

## Case Report

# Carcinosarcoma of female urethra with melanocytic differentiation

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**Abstract:** Carcinosarcoma arising from the female urethra is rare. We report an unusual case of urethral carcinosarcoma from a female patient with melanocytic differentiation. The tumor consists of a high-grade papillary serous carcinoma with psammoma bodies and a mesenchymal component with area of heterologous (cartilaginous) element. More interestingly, there are epithelioid tumor cells containing melanin pigment. On immunohistochemical stains, the epithelioid tumor cells are positive for S100, HMB45 and Mart-1, but negative for cytokeratin. This case represents an unusual carcinosarcoma with areas of melanocytic differentiation. Such rare tumors have been occasionally reported in the breast, uterus, kidney, and lung. These cases demonstrate the capacity of tumor cells to differentiate into divergent elements, supporting the concept of pluripotent tumor stem cells.

**Keywords:** Urethra, carcinosarcoma, melanocytic differentiation, pluripotent tumor stem cells

### Clinical history

The patient was a 50-year old African American female, who presented with urinary tract infection and urinary retention. Further evaluation revealed a urethral mass associated with a urethral diverticulum. Biopsy of the mass showed poorly differentiated clear cell carcinoma. A subsequent anterior exenteration including total cysto-urethrectomy, total vaginectomy, bilateral pelvic lymph node dissection, and ileal conduit urinary diversion was performed. Her past medical history was significant for a stage II left breast cancer with chemotherapy 4 years ago and a total hysterectomy with bilateral salpingo-oophorectomy for menorrhagia 3 months ago.

### Material and methods

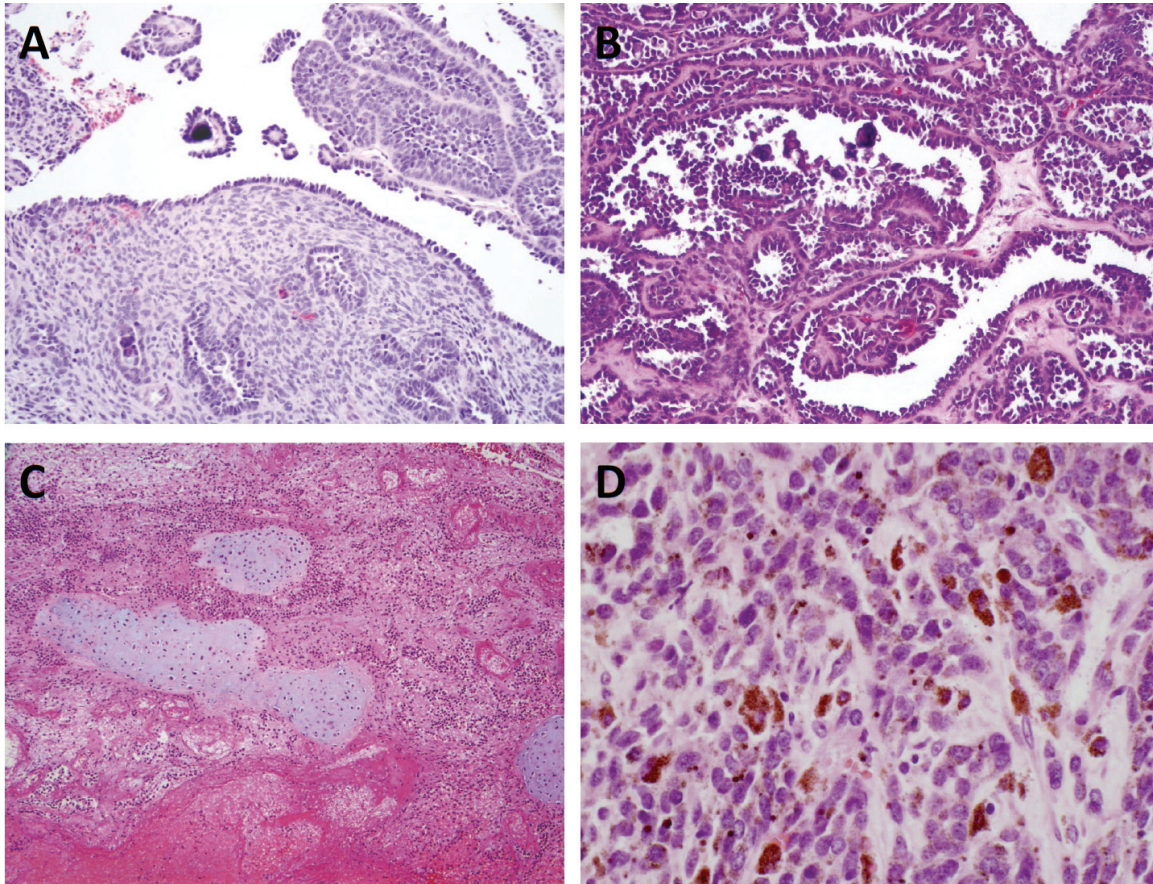
The urethra, bladder and anterior vagina were fixed in 10% buffered formalin. Representative sections were embedded in paraffin. Five-micrometer sections were cut and stained with hematoxylin and eosin [standard H&E]. Immunohistochemical studies were performed on

Ventana Autostainer, using antibodies for pan-cytokeratin, S-100, HMB-45 and Mart-1 (DAKO).

### Results

Grossly, the distal portion of the urethra has a 3x1x1 cm mucosal lesion as well as loose tumor within the lumen. On cut sections, the tumor appears friable with hemorrhage. There is mucosal dilatation of the urethra adjacent to the tumor, raising the possibility of a previous urethral diverticulum. The bladder and vaginal mucosa are free of tumor.

Microscopic examination showed predominantly a high grade papillary serous adenocarcinoma, with high nuclear grade, gland formation and psammoma bodies (**Figure 1A** and **1B**). In one area, sarcomatous components with heterologous [cartilaginous] element are present (**Figure 1C**), fulfilling the diagnosis of carcinosarcoma (malignant mesodermal mixed tumor). In addition, clusters of epithelioid cells containing melanin pigments are identified (**Figure 1D**). These cells are positive for S100, HMB45 and



**Figure 1.** Low (A) and high (B) power view of tumor showing high grade papillary serous adenocarcinoma with psammoma bodies. C. Area of sarcoma with heterologous element (cartilage); D. Area of epithelioid tumor cells containing melanin-pigments. The pigments are stained negative for iron (picture not shown).

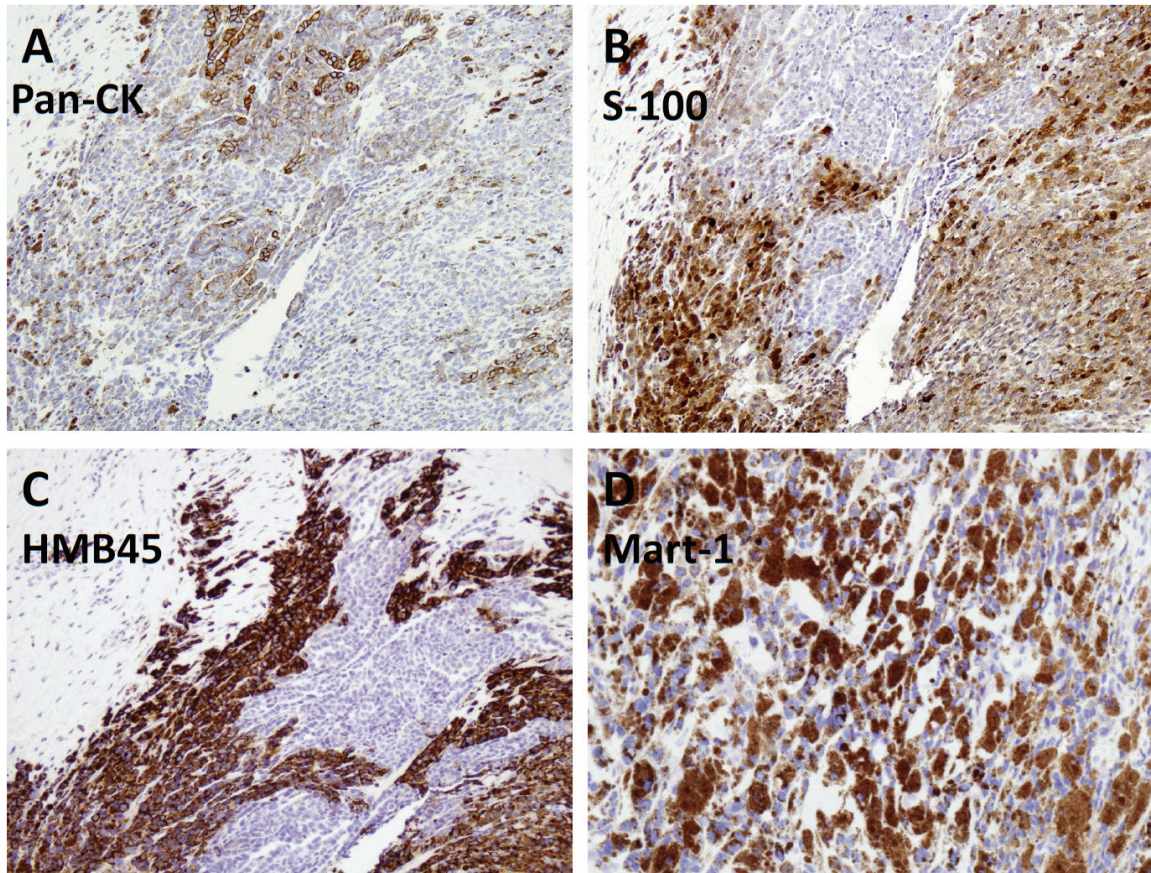
Mart-1, but negative for pan-cytokeratin staining (AE1/AE3) (Figure 2A, 2B, 2C, and 2D). The morphology and immunostaining pattern support melanocytic differentiation of those tumor cells.

#### Discussion

Carcinosarcoma is an aggressive tumor that can occur in almost any organ, with the uterus as one of the most common sites. Carcinosarcoma arising from the urethral tract is a rare entity. Only a few cases have been reported so far [1, 2, 3]. The unusual feature of this case is the presence of tumor cells with melanocytic differentiation. To the best of our knowledge, this is the first such case reported in female urethra, though carcinosarcoma with melanocytic differentiation has been reported in uterus [4, 5].

Previously, it was debatable whether carcinosarcoma is a biclonal or monoclonal neoplasm. Evidence of monoclonal origin of majority carcinosarcomas from uterus and ovaries supported the hypothesis that carcinosarcoma derives from the monoclonal pluripotent tumor stem cell via divergent histogenesis, so called divergent tumor theory [6, 7].

Combination of carcinoma and melanoma has been reported in the skin, oral cavity, lung, and breast [8-12]. Two cases of combined malignant melanoma and ductal carcinoma of the breast were reported by Padmore et al [11] with the hypothesis that a single tumor has bidirectional differentiation and the melanoma is differentiated from the primary breast ductal carcinoma. Further molecular testing on one similar case of breast carcinoma with melanocytic differentia-



**Figure 2.** One area of high grade tumor contained mixed epithelial and melanocytic components as the carcinoma-tous cells stained positive for cytokeratin, negative for S-100 (A); While the spindle melanocytic cells stained positive for S-100, negative for pan-cytokeratin (B); The cells stained positive for S-100 are also stained positive for HMB45 (C) and Mart-1 (D).

tion supported the theory that the malignant melanoma and breast carcinoma come from the same clonal tumor cells [12]. Those results are consistent with the divergent tumor theory.

In our case, the malignant melanoma is closely admixed with high grade carcinoma. We present it as another case supporting the tumor divergent theory.

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