CASE REPORT

Clear Cell carcinoma of the urinary bladder, A case report: Surgical and oncological management

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Summary
Introduction: Bladder cancer is a condition characterized by a broad spectrum of histological variants and clinical courses. The morphological description of histological variants is becoming increasingly important. The 75% of cases of these cancers are classified as pure urothelial carcinoma, while the remaining 25% is represented by other histological variants. The clear cell carcinoma is part of urothelial group and is a very rare entity. Oncological outcomes of this variant are still uncertain, but seems to be worst than for patients with pure urothelial carcinoma. Moreover it seems to metastatize more easily to the lymph nodes.

Case report: We present a case of a Caucasian 73 year old woman who, after an episode of gross hematuria, underwent an ultrasound of the urinary system, a cystoscopy and a total body computed tomography (CT) which confirmed the presence of a bladder neoplasms. A transurethral resection of the bladder (TURB) was performed: the result of the histological examination was "poorly differentiated clear cell carcinoma". Given the rarity of histological characterization, we required a PET-CT scan for more accurate staging, at which a suspected right pelvic lymph node was detected. We proposed a radical cystectomy with hysterectomy and extended lymphadenectomy. During the pre-hospitalization process, the patient developed anemia, with acute renal failure and bilateral hydronephrosis, which required the placement of bilateral nephrostomies; we performed the planned surgical procedure and the histological examination confirmed high grade urothelial carcinoma with a high percentage (more than 70%) of clear cell carcinoma, with a strong local aggression and lymph node metastases. We referred the patient to the oncologist who suggested a treatment plan within an immunotherapy based clinical trial and cisplatin.

Conclusions: The morphological description of histological variants in bladder cancer is gaining increasing importance, especially for infiltrating and aggressive forms. The clear cell carcinoma is a very rare entity part of the urothelial group; they would seem more aggressive forms with an early lymph node involvement. This evidence is confirmed by the clinical case described, in which we have seen a large local aggression with an involvement of the lymph nodes of the right side of the pelvis or the pre-sacral ones. In these cases, the multimodal approach is crucial.

Key words: Bladder cancer; Oncology; Uro-oncology; Rare tumors; Cystectomy.

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INTRODUCTION
Bladder cancer is a condition characterized by a broad spectrum of histological variants and clinical courses. Indicatively 75% of cases of these cancers are classified as pure urothelial carcinoma, while the remaining 25% is represented by other histological variants (1). The morphological description of histological variants is becoming increasingly important as underlined by the WHO 2016 classification (2), which introduced a particular category: "invasive urothelial carcinoma with divergent differentiation" for tumours showing a component of urothelial carcinoma combined with other morphologies (2-3). The real clinical importance of the histological variant is still under discussion, in fact the data are still insufficient to demonstrate a different clinical course compared to the conventional urothelial bladder carcinoma of the same stage and grade (2). Currently we can distinguish the histological variants in two large subgroups: urothelial and non-urothelial. The clear cell carcinoma is part of urothelial group and is a very rare entity, characterized by a glycogen-rich cytoplasmic pattern with tubulocystic, papillary, or diffuse growth patterns. This histological pattern must be distinguished from clear cell adenoscarcinoma of the urethra or bladder, or metastatic carcinoma originating from the kidney, prostate, or female genital tract; oncological outcomes of this variant are still uncertain, both for the rarity and for the short follow-up period, but seems to be worse than for patients with pure urothelial carcinoma (3-5). Moreover it is also one of the variants (together with the micropapillary histotype) that seems to metastatize more easily to the lymph nodes, suggesting theses variants are associated with lymphatic spread (6).

CASE REPORT
We present a case of a Caucasian 73 year old woman with a history of breast cancer, treated with left mastectomy and subsequent chemotherapy, diabetes mellitus and high blood pressure on medical therapy. She reported an episode of macrohematuria for which she underwent ultrasound of the urinary tract, which showed a thickening of the posterior wall of the bladder. It was therefore decided to perform a cystoscopy, which showed a large
therapy based clinical trial and cisplatin; unfortunately the patient rapidly worsened developing loss of appetite, constipation and pain in her right side. She underwent a total body CT scan that showed disease recurrence at the peritoneum, pelvis and ileal conduit which determined intestinal sub-occlusion and right hydrourteronephrosis. The clinical picture further worsened and the patient died almost four months after surgery.

**CONCLUSIONS**

The morphological description of histological variants in bladder cancer is gaining increasing importance, especially for infiltrating and aggressive forms. The role of this more accurate histological characterization in clinical practice is still under discussion. The clear cell carcinoma is a very rare entity part of the urothelial group, the oncological outcomes of this histotype are still uncertain, but they would seem more aggressive forms with an early lymph node involvement; this evidence is confirmed by the clinical case described, in which we have seen a large local aggression (with a rapid involvement of the ureteral hosts, the uterine cervix and the annexes) with an involvement of the lymph nodes of the right side of the pelvis of the pre-sacral ones. We have also witnessed a rapid recurrence of disease which quickly led to patient’s death. In these cases, the multimodal approach could be fundamental to improve the prognosis.

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