Short communication

Vaginal metastasis of renal clear cell carcinoma: a case report emphasizing the role of immunohistochemistry in differential diagnosis in the absence of a clinical history

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We present the case of a 71-year-old patient, with vaginal bleeding, dyspnea, headache, loss of appetite and weakness. Clinical examination revealed a pediculated vaginal mass of 25 mm diameter, of dark-red color and soft spongy consistency, with an ulcerated surface and originating from the anterior wall, which was surgically removed. The morphology was dominanted by large, round to polygonal tumor cells, arranged in a predominantly tubulo-cystic architecture, surrounding numerous blood vessels that dominated the appearance, suggesting a perivascular epithelioid cell tumor (PEComa) or hemangioblastoma but the presence of pleomorphic nuclei, numerous mitoses together with immunohistochemistry helped for a correct diagnosis of vaginal .

Key words: vaginal metastasis, renal cell carcinoma, immunohistochemistry.

Introduction

A 71-year-old patient with an unremarkable past medical history presented to the Gynecology Department for vaginal bleeding, dyspnea, headache, loss of appetite and weakness observed in the prior 3 months. Clinical examination revealed a pediculated vaginal mass, 25 mm in diameter, of dark-red color and soft spongy consistency, with an ulcerated surface and originating from the anterior wall, which was surgically removed (Fig. 1A). There was no evidence of adenopathy or involvement of vulva or cervix. Microscopically, large round to polygonal tumor cells were arranged in a predominantly tubulo-cystic architecture, with numerous surrounding thin-walled blood vessels that dominated the appearance. The tumor cells had ample eosinophylic or clear vacuolated cytoplasm, with large pleomorphic nuclei, containing nucleoli and numerous atypical mitotic figures. Areas of hyalin, necrosis, haemorhage, and inflammatory infiltrates were also identified (Fig. 1B-F). The morphology suggested a perivascular epithelioid cell tumor (PEComa) or hemangioblastoma, but other primary and metastatic lesions characterized by tumor cells with eosinophylic or clear cytoplasm such as clear cell or squamous cell carcinoma, yolk sac tumor, renal cell carcinoma (RCC), sarcomas or malignant melanoma were also in the differential diagnosis. Immunohistochemistry revealed that vascular markers (CD31, CD34, Factor VIII, Podoplanin) were only positive in endothelial cells, while tumor cells were negative. Tumor cells were also negative for CK7,

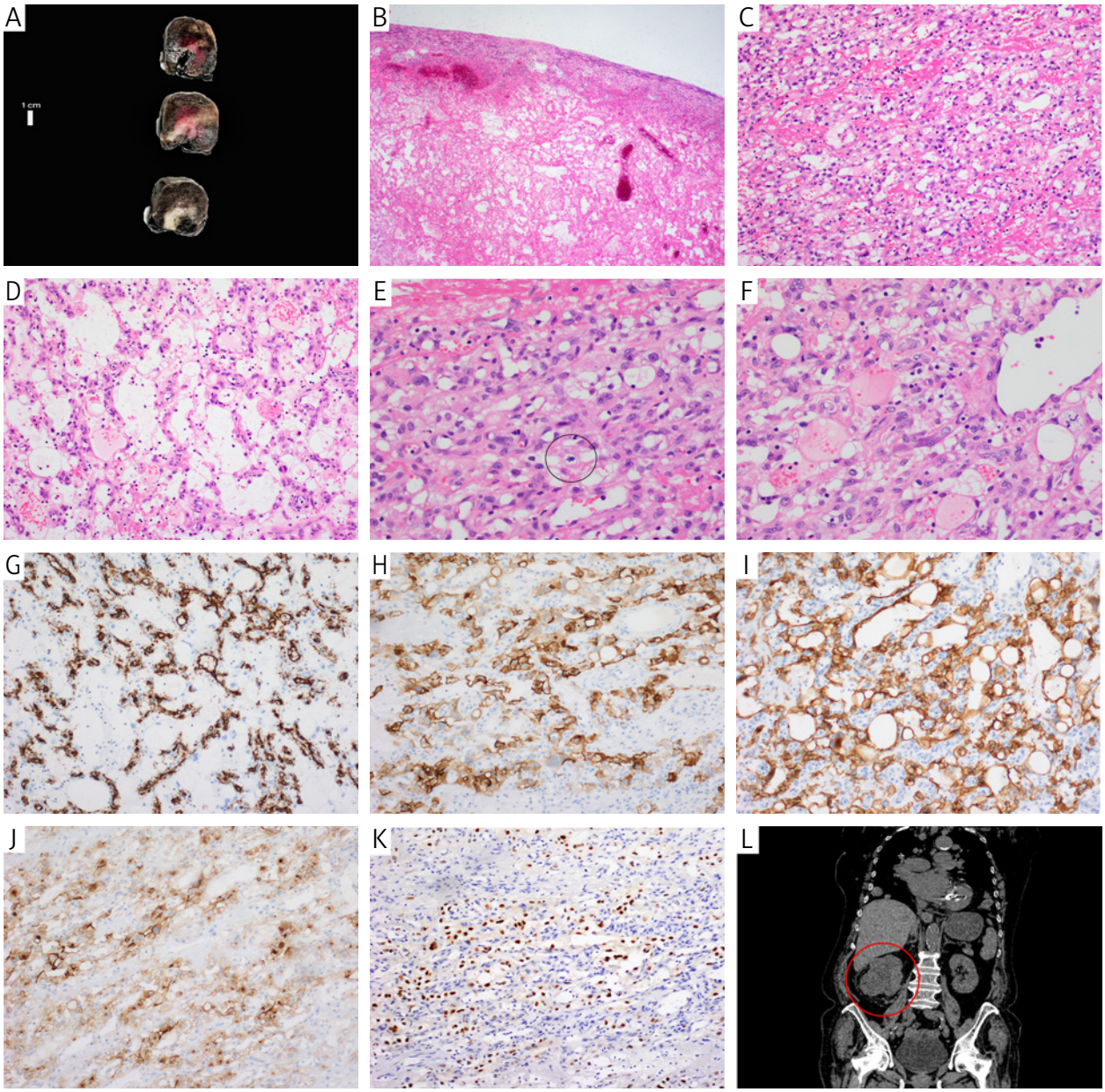

Fig. 1. Surgically removed vaginal mass of 25 mm diameter, of dark-red color and soft spongy consistency (**A**), with ulcerated surface (**B**); large tumor cells with ample eosinophylic or clear vacuolated cytoplasm, arranged in a predominantly tubulo-cystic architecture, (**C**) surrounding numerous blood vessels (**D**); numerous atypical mitotic figures (**E**); tumor cells with large pleomorphic nuclei, presenting nucleoli (**F**); tumor cells were negative for CD34 (**G**) but positive for EMA (**H**), CAIX (**I**), CD10 (**J**) and PAX 8 (**K**); abdominal computed tomography revealed a 100mm diameter right kidney mass (**L**)

p63, Vimentin, SALL4, α-fetoproteina, Melan-A, HMB45, AMACR, SMA, ER, PR. Tumor cells were instead positive for EMA, CAIX, CD10, PAX8 and focally for AE1/AE3 (Fig. 1G-K). The immunohistochemical profile together with tumor morphology were in favor of a metastasis from a RCC to the vagina. The patient was reffered to the Radiology Department for further investigations and abdominal computed tomography (CT) revealed a 100 mm diameter right renal mass with central necrosis, renal vein involvement and multiple lung nodules of 5-30 mm diameter (Fig. 1L). A subsequent nephrectomy confirmed the presence of a RCC, Fuhrman grade III/IV, sharing similar immunohistochemical and molecular profile with the vaginal metastasis. No systemic treatment was considered for the patient given her poor performance status.

Vaginal cancer represents approximately 1-2% of all genital tract malignancies with primary adenocarcinoma of the vagina comprising only 10% of all vaginal neoplasms; metastasis should always be considered when diagnosing an adenocarcinoma in the vagina [1]. Vaginal metastasis usually originate in the cervix, endometrium, ovary or colon. All

other metastases are extremely rare phenomena [2]. Hemangioblastoma is a rare, benign and highly vascular neoplasm usually occuring in the cerebellum, brainstem or spinal cord. Most are sporadic (70%), while familial cases (30%) are associated with loss or inactivation of the *VHL* gene, in association with von Hippel-Lindau (VHL) syndrome [3]. Microscopically, it is represented by neoplastic stromal cells with foamy cytoplasm, mild pleomorphism, hypechromatic nuclei, rare mitotic figures, with a background network of numerous small vessels and rare hyaline globules. Diagnosis is based on macroscopy (highly vascular tumor, of red color), morphology, clinical history of VHL syndrome or evidence of genetic alterations and immunohistochemistry (tumor cells are positive for Inhibin, CD56, S100 protein, CAIX and Vimentin and negative for AE1/AE3, EMA, PAX8, RCC, CD10). RCC accounts for 3% of all adult malignancies and 85% of all primary renal tumors and frequently metastasizes to lungs, lymph nodes, bone, and liver, while vaginal metastases are exceptional. Peham reported the first case of vaginal metastasis from RCC in 1906, and subsequently, less than 100 cases of vaginal metastasis of RCC were published [4, 5] with most cases being diagnosed as metachronous metastatic disease that was discovered long after radical nephrectomy. There are very rare reported cases of vaginal metastasis from RCC where the vaginal mass was discovered prior to the primary tumor, usually as a solitary mass and in these cases, the diagnosis was based on morphology (unlike the present case, was histologically resembling a clear cell carcinoma) and immunohistochemical profile (metastases of RCCs are positive for AE1/AE3, EMA, CD10, PAX8, RCC marker) [6]. In the present case, unlike previous cases published in the literature, the past medical history of the patient did not support a diagnosis of VHL syndrome or a primary RCC and the morphology was dominanted by numerous blood vessels surrounding tumor cells, suggesting a hemangioblastoma or PEComa, but the presence of pleomorphic nuclei, numerous mitoses together with immunohistochemistry provided a correct diagnosis of vaginal RCC metastasis, further confirmed by radiologic investigations.

The authors declare no conflict of interest.

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