in other countries. The other types are squamous cell carcinoma and primary adenocarcinoma (3,5,15). Similar to

the literature, in this study, infiltrating urothelial carcinoma was the most common neoplasm in the bladder. It accounts for 58.9 % of all cases of neoplastic lesions and 78 % of all invasive bladder carcinoma. Squamous cell carcinoma is the second commonest type (8.9 %), followed by adenocarcinoma in third place (7.8 %).

Secondary neoplasms of the bladder are most often caused by direct extension from near organs, such as, uterine cervix, uterus, prostate and rectum (5). Cervical cancer with bladder invasion is included in stage IVA (FIGO) and presents in about 2 % of all cervical cancers (10). A literature review of metastatic tumors in the bladder from 1953-2005 by Velcheti and Govindam (2007) found that the most common primary source of metastatic cancer in bladder is cancer of the genitourinary system, followed by colorectal and melanoma. This is consistent with the results of this study in which cervical cancer is the most frequent source of metastasis (87.5 %). The remaining 12.5 % derived from colorectal cancer (16).

Men are four times more likely to develop bladder cancer than women. This risk difference is due to environmental factors, smoking habits, sexual characteristics (anatomical differences), urinary habits and hormonal factors. Duration and intensity of smoking are associated with a risk of bladder carcinoma. Gradual cessation of smoking may reduce the risk of bladder carcinoma. In a prospective study in the Netherlands, 23 % of women and 50 % of men with bladder cancer were smokers (5,9,14). Several humans and animal studies revealed that the different risk between males and females was associated with differences in liver metabolism and with the differences in hormonal status (4). In this study, the ratio of male:female for neoplastic lesions was 4:1, while for malignant neoplastic lesions it was 3:1 (16). The same results were found in research conducted by Syafa'ah et al., in Dr. Mohammad Hoesin Palembang Hospital (2015), with the male:female ratio being 4:1 (17).

Bladder cancer is a disease found in the elderly. An estimated 80 % of new cases of urothelial carcinoma are found in people over the age of 60 years (3). In this study, invasive lesions were mostly found in the age range 60-69 years (29 %), followed by the age range 50-59 years (24.6 %) and 70-79 years (21.7 %). Factors contributing to this process are the accumulated effects of carcinogen exposure, disruption of DNA repair, immune system disorders, and possibly urinary retention (18,19). Theories of aging and genetic mutations explain that there is an accumulation of declining genetic material as age increases, particularly p53 inactivation (20). As the age increases, DNA mutation will accumulate, telomeres will progressively shorten, mitochondrial damage will happen, and there is also some other DNA damage that can interfere with the control of cell proliferation and control of cell damage (3). This damage is also supported by external factors of carcinogen exposure, especially cigarette smoke exposure. Another factor contributed to older age predominance, namely delayed definitive diagnosis. This is often caused by the similar symptoms of bladder carcinoma with other lesions, such as urinary tract infections and calculi (21).

CONCLUSION

There were 127 cases of bladder lesions examined in the Pathological Anatomy Laboratory of Sanglah Denpasar Hospital from 2013-2017. They consisted of 90 (70.9 %) neoplastic lesions and 37 (29.1 %) non-neoplastic lesions. Almost all of the non-neoplastic lesions were cystitis and its variants. For neoplastic lesions, infiltrating urothelial carcinoma is the most common histologic type (58.9 %). Neoplastic lesions were more common in males than females (ratio 3-4:1). The highest prevalence was found in the 60-69 age group.

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