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INCIDENCE OF URINARY TRACT TUMOURS IN A TWO-YEAR PERIOD (2010–2011) AT THE INSTITUTE OF PATHOLOGY, FACULTY OF MEDICINE, SKOPJE, MACEDONIA

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Abstract

We performed a retrospective analysis of tumours of the kidneys and the lower urinary tract diagnosed at the Institute of Pathology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Macedonia, in a two-year period (2010–2011), with the aim of highlighting the main morphological characteristics and to present the statistical features of these tumours. All the cases were diagnosed on paraffin sections from surgical specimens routinely stained with H&E, and immunohistochemically with a panel of monoclonal antibodies. The analysis revealed a total of 755 cases, of which 166 (14%) were located in the kidney including the renal pelvis, and 649 (86%) were tumours of the urinary bladder. Twelve of the renal tumours (11.3%) were benign, and the rest were malignant tumours. Most of them were adenocarcinomas (n = 77; 72.6%) and 17 cases (16%) were transitional cell carcinomas originating from the renal pelvis. The analysis of the lower urinary tract tumours showed a strong prevalence of malignant urothelial tumours (96%), with a male to female ratio of almost 4:1. Low grade morphology was a predominant feature (71.7%) and 51 cases (22.9%) were of high grade. The percentage of urothelial tumours of the kidney in our series is higher than in most of the reported series, which should lead to an expanded analysis.

Key words: urinary tract tumours, incidence, morphological features, benign and malignant tumours of the kidney, benign and malignant tumours of the upper urinary tract, benign and malignant tumours of the lower urinary tract.

Introduction

Both benign and malignant tumours affect the organs of the urinary system and are of great clinical importance [1]. They are traditionally divided into tumours of the kidney (including the renal pelvis) and tumours of the lower urinary tract.

The vast majority of kidney tumours are malignant, accounting for 75–85% of the detected tumour masses in the kidney, while the remaining 15–25% are benign tumours [2–4].

Lower urinary tract tumours can also be of benign or malignant biological behaviour, the latter being predominant and comprising about 99% of all bladder tumours [5].

We performed a retrospective analysis of the tumours of the kidneys and the lower urinary tract diagnosed at the Institute of Pathology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Macedonia, in a two-year period (2010–2011) with aim of highlighting the main morphological characteris-

tics, as well as to present the statistical features of these tumours. We also compared our findings with the data published in the literature.

Material and Methods

In a retrospective study we performed data analysis of all cases diagnosed with any entity belonging to the group of tumors of the kidney and the lower urinary tract at the Institute of Pathology, Medical faculty, University "Ss. Cyril and Methodius", Skopje, Macedonia, during 2010 and 2011.

All the cases were diagnosed on paraffin sections from surgical specimens routinely stained with H&E, as well as with a panel of monoclonal antibodies in difficult cases with several differential diagnoses, by using the Universal LSAB – PT LINK immunohistochemical technique. For establishing the diagnosis of renal cell carcinoma we used the following panel of antibodies: Renal cell carcinoma (RCC), CD10, Vimentin, Pan-Cytokeratin, CD34. In the cases that needed distinction between urothelial and prostatic cancer, we used the following monoclonal antibodies: thrombomodulin, CK7, CK18, CK20, beta-catenin, PSA, AMACR and p63. In two cases, to distinguish onconcytoma from chromophobe carcinoma, electron-microscopical analysis was carried out on ultrathin sections contrasted with uranyl acetate, by TEM JEOL 1400.

The cases were then classified into two large groups, tumours of the kidney and tumours of the lower urinary tract, using the nomenclature of the current WHO Classification of Tumours of the Urinary System and Male Genital Organs [6].

Statistical analysis of the obtained data was done with the Statistica software [7].

Results

The investigation revealed a total of 755 cases diagnosed as tumours of the urinary system in the period between 01.01.2010 and 31.12.2011. One hundred and six cases (14%) were located in the kidney including the renal pelvis, and 649 (86%) were tumours of the urinary bladder.

Kidney tumours

The renal tumours were more frequently found among men (n = 61; 57.5%), in comparison to women (n = 45; 42.4%). The average age at diagnosis was 60 in men (min. 34, max. 83) and 59 in women (min. 23, max. 80).

Twelve of the renal tumours (11.3%) were benign, 4 of which had oncocytic morphology (less than 4% of all cases), 2 were adenomas (1.9%) and the rest were angiomyolipomas (5.7%) (Figure 1).

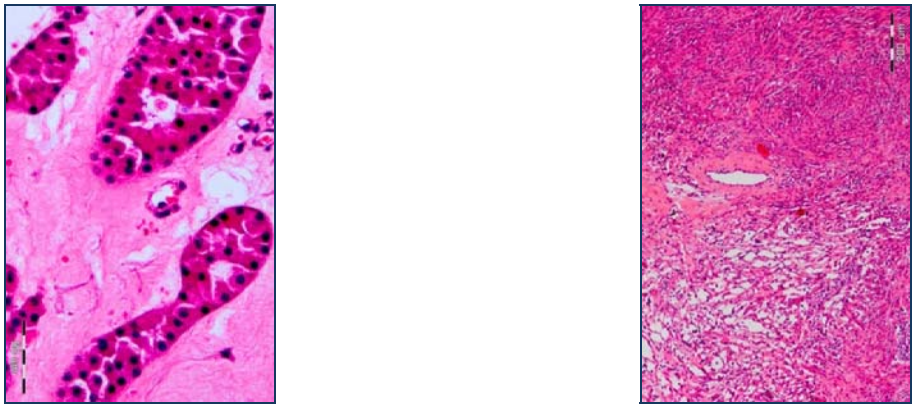

Figure 1 – Benign tumours of the kidney. A. Oncocytoma (HE, × 400); B. Oncocytoma, Electron microscopy (× 25000); C. Angiomyolipoma (HE, × 200)

The vast majority of the malignant tumours were adenocarcinomas (n = 77; 72.6%) and 17 cases (16%) were transitional cell carcinomas originating from the renal pelvis. In the group of the renal adenocarcinoma 72 cases had a morphology of clear-cell renal cell carcinoma, two cases were chromophobe carcinomas, and three cases had a morphology of papillary renalcell carcinoma. Immunohistochemically, chromophobe carcinoma was positive for pan-CK, EMA and negative for CD10 and Vimentin in opposite to clear-cell renal-cell carcinoma that was positive for Renal Cell Carcinoma, Vimentin and CD10 (Figure 2).

Figure 2 – Malignant tumours of the kidney. A. Clear-cell renal cell carcinoma (HE, × 200); B. Clear-cell renal cell carcinoma (Vimentin, × 200); C. Chromophobe carcinoma (HE, × 100); D. Chromophobe carcinoma (Vimentin, × 200)

The clear-cell renal-cell carcinomas were more frequently found in males (n = 47; 61%; male to female ratio 1.5 : 1. The average age at the time of diagnosis was 59 both in male (min. 34, max. 73) and female (min. 36, max. 80) patients.

Transitional cell carcinomas of the renal pelvis were more rarely found (n = 17; 16%) and had identical morphology to those originating from the lower urinary tract urothelium. The male to female ratio for these tumours was 2 : 1, and the average age at the time of diagnosis was 63 both in male (min. 36, max. 83) and female (min. 44, max. 71) patients. Only 4 cases were found to be of high grade papillary carcinoma, and in 5 cases infiltrative pattern was confirmed.

Most of the cases (41%) with a malignant tumour of the upper urinary tract were diagnosed in stage I, followed by stage II and III (23% and 28%, respectively), and fewest of them were in stage IV (5%). Only 3% were not staged, due to various reasons (Figure 3).

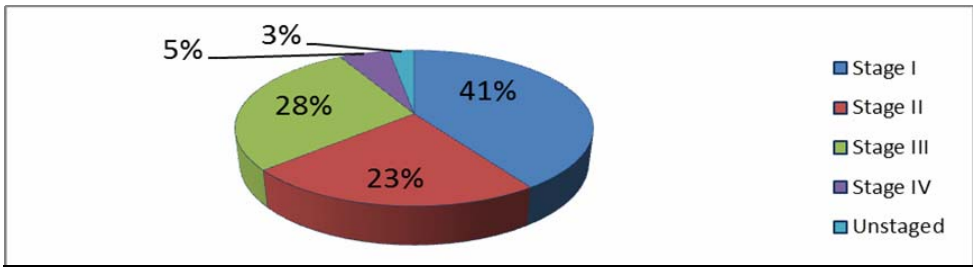

Figure 3 – Grouping of malignant tumours of the kidney according to stage

Lower urinary tract tumours

Of the total number of 649 cases of tumours in the lower urinary tract diagnosed during this period, 223 (34.4%) were diagnosed for the first time. The rest of the cases were re-operations from cases diagnosed in previous years.

The analysis showed a strong prevalence of newly-diagnosed tumours in the male population (177 male vs. 46 female), the ratio of which was almost 4 : 1. The average age at diagnosis was 65 in men (min. 29, max. 88) and 60 in women (min. 32, max. 89).

Only 9 cases (4%) were benign papillomas of the urinary bladder (Figure 4A), and most of the cases (96%) were malignant. Transitional cell carcinoma was present in 211 cases, and only three cases (1.3%) were primary squamous cell carcinomas of the bladder. Low grade morphology (grade I and II) was the predominant feature (71.7%) (Figure 4B) and 51 cases (22.9%) were high grade (grade III and anaplastic) (Figure 4C).

In more than 78% of the cases, the transitional cell carcinoma was superficial, and in the rest (about 21.3%) the tumour was infiltrative.

In 3 cases there were two synchronous neoplasms of the bladder and prostate. The use of immunohistochemical analysis for thrombomodulin, CK7, CK18, CK20, beta-catenin, PSA, AMACR and p63 was very helpful in distinguishing between these two carcinomas.

Figure 4 – Tumours of the lower urinary tract. A. Papilloma (HE, × 100); B. Low-grade transitional cell carcinoma (HE, × 40); C. High-grade transitional cell carcinoma (HE, × 100)

Analysis of the patients according to their regional distribution in Macedonia showed seven of the patients with TCC of the renal pelvis were from Skopje, 4 were from the eastern part, and 6 were from the central and western regions of the country. The vast majority of the cases with urinary bladder cancer were from Skopje (n = 93; 41.3%), 59 cases (26%) were from the eastern part of the country and 71 cases (31.5%) came from the central and western parts of the country.

Discussion

Benign tumours of the kidney were found in nearly 11% of the nephrectomies due to kidney tumours in our series, which is a lower incidence than the 13–25% reported in Western countries [3, 4, 8], but greater than the incidence of 7.1% reported in a large South Korean study [9].

Kidney cancer amounts to 2% of the total human cancer burden (WHO, 2004), with over 85–90% of the cases arising from the epithelium of the renal tubules – adenocarcinoma [10, 11]. Adenocarcinomas in our series were less frequent (72.6%). Most of the patients in worldwide cancer statistics (around 80%) are between 40 and 69 years of age, and are predominantly male, with a male to female ratio 2 : 1 [12]. In our series, males are predominant, too, with a male to female ratio 1.5 : 1, and the average age of the patients is within the worldwide statistical range.

From the epidemiological point of view, smoking, obesity and hypertension are well-established risk factors for renal adenocarcinomas (a combination of obesity and hypertension additionally increases the risk of renal adenocarcinoma) [13], while other risk factors include long-term haemodialysis due to end-stage renal disease [14], occupational exposure to trichloroethylene, asbestos and heavy metals [15, 16]. Besides the sporadic cases, which are the most common, there are also familial variants of renal adenocarcinoma (Von Hippel-Lindau syndrome, hereditary clear-cell and hereditary papillary carcinoma).

In contrast to the adenocarcinomas, the incidence of transitional-cell carcinomas of the renal pelvis was much higher in our series in comparison with the above-mentioned South Korean study (16% vs. 1%, respectively), as well as with other sources [1, 17, 18], but corresponded to the study by Guinan et al. (1992) [19], who reported that 15% of renal tumours in their series were renal pelvis TCC. This tumour is more common among male patients, with a male to female ratio of 3 : 2 in literature data [20] and a 2 : 1 ratio in our series. The mean age of patients developing upper urinary tract urothelial tumours is 65 years [21], which corresponds to the average age of our patients of 63 years, both in male and female patients.

Environmental factors, such as exposure to tobacco, some aromatic amines (due to which these tumours are also called "amino

tumours"), as well as intake of phenacetin increase the risk of these tumours [22–24]. Aristolochic acid and consumption of Chinese herbs also contribute to the higher incidence rate in endemic regions in comparison with the general population. However, the number of newly-diagnosed upper urinary tract urothelial carcinomas is reportedly increasing in the areas of Balkan Endemic Nephropathy [25]. According to our knowledge, no such areas have been defined in Macedonia, which corresponds to the fact that no regional pattern of distribution of our cases has been identified. Still, in comparison with the worldwide statistics, the incidence of these rather rare kidney tumours is much higher in our series.

Besides this, it has been estimated that 2–4% of patients with bladder TCC develop upper urinary tract TCC, whereas approximately 40% of patients with upper urinary tract TCC will develop bladder TCC, due to which both groups of patients should be closely monitored. However, we have not noticed any such case in our series.

Bladder cancer is the most common malignancy in the urinary tract and is the ninth most common malignancy worldwide [26]. It is more frequent than malignant tumours of the kidney and accounts for up to 7% of the total human cancer burden [18]. According to worldwide statistics, the average age at diagnosis is 65, which is in line with our findings, and the male to female ratio is 4: 1, also corresponding to our series.

The vast majority (more than 90%) of bladder neoplasms are urothelial tumours [27]. Cigarette smoking and occupational exposure to certain carcinogens (aromatic amines, polycyclic aromatic hydrocarbons, etc.) have been known to be responsible for bladder carcinogenesis [28, 29]. Certain dietary habits (low fruit and vegetable intake) [30], chronic inflammatory diseases of the bladder [31], Schistosomiasis, as well as a family history of bladder neoplasms have also been indicated as risk factors for bladder cancer.

Bearing in mind the limitations of our study (a short, two–year period, as well as a single-centre based study), we can still conclude that the percentage of urothelial tumours of the kidney in our series is higher than in most of the reported series, which should lead to an expanded analysis.

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Резиме

ИНЦИДЕНЦА НА ТУМОРИТЕ НА УРИНАРНИОТ ТРАКТ ВО ПЕРИОД ОД ДВЕ ГОДИНИ (2010–2011) НА ИНСТИТУТОТ ЗА ПАТОЛОГИЈА, МЕДИЦИНСКИ ФАКУЛТЕТ, СКОПЈЕ, МАКЕДОНИЈА

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Направена е ретроспективна анализа на туморите на бубрезите и на долниот уринарен тракт дијагностицирани на Институтот за патологија во период од две години (2010–2011), со цел да се направи пресек на основните морфолошки и статистички карактеристики на овие тумори. Сите случаи беа дијагностицирани на парафински пресеци од хируршки примероци рутински боени со хематоксилин и еозин, како и имунохистохемиски со панел на моноклонални антитела. Анализата покажа вкупно 755 случаи, од кои 166 (14%) потекнуваа од бубрегот, вклучувајќи ја и бубрежната карлица, а 649 (86%) беа тумори на мочниот меур. Дванаесет случаи од бубрежните тумори (11,3%) беа бенигни, а останатите беа малигни тумори. Поголемиот дел од нив беа аденокарциноми (n = 77; 72,6%), а 17 случаи (16%) карциноми со потекло од преодниот епител на бубрежната карлица. Анализата на туморите на долниот уринарен тракт покажа силна преваленца на малигни уротелни тумори (96%), со сооднос на мажи наспроти жени од 4 : 1. Доминантна карактеристика беше нискиот степен на малигнитет (71,7%), а кај 51 случај (22,9%) беше најден висок степен на малигнитет. Процентот на уротелни тумори на бубрегот во нашата серија е повисок од оној во сличните објавени студии, поради тоа е потребна продлабочена анализа.

Клучни зборови: тумори на уринарен тракт, инциденца, морфолошки карактеристики, бенигни и малигни тумори на бубрезите, бенигни ималигни тумори на горен уринарен тракт, бенигни и малигни тумори на долен уринарен тракт.