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Research Article

The Clinical and Laboratory Characteristics of Patients with Urological Cancers and Additional Primary Malignancies: A Single Institution Study

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Abstract

Objective: The objective of this study is to analyze the clinical and laboratory charateristics of patients with urological cancers with additional primary malignancies in a Taiwanese population.

Materials and Methods: The clinical and laboratory data for patients with urological cancers with other primary malignancies were collected during the study interval. Treatment types and site of additional primary cancers were also obtained and stratified. All primary malignancies were histologically verified.

Results: Among the patients with multiple primary malignancies, 8 patients with prostate cancer, 5 patients with urothelial cell carcinoma in bladder (UCC) and 1 patient with Renal Cell Carcinoma (RCC) were found. Gastric cancer and Hepatocellular Carcinoma (HCC) were the most common other primary malignancies in prostate cancer-bearing patients. Furthermore, the most common additional malignancies accompanied with UCC were gastric cancer and breast cancer. One patient with multiple primary neoplasms of RCC and HCC was also reported. Overall, there was a high occurrence in additional primary malignancies of the stomach and liver in patients diagnosed with urological cancers.

Conclusion: Patients with urological cancers seemed to be associated with the development of additional primary malignancies, especially in the stomach and liver. This should be considered in the management and follow-up of patients with urological cancers.

Keywords: Multiple Primary Malignancies; Prostate Cancer; Renal Cell Carcinoma; Urothelial Cell Carcinoma

Introduction

Multiple primary malignancies, first reported in the 1930s, were defined as: (1) each pathologically proved malignancy should be distinct and separate in anatomy; and (2) the secondary cancer should not be a metastasis or recurrence of the primary neoplasm [1]. In the past decade, the diagnostic rate of multiple primary malignancies has been emergently increased and become of concern. This phenomenon may be contributed to the development of medical technology and prolonging life span. The occurrence of additional primary neoplasms affecting all cancer patients was ranged from 6% to 15%, depending on their age and gender [2]. Previous retrospective studies had systematically demonstrated the prevalence and clinicopathological features of multiple primary malignancies in patients with lung cancer [3], gastric cancer [4,5], hepatic cancer [6,7] and colorectal cancer [8], respectively. According to accumulating meta-analysis of multiple primary malignancies, several pathological mechanisms had been implicated and etiological factors were classified as (1) chemotherapy- or radiotherapy-related; (2) genetic predisposing; and (3) environmental exposure factors [9]. The investigation data provided clinicians a deeper insight into the management of cancer patients with high risk factors of subsequent primary neoplasms.

Urological cancers, including cancers of the kidney, bladder, prostate and testicles, attributed to a major portion of all malignancies in European and American populations during

the past decades [10]. The prognosis of urological cancers was variable, depending on the clinical parameters of patients, tumor site and size, histological differentiation and treatment types. Of these cancers, prostate cancer also accounts for sixth most common cause of cancer mortality in Taiwan. However, few studies about urologic cancers with multiple primary malignancies were investigated. Therefore, we conducted this case series study to investigate clinical characteristics, laboratory data and treatment outcome of additional primary malignancies in Taiwanese patients with urologic cancers.

Materials and Methods

Between January 2009 and December 2013, clinical information of patients diagnosed with one of urological cancers and additional primary malignancies and receiving treatments and regular follow-up at the Far Eastern Memorial Hospital (FEMH) in New Taipei city, Taiwan, were obtained via a chart review in the study. All patients were Chinese residents. Clinical data included age, gender, family history of cancer, underlying comorbidities, date of diagnosis, tumor site, stage of each primary neoplasm, treatment of urological cancers and expiry date. To analyze patients with multiple primary malignancies, each primary malignancy was histopathologically verified; and 8 patients among 1381 suspected to have prostate cancer, 5 patients among 725 suspected to have urothelial cell carcinoma in bladder (UCC) and 1 patient among 42 suspected to have Renal Cell Carcinoma (RCC) were enrolled. Addiotnally, 1 patient with prostate cancer and 4 patients with bladder cancer were excluded from the group of multiple primary malignancies because of incomplete clinical data.

The first recorded laboratory data of each patient were collected during admission or follow-up in outpatient department when diagnosis of multiple primary malignancies with urological cancers was established. The laboratory data, including hematological, biochemical and metabolic parameters were requested. Among these indicators, hematological parameters included White Blood Cell Count (WBC), Hemoglobin (Hb), Platelet (PLT) and Neutrophil-To-Lymphocyte Ratio (NLR); biochemical parameters included Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), total bilirubin, creatinine, Blood Urea Nitrogen (BUN) and albumin; and metabolic parameters included fasting glucose, cholesterol, High Density Lipoprotein Cholesterol (HDL-C) and triglyceride. All laboratory values were measured by the automatic analyzer via standard laboratory procedures.

Data were presented as the mean ± standard deviation or case number (percentage). All statistical analyses were performed using the statistical software SPSS (version 19.0; SPSS Inc., Chicago, USA). Statistically significance was considered at $p < 0.05$.

Results

The clinical characteristics of patients with urological cancers and additional primary malignancies were listed in (Table 1).

Variables	Prostate Ca (n=8)	UCC (n=5)	RCC (n=1)
Age (y)	74.0±8.2 (61-86)	72.6±12.2 (57-91)	56
Gender			
Male	8 (100.0)	2 (40.0)	0 (0)
Female	0 (0)	3 (60.0)	1 (100)
FHC			
Yes	2 (25.0)	1 (20.0)	0 (0)
No	6 (75.0)	4 (80.0)	1 (100)
Stage			
I	0 (0)	1 (20.0)	0 (0)
II	6 (75.0)	2 (40.0)	0 (0)
III	1 (12.5)	2 (40.0)	1 (100)
IV	1 (12.5)	0 (0)	0 (0)
Comorbidities			
CVD	4 (50.0)	1 (20.0)	0 (0)

HTN	4 (50.0)	1 (20.0)	1 (100)
DM	1 (12.5)	0 (0)	1 (100)
CKD	0 (0)	1 (20.0)	1 (100)
PUD	1 (12.5)	0 (0)	0 (0)
COPD	1 (12.5)	0 (0)	0 (0)
Hepatitis B	1 (12.5)	2 (40.0)	1 (100)
Stroke	0 (0)	0 (0)	0 (0)
Survival rate (%)			
1-year	75.0	80.0	100
5-year	75.0	40.0	0

Prostate Ca: Prostate Cancer; UCC: Urothelial Cell Carcinoma in Bladder; RCC: Renal Cell Carcinoma; FHC: Family History of Cancer; CVD: Cardiovascular Disease; HTN: Hypertension; DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; PUD: Peptic Ulcer Disease; COPD: Chronic Obstructive Pulmonary Disease. Data were expressed as mean ± standard deviation (range) or case number (percentage).

Table 1: Clinical characteristics of patients with urological cancers and additional primary malignancies.

The mean age was 74.0±8.2 years (range: 61-86 years) at the diagnosis of prostate cancer and 72.6±12.2 years (range: 57-91 years) at the diagnosis of UCC; the age was 56 years at the diagnosis of RCC. All patients with prostate cancer and additional primary malignancies were male. Two patients with UCC and additional primary malignancies were male and other 3 were female. The patient with RCC and additional primary malignancies was female. Besides, 25% of prostate cancer-bearing patients (n=2) and 20% of UCC-bearing patients (n=1) had Family History of Cancer (FHC). There was no FHC in the patient with RCC. Among these patients, 75% of patients with prostate cancer were stage II (n=6); and 12.5% presented with stage III (n=1) and stage IV (n=1), respectively; and 87.5% (n=7) had the Gleason score more than 6. Among patients with UCC, both stage II and III accounted for 40% (n=2, respectively) and the other 1 was stage I. The UCC in high grade accounted for 75% (n=3). The stage in RCC-bearing patient was stage III. Both Cardiovascular Disease (CVD) and Hypertension (HTN) accounted for 50% of patients with prostate cancer (n=4, respectively); and 12.5% presented with Diabetes Mellitus (DM), peptic ulcer, Chronic Obstructive Pulmonary Disease (COPD) and hepatitis B, respectively. Comorbidities with hepatitis B accounted for 40% (n=2) and CVD, HTN and Chronic Kidney Disease (CKD) accounted for 20% (n=1) of patients with UCC, respectively. The RCC-bearing patient had comorbidities with DM, HTN, CKD and hepatitis B. The 1-year survival rate in these patients with urological cancers and additional primary malignancies was above 75%. The 5-year survival rate remained no significant change in patients with prostate cancer, but much decreased in patients with UCC and RCC.

The treatment of urological cancers in patients with multiple primary malignancies were shown in (Table 2).

Treatment types of urological cancers	No. (%)
Prostate Ca (n=8)	
TUR-P	3 (37.5)
Thulium laser prostatectomy	2 (25.0)
Radical prostatectomy	2 (25.0)
Cryoablation	1 (12.5)
Chemotherapy	2 (25.0)
Radiotherapy	3 (37.5)
UCC (n=5)	
TUR-BT	3 (60.0)
Partial cystectomy with pelvic lymphadenectomy	1 (20.0)
Chemotherapy	4 (80.0)
Radiotherapy	3 (60.0)
RCC (n=1)	
Laparoscopic nephroureterectomy	1 (100)
Chemotherapy	1 (100)
Radiotherapy	0 (0)

Prostate Ca: Prostate Cancer; UCC: Urothelial Cell Carcinoma in Bladder; RCC: Renal Cell Carcinoma; TUR-P: Transurethral Resection of The Prostate; TUR-BT: Transurethral Resection of The Bladder Tumor.

Table 2: Treatment of urological cancers in patients with multiple primary malignancies.

The most common treatment of prostate cancer in surgical intervention was transurethral resection of the prostate (37.5%, n=3); the subsequent ones were Thulium laser prostatectomy and radical prostatectomy (25%, n=2, respectively). Besides, 12.5% (n=1) received cryoablation, 25% (n=2) received chemotherapy and 37.5% (n=3) received radiotherapy. Among the patients with UCC, 60% (n=3) received transurethral resection of the bladder tumor and 20% (n=1) received partial cystectomy with pelvic lymphadenectomy. One patient with UCC did not received surgical treatment in consideration of his old age (20%, n=1). Also, 80% (n=4) had chemotherapy and 60% (n=3) had radiotherapy. The patient with RCC received laparoscopic nephroureterectomy and chemotherapy.

The site and occurrence of additional primary malignancies in patients with urological cancers were presented in (Table 3). All primary malignancies diagnosed in these urological cancer-bearing patients were metachronous. Of these patients, most of all were diagnosed with secondary primary cancers (92.9%, n=13); and one patient (7.1%, n=1) had tertiary primary malignancies with UCC. Gastric cancer (37.5%, n=3) was the most common other primary malignancy in patients with prostate cancer. Hepatocellular carcinoma (HCC) accounted for 40% (n=2), Colorectal Cancer (CRC), multiple myeloma (MM) and pancreatic cancer accounted for 20% (n=1), respectively. Among the patients with UCC, gastric and breast cancers were the most common other primary neoplasms (25%, n=2, respectively). Lung cancer and thyroid cancer accounted for 12.5% (n=1), respectively. The secondary primary cancer in the patient with RCC was HCC.

SPC	Prostate Ca	SPC	UCC	SPC	RCC
Gastric Ca	3 (37.5)	Gastric Ca	2 (25.0)	HCC	1 (100.0)
HCC	2 (25.0)	Breast Ca	2 (25.0)		
CRC	1 (12.5)	Lung Ca	1 (12.5)		
MM	1 (12.5)	Thyroid Ca	1 (12.5)		
Pancreatic Ca	1 (12.5)				

SPC: Secondary Primary Cancer; prostate Ca: Prostate Cancer; UCC: Urothelial Cell Carcinoma in Bladder; RCC: Renal Cell Carcinoma; gastric Ca: Gastric Cancer; HCC: Hepatocellular Carcinoma; CRC: Colorectal Cancer; MM: Multiple Myeloma; pancreatic Ca: Pancreatic Cancer; breast Ca: Breast Cancer; lung Ca: Lung Cancer; Thyroid Ca: Thyroid Cancer.

Table 3: Site of multiple primary malignancies in patients with urological cancers.

The laboratory data of these urological cancer-bearing patients with additional primary malignancies were shown in (Table 4). It seemed that these patients had mild anemia and liver function impairment when the diagnosis was established. It was also observed that those with prostate cancer and RCC had renal function impairment and hypoalbuminemia. Notably, the patient with RCC had a higher NLR of 4.28 when the diagnosis was established.

Variables	Prostate Ca	UCC	RCC
Hematological			
WBC (10^3/uL)	8.78±4.35	8.45±1.34	7.80
Hb (g/dL)	11.8±2.5	12.1±2.1	10.4
PLT (10^3/uL)	298.9±167.7	230.4±35.2	161
NLR	2.60±0.98	2.64±1.18	4.28
Biochemical			
AST (U/L)	45.4±24.7	70.2±29.0	102
ALT (U/L)	66.8±56.1	57.0±34.2	64

Total bilirubin (mg/dL)	2.01±2.51	1.10±0.85	0.7
BUN (mg/dL)	22.1±19.1	20.8±9.3	61
Creatinine (mg/dL)	1.77±1.55	0.99±0.39	3.81
Albumin (g/dL)	2.9±0.7	3.7±0.9	2.8
Metabolic			
Glucose (mg/dL)	98.6±11.0	105.0±25.6	185
Cholesterol (mg/dL)	182.5±93.6	160.8±47.7	217
HDL-C (mg/dL)	55.4±36.3	66.8±19.8	48
Triglyceride (mg/dL)	295.7±325.1	81.5±44.1	196

Prostate Ca: Prostate Cancer; UCC: Urothelial Cell Carcinoma in Bladder; RCC: Renal Cell Carcinoma; WBC: White Blood Cell Count; Hb: Hemoglobin; PLT: Platelet; NLR: neutrophil-to-lymphocyte ratio; AST: Aspartate Aminotransferase; ALT: Alanine Transaminase; BUN: Blood Urea Nitrogen; HDL-C: High Density Lipoprotein Cholesterol.

Table 4: Laboratory data of patients with urological cancers and additional primary malignancies.

Discussion

Multiple primary malignancies, albeit rare, has been increasing epidemiologically in recent years. Whenever diagnosed, multiple primary malignancies often bring challenges to clinicians and patients according to the limitation of therapeutic options. Besides, it has been proposed that cancer patients are at higher risk of developing a second primary cancer than the general population [11]. Hence, the stratification of risk factors and mechanisms in multiple primary malignancies became important. The pathogenesis of multiple primary malignancies has been proposed according to a myriad of etiological factors, such as the therapeutic effect on cancer with chemo- or radiotherapy, hereditary or genetic susceptibility, specific viral infections and environmental exposure to heavy metal and chemicals [9,12]. However, some multiple primary malignancies were categorized as idiopathic and further investigation should be considered.

The present study indicated that an increased risk ratio in development of the cancers in the stomach and liver was observed in prostate cancer-bearing patients. Furthermore, the most common other malignancies accompanied with UCC were found in the stomach and breast. A patient with multiple primary neoplasms of RCC and HCC was also reported. Overall, there was a high occurrence in additional primary malignancies of the stomach and liver in patients diagnosed with urological cancers.

Beisland, et al. [13] reported that about 19% of RCCs with additional primary malignancies were synchronous in a retrospective review of 255 patients with multiple primary malignancies during a 7-year period. Moreover, the most common other malignancies accompanied with RCC were observed in the prostate, bladder, lung, breast and colon [13]. Furthermore, Xu, et al. [14] and Ozturk, et al. [15] reported the coexistence of (MM) and (RCC) in three patients, though this condition is extremely rare. Whereas Hemelrijck, et al. [16] found there was the highest occurrence of the lung and colon cancers accompanied with prostate cancer in a 30-year period retrospective study with 1718 multiple primary cancer-bearing patients. Of these patients with prostate cancer, the most common secondary primary neoplasm was thyroid cancer in those treated with surgical intervention, HCC in those treated with radiotherapy, and urological cancers in those treated with hormone therapy when categorized with type of treatment [16]. Instead, Fan, et al. [17] reported that patients with prostate cancer tended to have a lower risk of developing second primary malignancies, but a significantly higher risk of subsequent thyroid cancer. These results were partially similar to the present study as all patients diagnosed with prostate cancer and HCC received radiotherapy in our series. Additionally, Pruthi, et al. [18] reported that patients with the bladder cancer had a higher risk for developing a secondary primary cancer of the kidney, lung, breast and prostate. Furthermore, Tian, et al. [19] reported that in patients developing UCC after renal transplantation may also have a risk of developing sarcoma, CRC and squamous cell carcinoma of skin. The difference in the frequency of urological cancers with additional primary malignancies between our study and previous investigations may contribute to the distinctions of nation, race, residential area, lifestyle and environmental exposure.

The major limitations of the present study were the small case number and the case series study design. The variability of cancer treatment and follow-up method by each physician and unavailability of long-term follow-up data were also restricted in

our series. Although the case number was limited in our study, we believed that our research could provide clinicians a newly insight into the relative risk for developing a secondary primary neoplasm and the following management of patients with urological malignancies in a Taiwanese population.

Conclusion

In conclusion, patients with urological cancers seemed to be associated with the development of additional primary malignancies, especially in stomach and liver. This should be considered in the management and follow-up of patients with urological cancers.

Conflict of Interest: None.

Author Contributions: Hung-Pin Chiu and Wei-Lin Wong worked as co-first authors. Po-Wen Ku contributed as corresponding author. All authors read and approved the manuscript.

References

1. Warren S, Gates O (1932) Multiple primary malignant tumors: a survey of the literature and statistical study. Am J Cancer 16: 1358-1414.
2. Luciani A, Ascione G, Marussi D, Oldani S, Caldiera S, et al. (2009) Clinical analysis of multiple primary malignancies in the elderly. Med Oncol 26: 27-31.
3. Bae MK, Byun CS, Lee CY, Lee JG, Park IK, et al. (2011) The role of surgical treatment in second primary lung cancer. Ann Thorac Surg 92: 256-262.
4. Ławniczak M, Gawin A, Jaroszewicz-Heigelmann H (2014) Synchronous and metachronous neoplasms in gastric cancer patients: a 23-year study. World J Gastroenterol 20: 7480-7487.
5. Eom BW, Lee HJ, Yoo MW, Cho JJ, Kim WH, et al. (2008) Synchronous and metachronous cancers in patients with gastric cancer. J Surg Oncol 98: 106-110.
6. Wu WC, Chen YT, Hwang CY, Su CW, Li SY, et al. (2013) Second primary cancers in patients with hepatocellular carcinoma: a nationwide cohort study in Taiwan. Liver Int 33: 616-23.
7. Fernández-Ruiz M1, Guerra-Vales JM, Castelbón-Fernández FJ, Llenas-García J, Caurcel-Díaz L, et al. (2009) Multiple primary malignancies in Spanish patients with hepatocellular carcinoma: analysis of a hospital-based tumor registry. J Gastroenterol Hepatol 24: 1424-1430.
8. Sun LC, Tai YY, Liao SM, Lin TY, Shih YL, et al. (2014) Clinical characteristics of second primary cancer in colorectal cancer patients: the impact of colorectal cancer or other second cancer occurring first. World J Surg Oncol 12: 73.
9. Wood ME, Vogel V, Ng A, Foxhall L, Goodwin P, et al. (2012) Second malignant neoplasms: Assessment and strategies for risk reduction. J Clin Oncol 30: 3734-3745.
10. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. (2008) Cancer statistics, 2008. CA Cancer J Clin 58: 71-96.
11. Travis LB, Demark Wahnefried W, Allan JM, Wood ME, Ng AK (2013) Aetiology, genetics and prevention of secondary neoplasms in adult cancer survivors. Nat Rev Clin Oncol 10: 289-301.
12. Utada M, Ohno Y, Hori M, Soda M (2014) Incidence of multiple primary cancers and interval between first and second primary cancers. Cancer Sci 105: 890-896.
13. Beisland C, Talleraas O, Bakke A, Norstein J (2006) Multiple primary malignancies in patients with renal cell carcinoma: a national population-based cohort study. BJU Int 97: 698-702.
14. Xu G, Yang M, Huang J, Jin J (2015) Coexistence of multiple myeloma and clear cell renal cell carcinoma: a case report and review of literature. Int J Clin Exp Pathol 8: 7627-7630.
15. Ozturk MA, Dane F, Kaygusuz I, Asmaz O, Uzay A, et al. (2009) Synchronous renal cell carcinoma and multiple myeloma: report of two cases and review of the literature. J BUON 14: 511-514.
16. Van Hemelrijck M, Feller A, Garmo H, Valeri F, Korol D, et al. (2014) Incidence of second malignancies for prostate cancer. PLoS One 9: e102596.
17. Fan CY, Huang WY, Lin CS, Su YF, Lo CH et al. (2017) Risk of second primary malignancies among patients with prostate cancer: A population-based cohort study. PLoS One 12: e0175217.
18. Pruthi DK, Nugent Z, Czaykowski P, Demers AA (2013) Urothelial cancer and the diagnosis of subsequent malignancies. Can Urol Assoc J 7: E57-E64.
19. Tian Y, Xiao J, Lin J, Zhang L, Guo HB, et al. (2013) [Urothelial carcinoma accompanied with other malignant tumor after renal transplantation: 9 cases report]. Beijing Da Xue Xue Bao Yi Xue Ban 45: 542-544.