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Invasive bladder urothelial carcinoma, plasmacytoid variant: case report

Carcinoma urotelial invasor de bexiga, variante plasmocitoide: relato de caso

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ABSTRACT

Invasive bladder urothelial carcinoma, plasmacytoid variant is a rare entity with scarce cases reported in the literature. We report a case of a 79 years old male, subjected to transurethral resection of bladder tumor, which histological examination revealed a pT1 high-grade urothelial carcinoma. Subsequently, he underwent radical cystoprostatectomy, which showed urothelial carcinoma with lack of cohesion, plasmacytoid variant, positive for citokeratin 7 (CK7), citokeratin 20 (CK20) and trans-acting T-cell-specific transcription factor (*GATA-3*), and negative for E-cadherin and CD138. It is important to recognize the plasmacytoid variant of the invasive urothelial carcinoma, since it avoids a potential misdiagnosis of metastatic cancer.

Key words: urinary bladder; transitional cell cancer; carcinoma.

INTRODUCTION

Bladder cancer is the 11th most common cancer worldwide, with an incidence of 429,793 (3.1%) cases and a mortality of 165,084 (2%) persons[1]. Among all the bladder cancers urothelial carcinoma is the most common[2]. The urothelium consists of transitional epithelium with the ability to undergo metaplasia under several circumstances[3], also seen in urothelial carcinoma, known for its diverse differentiation, mainly squamous or glandular[2, 4]. In recent years, new, distinct and uncommon variants of urothelial carcinoma have been described, expanding the morphologic spectrum, namely nested, microcystic, plasmacytoid, clear cell, micropapillary, lymphoepithelioma-like and lobular, among others, accounting for 5%-15% of the transitional cell carcinomas with clinical implications[2-6].

CASE REPORT

Clinical data

Male seventy-nine years old was referred to a urology consultation reporting moderate to severe lower urinary tract symptoms, with sonographic incidental discovery of a 2.5 cm lesion compatible with tumor on the left wall of bladder. Pathology revealed a pT1 high-grade bladder urothelial cancer.

The patient was treated with intravesical Bacillus Calmette-Guerin (BCG) and the follow-up schedules were regular cystoscopies. Six weeks after BCG's induction the patient developed bladder tuberculosis, starting antimicrobial treatment. Tumor recurrence was diagnosed eight months after the resection of the primary tumor. Staging with abdominal and pelvic computed tomography (CT) showed bilateral obstructive uropathy and an apparently organ-confined disease. Bilateral nephrectomy was immediately held. Surgical treatment was proposed – radical cystoprostatectomy with pelvic lymphadenectomy and ureteroileostomy. Surgical laparotomy found a *frozen pelvis*, and complete removal of the bladder was impossible. The sigmoid colon was distended with signs of obstruction. Intraoperative general surgery consultation was requested and decided to perform a palliative terminal colostomy. During the postoperative period the patient's condition deteriorated and he died.

Histological evaluation

The examination was performed on sections stained with hematoxylin and eosin (HE) and observed in light microscope

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– Nikon Eclipse 50i, and images were obtained using a Nikon-Digital Sight DS-Fi1 camera.

Ancillary techniques/immunohistochemistry

The studies were performed in a representative block of the lesion, using the avidin-biotin-peroxidase complex detection method and performed on Ventana Marker Platform Bench Mark ULTRA IHC/ISH using the following antibodies: cytokeratin 20 (CK20) – S20.8, Dako, Denmark); cytokeratin 7 (CK7) – OV-TL, Dako, Denmark; E-cadherin – NHC-38, Dako North America, CA, USA; prostate specific antigen (PSA) – polyclonal, Ventana, AZ, USA; estrogens – SP1, Ventana, AZ, USA; progesterone – 1E2, Ventana, AZ, USA; synaptophysin – SP11, Ventana, AZ, USA; chromogranin A – LK2H10, Ventana, AZ, USA; S100 – polyclonal, Ventana, AZ, USA; melan A – A103, Ventana, AZ, USA; human melanoma black 45 (HMB45) – HMB45, Ventana, AZ, USA; cluster of differentiation 138 (CD138) – B-A38, Cellmarque, CA, USA; trans-acting T-cell-specific transcription factor (*GATA-3*) – L50-823, Cellmarque, CA, USA.

Pathological findings

Transurethral resection of bladder tumor (TURBT) specimen

The tumor was composed of papillae (**Figure A**), covered with cells with mild to moderate nuclear pleomorphism and architectural disorganization, infiltrating the sub-urothelial connective tissue, arrested within the boundaries of the detrusor muscle, with no sign of invasion nor an aggressive histological component.

Radical cystoprostatectomy specimen

Gross evaluation revealed several fragments, the largest with 10 cm, showing irregular, slightly elevated and reddish mucosa, in section that shows a white, firm and fasciculate transmural tissue. Also, it was sent a segment of sigmoid colon with 17 cm, apparently with no changes.

Histologically the largest fragment corresponded to the wall of the bladder, with an infiltrating tumor that dissociate the muscle fibers reaching the serous membrane and the perivesical fat, composed of discohesive cells arranged in a linear pattern with eosinophilic cytoplasm, some with intracytoplasmic vacuoles, with higher nuclear/cytoplasm ratio, sometimes with the nuclei diverted to the periphery, occasionally with visible nucleoli (**Figures B** and **C**).

The smaller fragments corresponded to the hyperplasic prostate tissue without tumor infiltration.

In the sigmoid there was tumor infiltration in serous, subserosa and muscular layers.

The tumor cells were positive for CK20, CK7 and epithelial membrane antigen (EMA), and negative for E-cadherin (**Figure D**), CD138 and all the other markers.

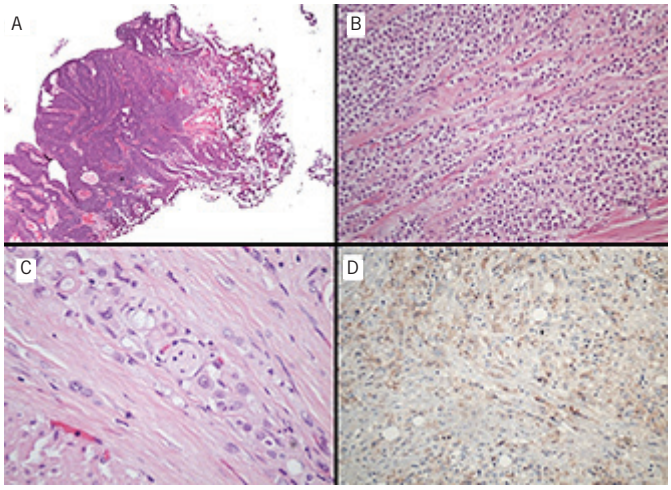

FIGURE – *Morphological and immunohistochemical characteristics of the resected specimens*

A) urothelial papillary neoplasia, HE 20×; B) invasive urothelial carcinoma with discohesive growth pattern, HE 200×; C) tumor cells showed eosinophilic cytoplasm and visible nucleoli, often with intracytoplasmic vacuoles and peripheral nucleus, HE 400×; D) negative for E-cadherin staining, 200×.

HE: hematoxylin and eosin.

DISCUSSION

Urothelial carcinomas have multiple morphological variants with different therapeutic and prognostic implications[4]. The plasmacytoid pattern of urothelial carcinoma is characterized by high-grade invasive urothelial carcinoma composed of discohesive cells forming linear single cells row, which is a well-known mimic of lobular breast cancer, becoming a potential pitfall for women and in small biopsies, especially in cases with little or no clinical information[2, 3, 7].

There is some confusion in the literature regarding the classification of invasive urothelial carcinomas with diffuse pattern, some named signet-ring cell urothelial carcinoma[3, 8], and plasmacytoid urothelial carcinoma[9]. In our case, only a few tumor cells had intracytoplasmic vacuoles with nuclei diverted to the periphery – not eccentric as in the signet-ring cell carcinoma

and lacked immunostaining in tumor cells for CD138, a feature, but not mandatory, of plasmacytoid tumors[8, 9].

Our case presented tumor dissemination to the omentum and colon, which reflects a more aggressive pattern when compared to the conventional urothelial carcinoma, which may be explained by the loss of E-cadherin linked to high-grade tumor and aggressive behavior[10]. The lack of E-cadherin expression in urothelial plasmacytoid and signet-ring cell carcinomas gave rise to the idea that they could be part of the same spectrum of high-grade invasive urothelial carcinomas[10]. However, the morphological and immunohistochemical differences between them provide us with information that they are probably distinct on subtypes of urothelial carcinomas[3, 7-10].

The differential diagnosis includes bladder extension by prostate carcinoma – ruled out by negative stain for PSA. A metastatic gastric carcinoma (diffuse-type) should also be considered (ruled out by the absence of gastric tumor in clinical history/evaluation and *GATA-3* immunohistochemistry expression)[2, 7], and regardless of their rarity, breast metastasis must also be excluded – negative for estrogens and progesterone receptors[3]. The presence of a previous usual papillary urothelial neoplasm with an invasive component provides a solid support of a bladder origin for the tumor[7], despite absence of an aggressive morphological subtype in previous TURBT (possible lack of representativeness).

The plasmacytoid pattern of invasive urothelial carcinoma represents a rare and aggressive morphological variant in which the correlation between the histological and clinical findings is extremely important to provide an accurate diagnosis of primary bladder cancer, avoiding diagnosis of secondary tumor, particularly in females and small biopsies. Awareness of this entity is fundamental for an early and accurate diagnosis.

CONFLICT OF INTEREST

None of the contributing authors has any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

RESUMO

*Carcinoma urotelial invasor da bexiga, variante plasmocitoide, é uma entidade rara, com poucos casos descritos na literatura. Relatamos o caso de um homem, 79 anos, submetido à ressecção transvesical de tumor da bexiga, cuja histologia revelou carcinoma urotelial de alto grau pT1. Posteriormente, foi submetido à cistoprostatectomia radical, que mostrou carcinoma urotelial invasor, descoeso, de tipo plasmacitoide, positivo para citoqueratina 7 (CK7), citoqueratina 20 (CK20) e fator de transcrição de ação "trans" específico de células T (*GATA-3*) e negativo para E-caderina e CD138. É importante reconhecer a variante plasmocitoide do carcinoma urotelial invasor, uma vez que se evita potencial diagnóstico errado de doença metastática.*

Unitermos: *bexiga urinária; carcinoma de células de transição; carcinoma.*

REFERENCES

1. World Health Organization. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. [Accessed on: Nov. 2014]. Available at: http://globocan.iarc.fr/Pages/fact_sheets_population.aspx.

2. Bostwick DG, Cheng L. Urologic surgical pathology. 2 ed. Mosby: Elsevier; 2008. p. 272-99.

3. Baldwin L, Lee AH, Al-Talib RK, Theaker JM. Transitional cell carcinoma of the bladder mimicking lobular carcinoma of the breast: a discohesive variant of urothelial carcinoma. Histopathology. 2005; 46: 50-6.

4. Nigwekar P, Amin MB. The many faces of urothelial carcinoma – an update with an emphasis on recently described variants. Adv Anat Pathol. 2008; 15(4): 218-33.

5. Amin MB, McKenney JK, Paner GP, et al. ICUD-EAU international consultation on bladder cancer 2012: pathology. Eur Urol. 2013; 3(63): 16-35.

6. Paner GP, Annaiah C, Gulmann C, et al. Immunohistochemical evaluation of novel and traditional markers associated with urothelial differentiation in a spectrum of variants of urothelial carcinoma of the urinary bladder. Human Pathol. 2014; 45(7): 1473-82.

7. Galia A, Amico P, Emmanuele C, Tranchina MG, Pepe P, Fraggetta F. Primary invasive urothelial carcinoma of the bladder. Pathol – Res and Pract. 2013; 209: 327-9.

8. Wang Z, Lu T, Du L, et al. Plasmacytoid urothelial carcinoma of the urinary bladder: a clinical pathological study and literature review. Int J Clin Exp Pathol. 2012; 5(6): 601-8.

9. Rahman K, Menon S, Patil A, Bakshi G, Desai S. A rare case of plasmacytoid urothelial carcinoma of bladder: diagnostic dilemmas and clinical implications. Indian J Urol. 2011; 27(1): 144-6.

10. Lim MG, Adsay NV, Grignon DJ, Osunkoya AO. E-Cadherin expression in plasmacytoid, signet ring cell and micropapillary variants of urothelial carcinoma: comparison with usual-type high-grade urothelial carcinoma. Mod Pathol. 2011; 24: 241-7.

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