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Case Report

Complex Urothelial Carcinoma with Micropapillary and Nested Variant with Tubular Differentiation and Omental Metastasis in a Dog: A Case Report

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Abstract

In this presentation, the pathological examination of a complex micropapillary and nested urothelial carcinoma, tubular variant, diagnosed in the renal pelvis of a 1.5-year-old male Wolfdog, along with omental metastasis, is presented. The owner brought their dog to Selçuk University Veterinary Faculty Animal Hospital with complaints of bloody urine and a mass in the abdominal region upon palpation. During the clinical examination, a large mass was detected in the left kidney during the ultrasonographic examination. During the surgical removal of the kidney, masses were also observed in the omentum and samples were taken. The tissues were sent to the Pathology Laboratory of Selçuk University Faculty of Veterinary Medicine for histopathological examination. Macroscopic examination revealed that the mass in the kidney was 20x13x11 cm in size, creamy pink in colour, soft in consistency, and multilobular in structure. Microscopic examination revealed that significant atypia, pleomorphism, mitotic figures, cells with nuclei pushed to the periphery, signet ring cells, and Melamed-Wolinska bodies in the tumour cells. The diagnosis was nested variant urothelial carcinoma and omentum metastasis, showing micropapillary and tubular differentiation due to the presence of tubular and micropapillary structures formed by tumour cells.

Keywords: Cytology, histopathology, immunohistochemistry, micropapiller, urothelial carcinoma,

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Introduction

Kidney tumors are rare in all animal species and are usually detected in older animals between 7-9 years of age. Kidney tumors arise from renal tubular epithelial cells, renal pelvis, and embryonal tissues. The most common kidney tumors are renal cell carcinoma and nephroblastoma. Urothelial carcinoma (UC), also known as transitional cell carcinoma, is an aggressive tumor that arises from the transitional epithelial cells lining the urinary tract and is rarely observed in humans and all animal species. It is most seen in the bladder and less frequently in the upper urinary tract (renal pelvis and ureters) and is invasive. It is more common in female dogs than in male dogs. Due to their genetic predisposition, the incidence of this tumor is significantly higher in Scottish Terriers, West Highland White Terriers, Fox Terriers, Airedales, Shetland Sheepdogs, and Beagles compared to other breeds. It is a tumor with a high risk of metastasis. The most common metastases are to the lungs and lymph nodes, while metastases to the large intestine, abdominal wall, eyes, and leg skeletal muscle have also been reported (Mutsaers et al 2003, Wilson et al 2007, Moore and Frimberger 2009, Grader et al 2016, Meuten and Meuten 2016, Yönez et al 2016, De Brot et al 2018, Van Der Weyden et al 2021, Ates et al 2022, Hernández et al 2025).

Clinically, hematuria, stranguria, and pollakiuria can be observed in UC. Nonspecific symptoms such as anorexia, weight loss, abdominal pain, and depression are more common (Klein et al 1988, Goldsmid et al 1992, Militerno et al 2003, Moore and Frimberger 2009, Fulkerson and Knapp 2015). Clinical examination reveals an abdominal mass, kidney enlargement, and hydronephrosis (Wimberly and Lewis 1979). Many risk factors such as genetic disorders, cyclophosphamide exposure and obesity play a role in its etiology (Burger et al 2013, Montella et al 2015, Alouini 2024).

Macroscopically, it can appear as a cauliflower-shaped, raised mass that often extends into the lumen. It can also be solid or cystic. The mass has a soft consistency that can be easily broken down. Marked renomegaly and widespread atrophy of the cortical and medullary parenchyma may be observed in the kidney containing the tumor. Histopathologically, tumor cells are round or polygonal, have prominent nuclei, and are pleomorphic. Mitotic figures are common. The histopathological appearance of the tumor varies depending on its grade and variant. Papillary, micropapillary, microcystic, glandular, squamous, sarcomatoid, rhabdoid, plasmacytoid, giant cell, clear cell, signet ring cell, small cell, and lymphoma-like variants have been described (Maranchie et al 2000, Militerno et al 2003, Yang et al 2013, Lin et al 2018, Lohith 2018, Matsumoto et al 2018, Alderson et al 2020, Park and Kang 2020, Van Der Weyden et al 2021). This study was deemed worthy of presentation because of the simultaneous observation of two rare variants of the rare UC: the micropapillary version and the nested variant with tubular differentiation.

Case presentation

Case History

In of the left kidney of a 1.5-year-old male Wolf Dog is described based on clinical and pathological findings. The patient's owner submitted the dog for examination at the Selcuk University Faculty of Veterinary Medicine, citing symptoms including bloody urine and a palpable abdominal mass that had persisted for a duration of two months. At the examination with palpation, there was tenderness in the abdominal area, and a mass was detected on the left side of the abdomen. During clinical examination, ultrasonographic evaluation of the abdominal region revealed a large mass in the left kidney, and based on this finding, surgical intervention was planned. Intraoperatively, multiple miliary lesions were also observed on the surface of the right kidney, and masses were detected in the omentum. The left kidney was completely excised, and tissue samples from the omental lesions were collected for histopathological evaluation and submitted to the Department of Pathology.

Material and Method

Cytological samples were obtained by fine needle aspiration (FNA) from both kidney and omentum tissues before fixation and then stained with Giemsa. After cytological sampling, kidney and omentum tissues were fixed in 10% formaldehyde solution for one day and routine tissue processing procedures were applied. Then, 5-micrometer-thick sections were cut from the paraffin-embedded tissues using a microtome and placed on adhesive slides. Tissue sections were stained with hematoxylin-eosin (HE) stain and proliferating cell nuclear antigen (PCNA,

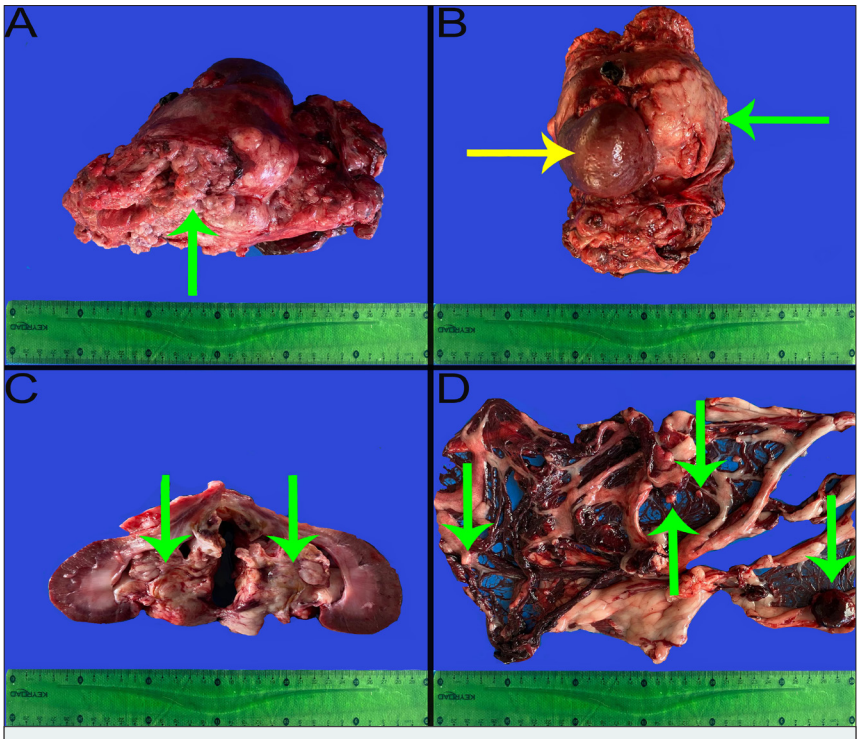

Figure 1. A-B. Large, rough, irregular surfaced, creamy-pale pink colored and hard in consistency tumoral mass extending into the renal pelvis in the left kidney (green arrows), normal kidney tissue (yellow arrow). C. Irregular cream-colored tumor mass located in the pelvis on sagittal section of the kidney (green arrows). D. Tumor masses located on the omentum (green arrows)

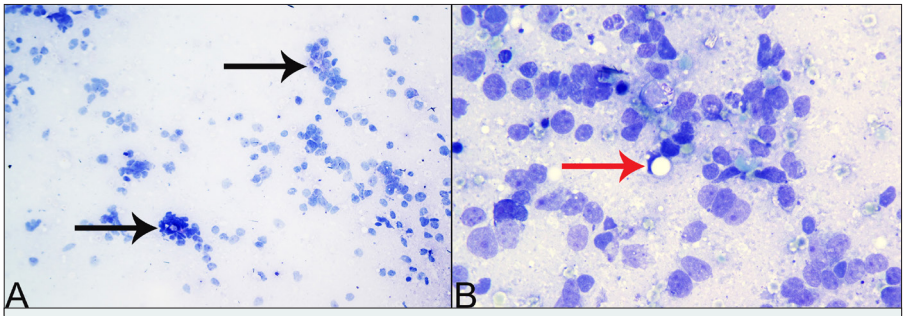

Figure 2. A. Atypical tumor cells (black arrows), Giemsa Staining, x400, FNA. B. Signet-ring cell (red arrow), Giemsa Staining, x1000, FNA

1:100, DAKO) by immunohistochemistry according to previously reported methods (Bulut et al 2023, Ekici et al 2024, Kanat 2024, Kayıkcı et al 2024, Sensoy and Güneş 2024). Then the sections examined under a light microscope and photographed (Olympus BX51, Tokyo, Japan).

Results and discussion

The mass in the renal pelvis was 20x13x11 cm, creamy pink in color, firm, irregularly contoured, and multilobular. There were areas of bleeding on its surface and necrotic areas were present in the center of the mass on the cut surface. The masses in the omentum were of various sizes, smoothly contoured, and creamy pink in color and firm. In this case, UC was detected in the renal pelvis and omental tissues. The mass was creamy-pale pink colored and soft consistency (Figure 1). UC is most observed in the urinary bladder in dogs. Urothelial carcinoma, which originates from the renal pelvic epithelium in dogs, is a rare tumor and has been reported to occur mostly in older animals (average age 7-9 years) (Militerno et al 2003, De Brot et al 2018, Park and Kang 2020). In this case, the tumor mass was taken from a 1.5-year-old crossbreed Wolfdog breed dog from the renal pelvis region, which is reported to be rarely observed (Figure 1A-C). Clinical findings such as renomegaly, abdominal mass, hematuria and abdominal pain, as well as nonspecific findings such as anorexia, weight loss and depression can be observed in humans, cats and dogs (Klein et al 1988, Militerno et al 2003). In the dog in this presentation, tenderness and a mass were detected in the abdominal region during palpation. While lung metastases were the most common,

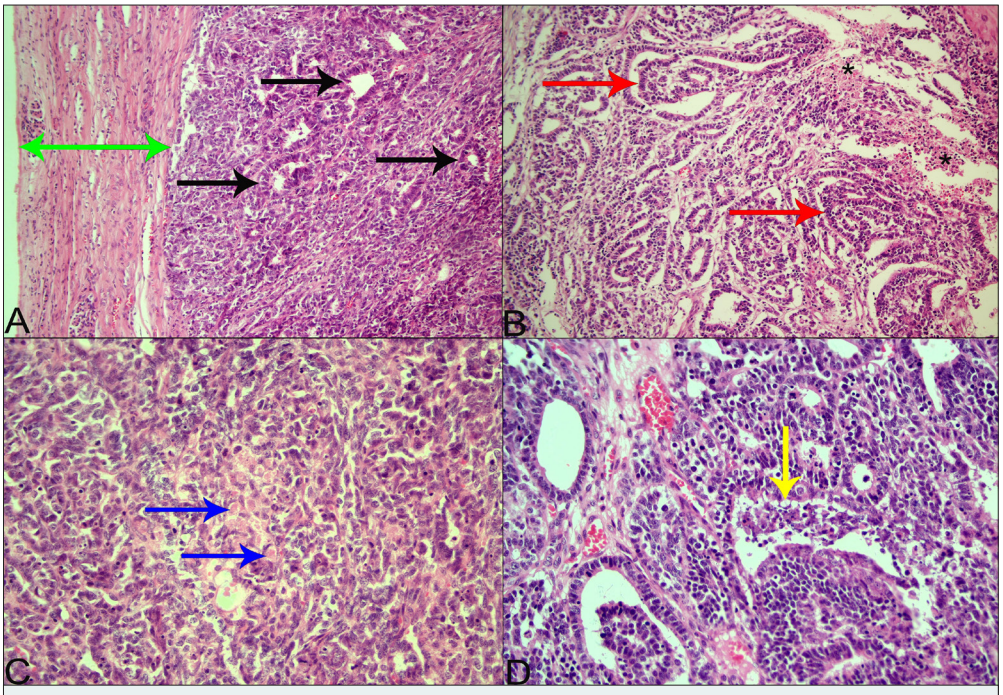

Figure 3. A. Tubular structures formed by atypical tumor cells (black arrows) and stromal fibrosis (green arrow), x200, H&E. B. Micropapills (red arrows) and large necrotic areas (asterisks) formed by tumor cells, x200, H&E. C. Intracytoplasmic eosinophilic Melamed-Wolinska bodies in tumor cells (blue arrows), x400, H&E. D. Signet ring cells (yellow arrow), x400, H&E

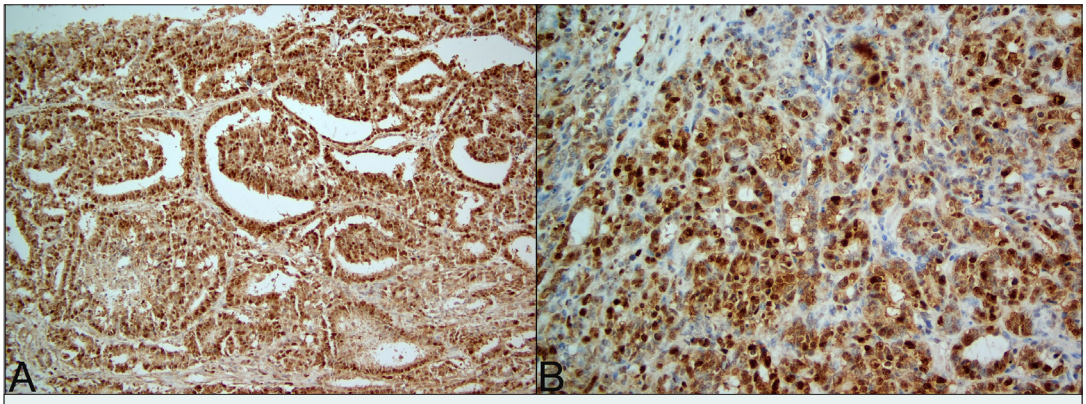

Figure 4. A-B. PCNA positive staining in the nuclei of tumor cells (black arrows), A. X200, B. X400, IHC-DAB

metastases to the large intestine, abdominal wall, eye, and leg skeletal muscle have also been reported (Mutsaers et al 2003, Wilson et al 2007, Moore and Frimberger 2009, Grader et al 2016, Yönez et al 2016, De Brot et al 2018, Van Der Weyden et al 2021, Hernández et al 2025). In this case, omentum metastasis was detected, which is rarely reported (Figure 1D).

Cytological and histopathological examination reveals Melamed-Wolinska bodies and signet ring cells containing large cytoplasmic vacuoles. Melamed-Wolinska bodies are intracytoplasmic eosinophilic structures, a characteristic finding in the diagnosis of UC and leading directly to the diagnosis. Signet ring cells are ring-like vacuoles formed by mucin-containing vacuoles in the cytoplasm of tumor cells, displacing the cell nucleus toward the periphery (Meuten and Meuten 2016, Shilpa et al 2019). In this case, both cytological and histopathological examinations revealed intracytoplasmic eosinophilic Melamed-Wolinska bodies (Figure 3C) and signet ring cells with large, sharp-edged spaces in their cytoplasm (Figure 2B, Figure 3D)

In UC, tumor cells show marked atypia and pleomorphism. The nuclear-to-cytoplasmic ratio is increased, and mitotic figures are common. Cytoplasmic vacuoles are commonly observed in tumor cells (Knapp et al 2020). Nested, papillary, micropapillary, microcystic, glandular, squamous, sarcomatoid, rhabdoid, plasmacytoid, giant cell, clear cell, signet ring cell, small cell, and lymphoma-like variants of UC have been described in the literature (Lin et al 2018, Lopez-Beltran et al 2019, Park and Kang 2020, Van Der Weyden et al 2021). In this study, two rare variants of urothelial carcinoma, the micropapillary variant and the nested variant with tubular differentiation, were observed together (Figure 3A-B).

PCNA is a nuclear protein predominantly found in the G1, S, and G2 phases of the cell cycle, is an important indicator of cell proliferation, and is widely observed to be expressed in tumours. PCNA indices assess the biological behaviour, aggressiveness, and prognosis of cells. A high PCNA index often indicates accelerated growth, advanced stage, and a poor prognosis in neoplasms (Stoimenov and Helleday 2009, Yıldırım et al 2014). PCNA expression, mitotic index, tumour grade, and cell differentiation levels were found to change significantly across different tumour grades. This situation suggests that PCNA expression could be useful in predicting prognosis in animal tumours (Ahmed and Sözmen 2020, Lv et al 2021). In this case, immunohistochemical staining was conducted utilizing the PCNA antibody to assess proliferative activity. Following staining, sections were assessed using a light microscope, with strong positive immunoreactivity identified as nuclear brown staining. In this case, the presence of strong positive staining reflects the high proliferative activity of UC, indicating that UC is an aggressive and invasive tumor (Figure 4A-B).

Conclusion

Urothelial carcinoma originating from the renal pelvis epithelium in dogs is a very rare tumor and only a few cases have been reported in the literature. In this case report, a rare case of micropapillary and nested variant with tubular differentiation urothelial carcinoma of the renal pelvis and omentum metastasis in a dog was described clinically, cytologically and histopathologically. Urothelial carcinoma is a tumor that frequently develops in the bladder in dogs and is often diagnosed late. Despite their benign histology, these tumors are frequently invasive and associated with a poor prognosis. Early diagnosis and histopathological typing of this invasive tumor are crucial for prognosis and treatment.

Declarations

Competing Interests

The authors declared that there is no conflict of interest.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author.

Ethical Statement
Informed consent was obtained from the animal owner.

Author Contributions
Motivation / Concept: OO, Design: OO, Control/Supervision: OO, Data Collection and Processing: AB, MMSG; Analysis and Interpretation: AB, MMSG; Literature Review: AB, MMSG; Writing the Article: AB; Critical Review: OO

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