Annals of Diagnostic Pathology 40 (2019) 176–179

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

journal homepage: www.elsevier.com/locate/anndiagpath

Letter to the Editors

Immunohistochemical stains to detect residual tumor in cystectomy specimens taken shortly after transurethral resection of bladder tumors

ARTICLE INFO

Keywords:
Urothelial carcinoma
Immunohistochemistry
pT0
GATA3

Sir,

Trans-urethral resection of urinary bladder is carried out for diagnostic and therapeutic purposes in case of urinary bladder lesions. In 5–20% of cases, TUR leads to complete resection of urothelial carcinoma. In those cases, the following resection specimen does not show any residual tumor cells, and it is classified as pT0 [1]. However, TUR procedure may also lead to an inflammatory response consisting in granulomata or cystitis with giant cells or atypical mononuclear cells [2,3], which may masquerade residual cancer in haematoxylin and eosin (H&E) stained slides and determine understaging in the surgical specimen.

Herein we show the utility of immunohistochemistry to avoid understaging of bladder carcinoma in surgical specimens obtained shortly after TUR and showing post-TUR cystitis. Among 21 urinary bladders surgically resected for urothelial carcinoma during the last year, we observed cystitis with giant cells or atypical mononuclear cells with no readily apparent residual cancer in a total of 4 (19%) cases. Residual cancer was found in all the 17 remaining cases, with different pT stage (pT2a: 3 cases; pT2b: 2 cases; pT3a: 6 cases; pT3b: 3 cases; pT4a: 3 cases). All cases with cystitis were obtained from male patients submitted to TUR procedure 1 to 2 months before surgery. None had received neo-adjuvant treatments. In all 4 cases, inflammatory infiltrate was present in the anatomical site of TUR and it involved the mucosa and suburothelial connective layer, but not the muscularis propria. In 3 cases, the mucosa was ulcerated with a fibrous scar and showed multinucleated giant cells, lymphocytes and plasma cells (Fig. 1a). In the other case, we found medium/large sized cells with eccentric atypical nucleus, prominent nucleolus and abundant eosinophilic cytoplasm, in the thickness of mucosa (Fig. 2a).

In all 4 surgical specimens we performed immunohistochemistry against wide spectrum cytokeratin, GATA3 and p63, to identify residual cancer.

Two cases (cases 1 and 2) with giant cells cystitis had no cells positive for cytokeratin AE1/AE3, p63 and GATA3, apart from normal urothelium, and were classified as pT0. The other case (case 3) with giant cells cystitis was classified as pT3a stage due to the presence of aggregates or single tumor cells positive for cytokeratin, GATA3 and p63 in the muscularis propria (Fig. 1b) and in the perivesical adipose tissue.

Finally, immunohistochemistry showed that medium/large sized cells seen in the latest case (case 4) were positive for CKAE1/AE3, GATA3 and p63, thus demonstrating that they were neoplastic cells infiltrating the lamina propria of the urinary bladder (Fig. 2b). In addition, it disclosed small aggregates of neoplastic cells (positive for CKAE1/AE3, GATA3 and p63) in the muscularis propria (Fig. 2c), in the peri-vesical adipose tissue and in the vessels lumen, leading to classification as pT3a (Fig. 2c).

In conclusion, TUR may give rise to apparent complete resection. However, aggregates or single cancer cells may remain within the muscularis propria or in the adipose tissue. Due to their small size, they are not easily identifiable with H&E stain alone. Thus, im-

https://doi.org/10.1016/j.anndiagpath.2018.09.008

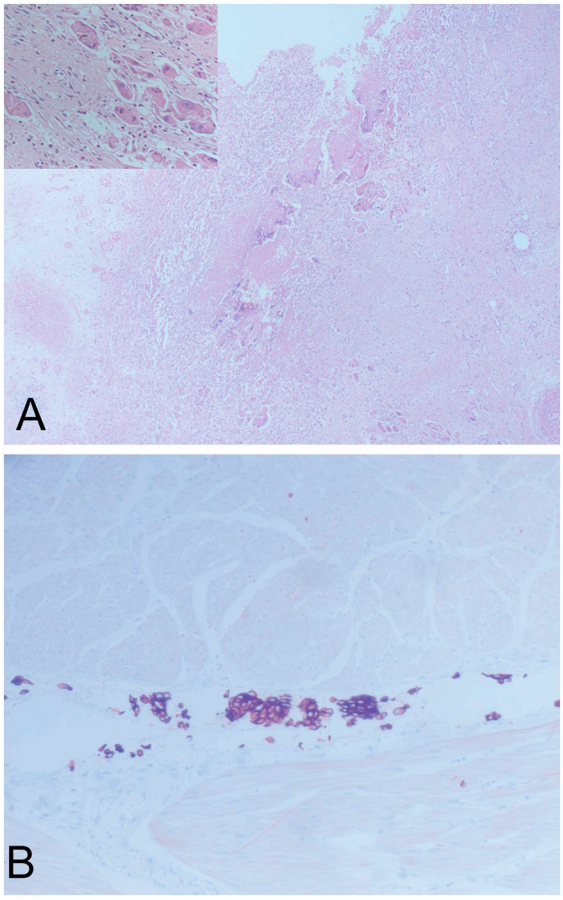

Fig. 1. a. Cystitis with fibrous scar and giant cells (inset in the left upper corner) in the TUR site in a bladder surgical specimens. No neoplastic cells were evidenced at H&E stain (H&E stain; original magnification ×100). b. Cytokeratin AE1/AE3 immunohistochemistry revealed aggregates of neoplastic cells, not seen at H&E stain, in the muscularis propria (CKAE1 stain; original magnification, ×200).

munohistochemistry against epithelial markers (CKAE1/AE3) may be essential for their identification and to avoid pT understaging in the surgical specimen. When tumor cells are only seen in the muscularis propria and in the perivesical fat, immunohistochemistry against urothelial markers (GATA3 and p63) may be useful to confirm urothelial primitivity.

We may hypothesize that residual cancer cells not identified by H&E alone may account for bad outcome reported in some patients with pT0 bladder carcinoma after radical cystectomy [4,5]. Thus, we suggest that immunohistochemistry may be required to detect residual carcinoma in urinary bladder surgical specimens after TUR, when cancer is not readily identifiable, and to avoid understaging.

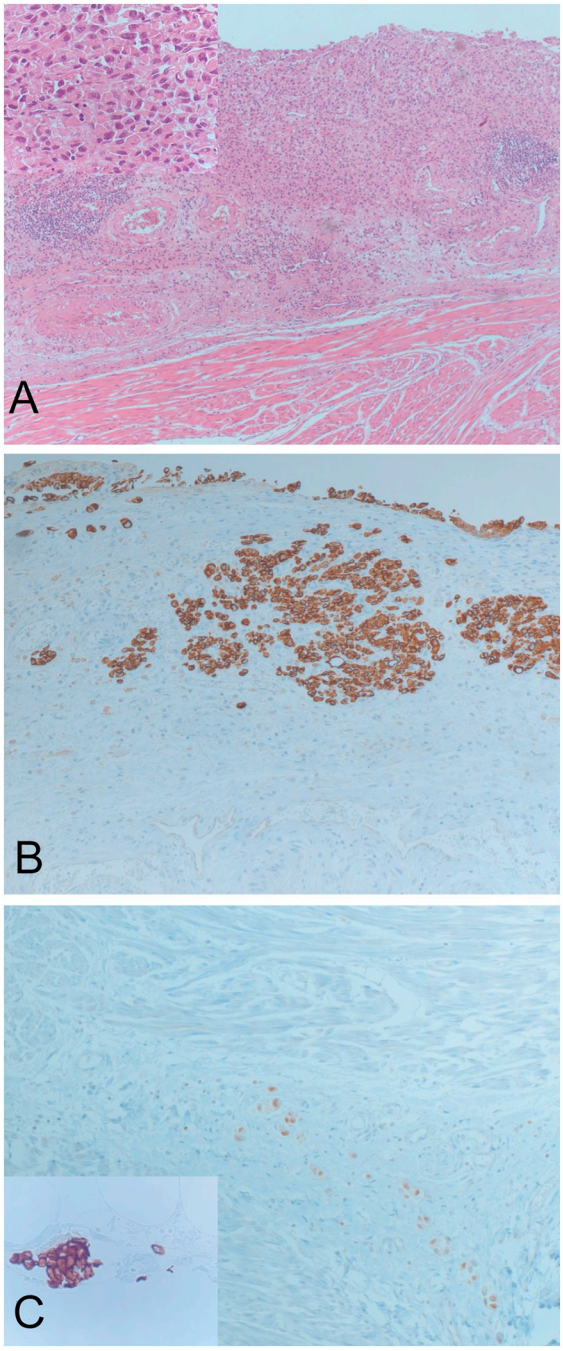

Fig. 2. a. Atypical cells in the lamina propria of urinary bladder (H&E stain; original magnification ×40) shown at higher magnification in the inset in the left upper corner (H&E stain; original magnification ×400); b. Cytokeratin AE1 immunohistochemistry revealed demonstrated that they were epithelial cells (CKAE1 stain; original magnification, ×200). c. GATA3 immunostain highlighted aggregates of neoplastic cells in the muscularis propria (GATA3 stain; original magnification, ×100). In the inset in the left upper corner, cytokeratin AE1 stain reveals vascular invasion in the peri-vesical adipose tissue (CKAE1 stain; original magnification, ×400).

Declarations of interest

None.

References

[1] Lee SE, Jeong IG, Ku JH, Kwak C, Lee E, Jeong JS. Impact of transurethral resection of bladder tumor: analysis of cystectomy specimens to evaluate for residual tumor. Urology 2004;63:873–7.
[2] Spagnolo DV, Waring PM. Bladder granulomata after bladder surgery. Am J Clin Pathol 1986;86:430–7.
[3] Grignon DJ, Sakr W. Inflammatory and other conditions that can mimic carcinoma in the urinary bladder. Pathol Annu 1995;30:95–122.
[4] Rouprêt M, Drouin SJ, Larré S, et al. Bladder Cancer Committee of the French National Association of Urology ("CC-AFU Vessie"). Oncologic outcomes and survival in pT0 tumors after radical cystectomy in patients without neoadjuvant chemotherapy: results from a large multicentre collaborative study. Ann Surg Oncol 2011;18:3833–88.
[5] Palapattu GS, Shariat SF, Karakiewicz PI, et al. Bladder Cancer Research Consortium. Cancer specific outcomes in patients with pT0 disease following radical cystectomy. J Urol 2006;175:1645–9.

Valeria Barresi*, Carmela Mirella Nunnari, Simona Lionti
Department of Human Pathology, University of Messina, Italy
E-mail address: vbarresi@unime.it (V. Barresi)

* Corresponding author at: Department of Human Pathology, Polyclinic G. Martino, Pad D, Via Consolare Valeria, 98125 Messina, Italy.