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Metastatic genitourinary cancer diagnosed by body fluid cytology: clinicopathologic and cytomorphologic correlation

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Introduction Malignant effusions secondary to genitourinary cancers constitute less than 5% of metastatic malignancies. Because of their rarity, definitive cytodiagnosis may be challenging. Our study aims to examine the incidence of malignant fluids secondary to genitourinary cancers in our institution, and to characterize their clinicopathologic and cytomorphologic features.

Methods A search of our database was undertaken for all body fluids reviewed from January 2003 through April 2014 at our institution.

Results During this 11.3-year study period, our search revealed 8255 body fluids. Of these, 1341 (16.2%) were malignant with only 15 (0.2%) due to a genitourinary primary, constituting a mere 1.1% of all malignant fluids. Eight cases (53%) were urothelial carcinomas, 6 (40%) were renal cell carcinomas, and 1 was a bladder leiomyosarcoma (7%). No prostate cancers were found. Seven (47%) involved the pleura, 6 (40%) were in the peritoneum, and 2 (13%) were in the cerebrospinal fluid (CSF). None were detected in the pericardium. Genitourinary metastases comprised 1.9% of peritoneal, 0.8% of pleural, 1.9% of CSF malignant fluids.

Conclusion Metastatic genitourinary cancers in body fluids are rare, making up only 0.2% of all fluids and 1.0% of all malignancies. The cytomorphologic features of metastatic urothelial and renal cell carcinoma, although similar to those described in the literature, are nonspecific. To our knowledge, this is the first reported case of metastatic bladder leiomyosarcoma in ascites diagnosed by effusion cytology. Because leiomyosarcoma in body fluids can demonstrate epithelioid features and cohesiveness, it may be confused with metastatic carcinomas.

Introduction

Genitourinary (GU) cancers were estimated to constitute 21.5% of cancers diagnosed in the United States in 2015,

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Table 1 Immunohistochemical stains for metastatic genitourinary cancers effusions.

Antibody	Vendor	Dilution	Pretreatment	Instrument
Caldesmon	Dako	1:100	High pH	Leica Bond III
CD10	Dako/Leica	1:50	High pH	Dako/Leica Bond III
CK 7	Dako	1:400	Protease K	Dako
CK 5/6	Dako	1:100	High pH	Dako
Desmin	Leica	Prediluted	High pH	Leica Bond III
p63	Dako	1:100	Low pH	Dako
PAX-2	Santa Cruz Biotech	1:100	High pH	Dako
PAX-8	Proteintech/Cell Marque	1:100	Low pH/High pH	Dako/Leica Bond III
RCC	Dako	1:100/1:50	Protease K/Enzyme	Dako/Leica Bond III
SMA	Leica	Prediluted	None	Leica Bond III
Vimentin	Dako	Prediluted	Low pH	Dako

Abbreviations: CD, cluster of differentiation; CK, cytokeratin; PAX, paired box gene; RCC, renal cell carcinoma marker; SMA, smooth muscle actin.

with prostate cancer (13.3%) being most common in men, followed by urinary bladder (4.5%) and kidney/renal pelvis (3.7%) cancers in both men and women combined.[1] In contrast, metastatic GU cancer is only rarely diagnosed in body fluid cytology, compared to the more frequently encountered lung, breast, and ovarian cancers.[2] The incidence of metastatic renal cell carcinoma, urothelial carcinoma, and prostatic adenocarcinoma in malignant serous effusions has been reported to be only 1.7%, 1.2%, and 0.2%, respectively.[3] In one study, metastatic prostatic cancer was identified in only 2.3% of malignant pleural effusions,[4] and metastatic urothelial carcinoma to the cerebrospinal fluid (CSF) was detected in fewer than 0.4% of cases.[5]

Because of the rarity of such metastatic involvement of body fluids by GU cancers, definitive cytodiagnosis may be challenging. Significant overlap in the cytomorphologic features of urothelial and pulmonary carcinomas has been noted in both pleural and peritoneal fluids.[6-8] Huang et al[9] also described morphologic similarities not only between metastatic urothelial carcinoma and adenocarcinoma, but also with poorly differentiated squamous cell carcinoma, malignant melanoma, and even reactive mesothelial cells in effusions. Additionally, metastatic renal cell cancer cells

Table 2 Genitourinary metastases in body fluid cytology (2003-2014).

Patient	Age, Sex	Primary cancer	Primary site	Grade	Stage	Body fluid site	Time to metastasis (years)	Metastasis to other sites	Time from effusion to death (weeks)
1	68, F	Urothelial CA	Bladder	G3-4	IV	Peritoneal	4.9 mo	Retroperitoneal lymph nodes	0.6
2	76, M	Urothelial CA	Bladder	G3-4	IV	Peritoneal	1.2	Retroperitoneal, iliac lymph nodes	1.7
3	80, M	Urothelial CA	Bladder	G4	IV	Peritoneal	1.3	Prostate, urethra	1.6
4	72, F	Urothelial CA	Bladder	G3	IV	Pleural	0	Liver, skull, humerus, acetabulum, ribs	1
5	97, M	Urothelial CA	Bladder	G3-4	I	Pleural	6.1	-	11.7
6	61, M	Urothelial CA	Left renal pelvis	G3-4	IV	Pleural	0	Lung	43.4
7	60, M	Urothelial CA	Bladder	G3	IV	CSF	0.8	-	5.7
8	69, M	Urothelial CA	Bladder	G3-4	IV	CSF	1.3	Cerebellum	1.3
9	58, M	RCC, clear cell	Bilateral kidneys	N/A	IV	Pleural	1.9 mo	Lungs, skin, scalp, right thigh soft tissue	N/A
10	57, M	RCC, clear cell	Right kidney	G2	III	Pleural	2.6	Lung	9.7
11	69, F	RCC, clear cell	Left kidney	G4	III	Pleural	6.8	Liver, ribs, adrenal gland	1
12	64, M	RCC, clear cell	Left kidney	G2	IV	Pleural	12	Lung, femur, patella	1.4
13	47, M	RCC, clear cell	Left kidney	G3	III	Peritoneal	0.8	Lung, liver	4.4
14	60, M	RCC, clear cell	Left kidney	G2	II	Peritoneal	8.2	Liver	20.4
15	48, F	Leiomyosarcoma	Bladder	G3-4	IV	Peritoneal	0	-	10.9

Abbreviations: CA, cancer; CSF, cerebrospinal fluid; mo, months; RCC, renal cell carcinoma;.