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Clinical and Pathological Analysis of Non-Epithelial Tumours of the Genitourinary System: A Single Centre Experience

Genitoüriner Sistemin Epitelyal Olmayan Tümörlerinin Klinik ve Patolojik Analizi: Tek Merkez Deneyimi

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ÖZET

Amaç: Genitoüriner sistem tümörlerinin çoğunluğu epitelyal kökenli iken, epitelyal olmayan tümörler genitoüriner sistemde izlenen tümörlerin yalnızca küçük bir bölümünü temsil eder. Bu çalışmada, bu nadir tümörlere yönelik tanı yaklaşımına katkıda bulunmayı ve bunların hasta prognozu üzerindeki etkilerine dikkat çekmeyi amaçladık.

Gereç ve Yöntemler: 2021-2023 yılları arasında genitoüriner sistem biyopsisi yapılan hastaların hasta kayıtlarına hastane veri tabanından ulaşıldı. Histopatolojik değerlendirmeye göre epitelyal tümör veya non-neoplastik doku tanısı konulan hastalar çalışma dışı bırakıldı. Epitelyal olmayan tümör tanısı almış hastaların demografik bilgilerine hastane veri tabanından, tümörle ilgili verilere ise patoloji raporlarından ulaşıldı.

Bulgular: Belirtilen dönemde, genitoüriner sistemde epitelyal olmayan tümör tanısı almış 20 vaka tespit edildi. Vakaların çoğu erkek hastalardan oluşmaktaydı. En sık görülen tümör lokalizasyon yeri böbrekti. Vakalar arasında 11 hastaya kötü huylu tümör tanısı konuldu, 9 hastaya ise iyi huylu tümör tanısı konuldu. Leiomyosarkom en sık görülen kötü huylu tümör olarak izlenirken, anjiyomyolipom en sık görülen iyi huylu tümördü. Diğer malign tümörler arasında rabdomyosarkom, liposarkom, andiferansiye pleomorfik sarkom, paraganglioma, malign soliter fibröz tümör ve diffüz büyük B hücreli lenfoma yer almaktaydı. İyi huylu epitelyal olmayan tümörler arasında ise anjiyoleiomyoma, schwannoma, renomedüller interstisyel hücreli tümör, leiomyoma ve anjiyofibrom mevcuttu. İyi huylu tümörü olan hastalara parsiyel rezeksiyon, transüretral rezeksiyon, eksizyonel biyopsi gibi cerrahi işlemler uygulanırken, kötü huylu tümörü olan hastalara radikal rezeksiyon, parsiyel rezeksiyon, trucut biyopsi ve transüretral rezeksiyon işlemleri uygulandı. Çalışma periyodunun sonunda (1 ila 38 ay arasında), iyi huylu tümör tanısı alan tüm hastalar hayattaydı, kötü huylu tümörü olan üç hasta ise hayatını kaybetmişti.

Sonuç: Genitoüriner sistemde, epitelyal olmayan tümörler nadir olarak izlenir ve geniş bir histolojik çeşitlilik gösterir. Kesin tanı histopatolojik incelemeye dayanır. Bu nadir tümörler için doğru tanı ve doğru tedavi stratejisi hastanın sağ kalımını önemli ölçüde değiştirir.

Anahtar Kelimeler: Genitoüriner sistem, epitelyal olmayan tümörler, malign, benign

ABSTRACT

Objective: While the majority of tumours in the genitourinary system originate from epithelial origin, non-epithelial tumours constitute only a minor subset. This study was conducted to improve diagnostic approaches for these rare tumours and to emphasize their impact on patient outcomes.

Materials and Methods: The patient records of patients who underwent genitourinary system biopsy between 2021 and 2023 were accessed from the hospital database. Patients diagnosed as epithelial tumour or non-neoplastic tissue according to histopathological evaluation were excluded from the study. Demographic data of patients diagnosed with non-epithelial tumours were obtained from the hospital database and tumour-related data were obtained from pathology reports.

Results: During the specified period, a total of 20 patients were identified, most of whom were male. The kidney was the most frequently affected site. Malignant tumours were diagnosed in 11 patients, and benign tumours in 9. Leiomyosarcoma was the most common malignant tumour, while angiomyolipoma was the most frequently observed benign tumour. Other malignant tumours included rhabdomyosarcoma, liposarcoma, undifferentiated pleomorphic sarcoma, paraganglioma, malignant solitary fibrous tumour, and diffuse large B-cell lymphoma. Benign tumours included angioleiomyoma, schwannoma, renomedullary interstitial cell tumour, leiomyoma, and angiofibroma. Surgical procedures varied depending on tumour type and included excisional biopsy, partial resection, and radical resection. During the follow-up period (ranging from 1 to 38 months), survival was achieved in all patients with benign tumours, whereas three patients with malignant tumours died.

Conclusion: Non-epithelial tumours of the genitourinary system are rare and display significant histological heterogeneity. Definitive diagnosis relies on histopathological evaluation. Appropriate diagnostic and therapeutic strategies may significantly influence patient survival.

Keywords: Genitourinary system, non-epithelial tumours, malignant, benign

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INTRODUCTION

Non-epithelial tumours of the genitourinary system (GUS) are considered diagnostically challenging due to their rarity and wide morphological spectrum (1,2). These tumours may arise in various anatomical locations within the GUS, including the kidneys, bladder, prostate, testes, and paratesticular region. In the existing literature, only individual case reports have been presented on this topic. Therefore, the objective of this study was to evaluate the clinical and histopathological features of non-epithelial tumours occurring in the GUS and to underline the diagnostic difficulties they may present.

MATERIALS AND METHODS

Patient records of those who underwent biopsy of the genitourinary system between 2021 and 2023 were accessed from the hospital database. Patients diagnosed with epithelial tumours or non-tumoral tissue based on histopathological evaluation were excluded from the study. Tumours located in the entire genitourinary system—including the kidney, ureter, bladder, prostate, urethra, testis, and paratesticular region—were included, while those originating from the female genital tract were excluded. As a result, twenty patients diagnosed with non-epithelial tumours of the genitourinary system were identified.

Demographic data such as age and gender were retrieved from hospital records. Tumour-related information, including histopathological diagnosis, tumour size, anatomical location, metastasis status at diagnosis, and details of surgical intervention, was extracted from pathology reports. All pathological specimens were re-evaluated. Postoperative follow-up was performed at regular intervals. Survival data were obtained from patient files. Basic statistical methods (means, percentages) were used for the analysis of variables such as age, gender, histopathological diagnosis, tumour size, and anatomical location. Ethical approval for the study was obtained from the local Clinical Research Ethics Committee on 17 July 2024 (approval number: 17.07.2024/08).

RESULTS

The demographic characteristics of the patients are summarized in Table 1. A majority of the patients were male (13; 65%), and the remaining were female (7; 35%). Tumours were diagnosed in adulthood in 18 cases, while 2 cases involved pediatric patients. The patients' ages ranged from 11 to 89 years, with a mean age of 53.1 years. Additionally, one patient was diagnosed with Von Hippel–Lindau syndrome (VHL). The kidney was identified as the most common tumour site, accounting for 35% of cases (7 patients). Other locations included the bladder (5 cases), paratesticular region (3 cases), testis (3 cases), prostate (1 case), and urethra (1 case). The mean tumour diameter was 6.71 cm. Benign tumours had an average size of 3.3 cm, whereas malignant tumours averaged 9.4 cm

Table 1. Clinical and pathological features of the patients

Patient No	Age	Sex	Tumor type	Diameter (cm)	Localization	Metastasis	Operation	Survival	Follow-up
1	89	M	Angioleiomyoma	1	Bladder	None	TUR	Alive	9
2	78	M	MSFT	16	Bladder	None	Partial cystectomy	Alive	21
3	53	M	Paraganglioma	0.7	Bladder	None	TUR	Alive	12
4	40	M	Leiomyosarcoma	6.9	Prostate	None	Trucut biopsy	Alive	9
5	69	F	AML	2.5	Kidney	None	Partial nephrectomy	Alive	18
6	52	F	AML	11	Kidney	None	Partial nephrectomy	Alive	38
7	23	M	Schwannoma	5	Paratesticular region	None	Excisional biopsy	Alive	25
8	37	M	RMICT	1.2	Kidney	None	Partial nephrectomy	Alive	27
9	45	F	AML	2.5	Kidney	None	Partial nephrectomy	Alive	34
10	63	F	Leiomyosarcoma	17	Kidney	None	Radical nephrectomy	Alive	10
11	69	M	UPS	8	Kidney	Present	Trucut biopsy	Ex	7
12	32	M	Leiomyoma	2.5	Kidney	None	Partial nephrectomy	Alive	26
13	76	M	Liposarcoma	10	Paratesticular region	None	Radical orchiectomy	Alive	7
14	11	M	Angiofibroma	3.3	Paratesticular region	None	Excisional biopsy	Alive	8
15	16	M	Rhabdomyosarcoma	7.2	Testis	None	Partial orchiectomy	Alive	19
16	73	M	Leiomyosarcoma	10	Testis	None	Radical orchiectomy	Alive	28
17	75	M	DLBCL	13	Testis	Present	Radical orchiectomy	Ex	1
18	80	F	UPS	10.5	Bladder	None	Radical cystectomy	Ex	2
19	43	F	Leiomyoma	1.5	Urethra	None	Excisional biopsy	Alive	24
20	39	F	Paraganglioma	4.4	Bladder	None	TUR	Alive	1

M: Male, F: Female, TUR: Transurethral resection, MSFT: Malignant solitary fibrous tumor, AML: Angiomyolipoma, RMICT: Renomedullary interstitial cell tumor, UPS: Undifferentiated pleomorphic sarcoma, DLBCL: Diffuse large B-cell lymphoma

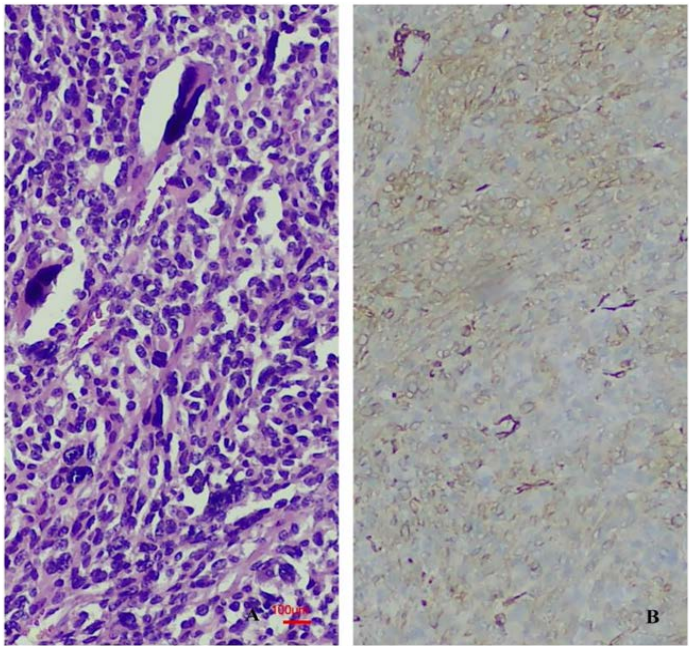

Figure 1. A) Leiomyosarcoma, composed of spindle-shaped smooth muscle cells, some of which have a bizarre appearance, HE x200. B) Positive staining of tumor cells with smooth muscle actin, SMA x200.

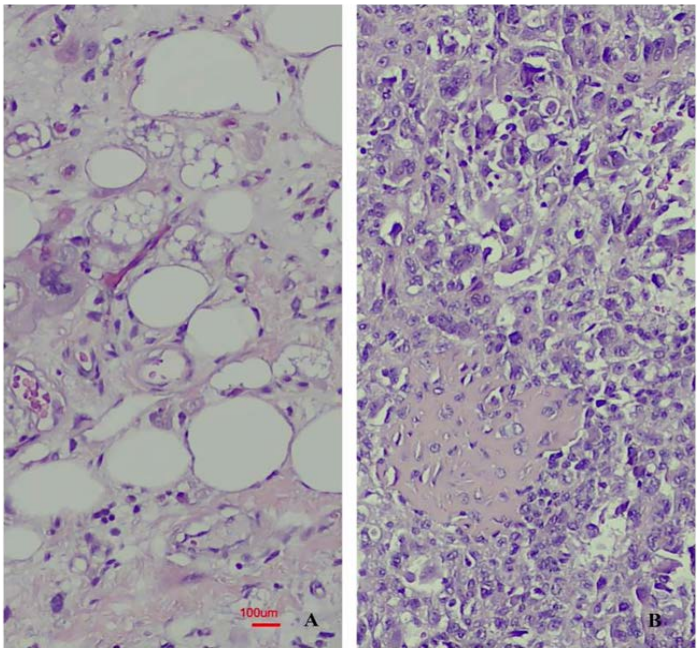

Figure 2. A) Areas of well-differentiated liposarcoma containing lipoblasts, HE x200. B) Dedifferentiated liposarcoma displaying regions of osteoblastic differentiation, HE x200.

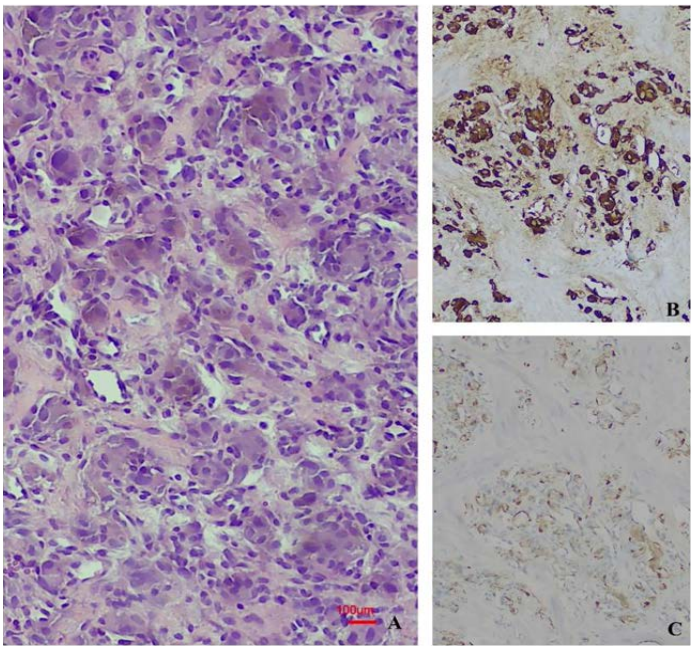

Figure 3. A) Paraganglioma exhibiting a nested pattern, HE x200. B) Neoplastic cells are positive for chromogranin A, x200. C) Sustentacular cells are positive for S100, x200.

in diameter. Of the total 20 patients, malignant tumours were diagnosed in 11 (55%) and benign tumours in 9 (45%).

Leiomyosarcoma was identified as the most common non-epithelial malignant tumour, accounting for 37.5% of all malignant cases (Figure 1). Other malignant tumours included rhabdomyosarcoma, liposarcoma (Figure 2), undifferentiated pleomorphic sarcoma, paraganglioma (Figure 3), malignant solitary fibrous tumour, and diffuse large B-cell lymphoma (DLBCL). Angiomyolipoma was the most frequently observed benign non-epithelial tumour, comprising 33.3% of benign cases (3 patients). Additional benign tumours included angioleiomyoma, schwannoma, renomedullary interstitial cell tumour, leiomyoma, and angiofibroma.

Among patients with benign tumours, partial resection was performed in 5 cases (55.5%), transurethral resection in 1 case, and excisional biopsy in 3 cases. In patients with malignant tumours, radical resection was conducted in 5 cases (45.4%), while partial resection, trucut biopsy, and transurethral resection were each performed in 2 cases. At the time of diagnosis, metastasis was present in 2 patients. The median follow-up period was 16.3 months. By the end of the follow-up (ranging from 1 to 38 months), all patients with benign tumours were alive, while 3 patients (27.3%) with malignant tumours had died.

DISCUSSION

Due to their rarity, non-epithelial tumours of the

genitourinary system (GUS) have primarily been reported in the literature through case reports or small series focused on specific organs (3–8). As a result of the limited number of comprehensive studies, data concerning their prevalence and incidence remain insufficient. In a study involving 48 cases of urological soft tissue sarcomas, the retroperitoneum was reported as the most frequent tumour location, with a male predominance and leiomyosarcoma being the most observed histological type. The average tumour diameter was noted as 9.5 cm (4). In the present study, most patients were male, the kidney was identified as the most frequent location, and leiomyosarcoma was the most common tumour type. The mean diameter of malignant tumours was found to be 9.4 cm. Another study analysing 28 bladder-based non-epithelial tumours reported 17 malignant and 11 benign cases. Small cell carcinoma and cavernous hemangioma were the most prevalent malignant and benign types, respectively (6). In the current series, paraganglioma was the most frequent malignant tumour in the bladder, while angioleiomyoma was the only benign tumour encountered in this site.

According to the World Health Organization (WHO) 5th edition classification of urinary and male genital tumours, non-epithelial tumours of the urogenital system are categorized as mesenchymal, hematolymphoid, melanocytic, and paragangliomas under neuroendocrine neoplasms. B-cell lymphomas and histiocytic tumours are classified within hematolymphoid neoplasms, whereas mucosal melanoma falls under melanocytic lesions (9). Mesenchymal tumours include fibroblastic, myofibroblastic, vascular, pericytic, smooth muscle, skeletal muscle tumours, and those of uncertain differentiation. Paragangliomas, as non-epithelial neuroendocrine tumours, are also classified under neuroendocrine neoplasms (9). Leiomyosarcoma has been identified as the most frequent histological subtype among non-epithelial tumours of the genitourinary tract (10). While commonly found in the retroperitoneum, its presence in the pelvis is less frequent. Within the GUS, these tumours are generally located in the bladder, prostate, and kidney, with primary paratesticular cases being extremely rare (11). In this study, leiomyosarcoma was the most prevalent histopathological diagnosis, with cases in the prostate, testis, and kidney.

Histologically, genitourinary leiomyosarcomas resemble those from other sites, consisting of intersecting fascicles of elongated spindle cells with blunt-ended nuclei. Well-differentiated tumours exhibit mild cytologic atypia and abundant eosinophilic cytoplasm, whereas poorly differentiated forms present with pleomorphism, necrosis, or increased mitotic activity (12). Adult genitourinary sarcomas are typically graded as low- or high-grade, with most leiomyosarcomas in the GUS—except those of the paratesticular region—being high-grade (13). These tumours generally show immunoreactivity for smooth muscle markers such as smooth muscle actin (SMA), desmin, h-caldesmon, and calponin, and are negative for S100. Embryonal rhabdomyosarcoma (ERMS) represents the most common urinary tract sarcoma in children, commonly affecting the urethra, bladder, and prostate (14). It is also the leading mesenchymal tumour of the paratestis in pediatric patients and may arise in the testicular parenchyma through somatic transformation of a teratoma (15). Although rare, renal involvement in children may occur through heterologous differentiation of Wilms tumour. In adults, bladder ERMS typically reflects sarcomatoid differentiation of urothelial carcinoma. In this series, ERMS was identified in an adolescent patient with testicular involvement.

ERMS displays variable cellularity, characterized by a range from spindle to fusiform cells within a loose myxoid stroma, with rhabdomyoblasts frequently present. In the botryoid subtype of ERMS, polypoid nodules with low cellular density are found near an epithelial surface, forming a dense layer of tumor cells known as the cambium layer. Alveolar RMS is composed of monomorphic round cells arranged in sheets or an alveolar pattern, separated by fibrous septa. Pleomorphic RMS features polygonal, round, and spindle-like cells with prominent nuclear pleomorphism. The spindle cell/sclerosing RMS subtype is defined by intersecting fascicles of monomorphic spindle cells in a dense, hyalinized matrix.
All rhabdomyosarcomas demonstrate skeletal muscle differentiation, with desmin positivity nearly universal and nuclear expression of myogenin and MYOD1 observed in most cases, albeit variably (16). Dedifferentiated liposarcoma (DDLPS) most commonly arises in the retroperitoneum but has also been documented in the spermatic cord, mediastinum, trunk, head, and neck. Within the GUS, case reports describe DDLPS in the paratesticular region and kidney (17,18). In the current case series, the tumour was located in the paratesticular area.

The histologic hallmark of DDLPS is an abrupt transition from an atypical lipomatous tumor/well-differentiated liposarcoma to a non-lipogenic, typically high-grade sarcoma. Dedifferentiated areas can display a variety of histologic patterns, most commonly resembling undifferentiated pleomorphic sarcoma or moderate to high-grade myxofibrosarcoma (19). Nearly all cases show diffuse nuclear expression of MDM2 and/or CDK4 (20). Undifferentiated sarcomas are rare and can appear in various anatomical sites without significant age or sex predilection. The pleomorphic subtype is more prevalent in older adults. In this study, such tumours were located in the kidney and bladder. These tumours lack distinct histological patterns and often exhibit pleomorphic multinucleated giant cells.

Solitary fibrous tumors (SFTs) of the GUS can arise in various anatomical sites, with cases reported in the kidney, urinary bladder, prostate, seminal vesicles, and penis. SFT is a fibroblastic tumor characterized by randomly arranged spindle cells in a "patternless" pattern with staghorn-like vascularization and defined by NAB2-STAT6 gene rearrangement. Immuno histochemically, most SFTs are positive for CD34 and STAT6, though PAX8 expression in some cases may lead to diagnostic confusion with sarcomatoid renal cell carcinoma, warranting consideration in the differential diagnosis of renal spindle cell tumors (21,22). Risk models based on factors such as patient age (≥ 55 years), mitotic rate (≥ 2 mitoses/mm^2), tumor size,

and presence of necrosis help estimate the risk of metastasis (23). In the current series, the SFT was in the bladder and classified as malignant based on risk stratification.

Paragangliomas (PGLs) are neuroendocrine neoplasms typically found in the retroperitoneum, pelvis, or bladder wall, associated with paraganglia presence. In the GUS, PGLs are infrequently observed in locations such as the prostate, seminal vesicles, kidneys, and paratestis. A significant proportion of PGLs 30-40% in adults and a higher percentage in children are linked to inherited conditions. Indicators such as young age, multiple tumors, and extra-adrenal tumors suggest the possibility of a germline mutation (24). PGLs display a distinctive Zellballen growth pattern, consisting of nests separated by a fibrovascular network and supported by sustentacular cells. Some PGLs, particularly those with clear cytoplasm, may mimic carcinomas of the bladder, prostate, or kidney (25). They typically show strong positivity for neuroendocrine markers like synaptophysin and chromogranin A, with S100 staining in sustentacular cells, while most are negative for cytokeratin. In our cases, the tumors were located in the bladder, with one patient being monitored for VHL. DLBCL can develop in any part of the GUS, with the kidney being the most frequent site (26). It is more prevalent within the GUS compared to other lymphoma types yet constitutes less than 1% of all genitourinary tumors (27). There is a slight male predominance in the incidence of primary genitourinary lymphomas (26).

DLBCL constitutes a morphologically and immuno phenotypically diverse group of aggressive lymphomas. It is characterised by sheets of large lymphoid cells with varying numbers of small lymphocytes, histiocytes, and other inflammatory elements. The tumour cells may exhibit centroblast or immunoblast features and can demonstrate variable pleomorphism (28). Among benign tumours of the GUS, a wide variety of histogenetic origins are observed, including cellular angiofibroma, hemangioma, glomus tumour, myointimoma, myopericytoma, PEComa, and leiomyoma. In addition to the general non-epithelial tumours encountered throughout the GUS, certain organs harbour specific tumour types. For instance, the kidney may host unique entities such as renomedullary interstitial cell tumour, juxtaglomerular cell tumour, and ossifying renal tumour of infancy.

This study was limited to cases from a single institution over a defined period. Expanding the study across multiple centres or extending the timeframe could potentially uncover additional mesenchymal tumours. For optimal patient care, it is crucial to maintain awareness of the morphological features of rare tumours and remain informed about emerging entities, even if direct morphological familiarity is lacking.

CONCLUSION

In addition to the numerous epithelial tumours, a broad spectrum of less common non-epithelial tumours can be encountered in the genitourinary tract. Accurate identification of these lesions is of critical importance, as it directly influences treatment protocols, surgical planning, and prognosis. A definitive diagnosis must be established through histopathological examination.

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