Pathology – Research and Practice 209 (2013) 255–259

Contents lists available at SciVerse ScienceDirect

Pathology – Research and Practice

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

Teaching cases

Polyomavirus (BK)-associated pleomorphic giant cell carcinoma of the urinary bladder: a case report

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ARTICLE INFO

Article history:
Received 1 November 2012
Received in revised form
11 December 2012
Accepted 30 January 2013

Keywords:
Pleomorphic giant cell carcinoma
Bladder

ABSTRACT

This report describes the morphological features of a pleomorphic giant cell carcinoma with focal trophoblastic differentiation of the urinary bladder in a male, 12 years post living related donor renal transplant. The voided urine cytology demonstrated rare decoy cells admixed with markedly atypical urothelial cell clusters, papillae and giant cells. Cystoprostatectomy demonstrated a nodular mass involving the trigone and right lateral-posterior wall, adjacent to the ureteral orifice. Hematoxylin-eosin stained sections showed two synchronous malignancies: (a) pleomorphic giant cell carcinoma with focal trophoblastic differentiation of the urinary bladder, metastatic to the omentum and (b) prostatic adenocarcinoma, Gleason score 3 + 4 = 7, involving the right prostate lobe. Strong diffuse expression of polyomavirus large T antigen was demonstrated in the primary and metastatic pleomorphic giant cell carcinoma, supporting a possible role for polyomavirus (BK) in the oncogenetic pathway. The prostatic adenocarcinoma was negative for polyomavirus large T antigen. Our findings of p63, CK7 and CK903 expression in pleomorphic giant cell carcinoma suggest that the tumor is of urothelial derivation. This is the first report describing the morphological features of urinary bladder pleomorphic giant cell carcinoma with trophoblastic differentiation, positive for polyomavirus large T antigen, arising in the background of BKV reactivation.

Introduction

In urinary bladder, pleomorphic giant cell carcinoma has been acknowledged in classic and more recent review articles on unusual variants of bladder cancer, including the current WHO classification of infiltrating urothelial tumors [3,7,17–20]. However, to our knowledge, only one original study concerning this unusual form of bladder carcinoma has been reported in the English language literature [20].

Polyomavirus hominis 1, better known as BK virus (BKV), infects up to 90% of the general population [10]. The introduction during the past two decades of new more potent immunosuppressive regimens has led to a significant increase in BKV-associated pathology, including but not limited to BKV allograft nephropathy (BKAN), ureteral stenosis, and hemorrhagic cystitis [5,10]. Although the cytologic features of BKV urinary tract infection (decoy cells) are well described [5], the literature describing BKV-associated urinary tract malignancies is scant, and the role of BKV in the development of human urinary tract tumors is still debated [1,5,8–11,13,14,16,23,24,26].

Herein, we report a case of BKV large T antigen-positive pleomorphic giant cell carcinoma that arose in the urinary bladder of a male kidney transplant recipient. The clinical significance of the findings is discussed, and relevant literature is reviewed.

Material and methods

Cytology

An unfixed urine sample received for cytologic assessment was prepared by the Cytospin method. Two cytospins were stained with Papanicolaou stain, screened by a cytotechnologist and subsequently reviewed and reported by the pathologist.

Histology

Representative tissue sections from the biopsies and cystoprostatectomy specimens were fixed in 10% buffered formalin and embedded in paraffin. For routine microscopy, 4-μm-thick sections

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http://dx.doi.org/10.1016/j.prp.2013.01.008

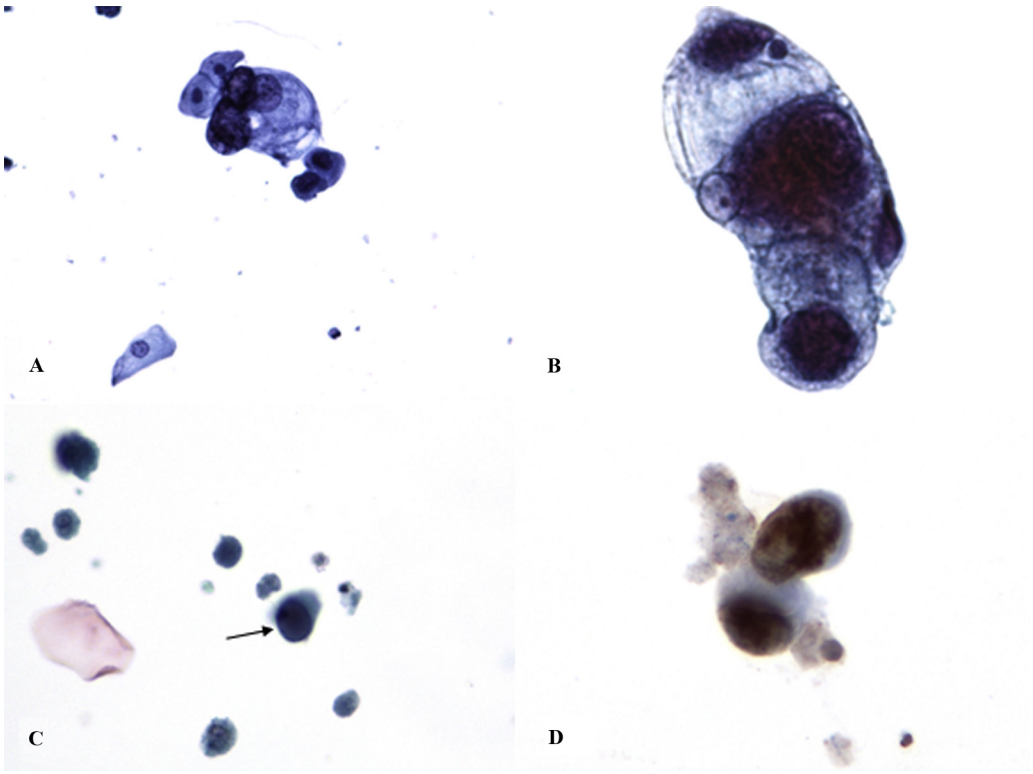

Fig. 1. Voided urine cytospin. (A) Note neoplastic multinucleated giant cell. Papanicolaou stain, 400×. (B) Neoplastic giant cell with markedly atypical morphology. Papanicolaou stain, 1000×. (C) Decoy cell (arrow), Papanicolaou stain, 1000×. (D) Polyomavirus large T antigen expression in neoplastic cells. SV40 stain, 1000×.

were stained with hematoxylin-eosin. The tumors were classified and graded according to previously described diagnostic criteria [3,17].

Immunohistochemistry

Immunohistochemical staining was performed using an automated immunostainer (BenchMark, Ventana, Tucson, AZ) and ultraview universal indirect biotin-free DAB detection kit. The following antibodies were used: Polyomavirus SV40 T Antigen (dilution 1:200, mouse monoclonal, Calbiochem), CK7 (prediluted, mouse monoclonal, Ventana), CK20 (prediluted, mouse monoclonal, Cell Marque), p63 (prediluted, mouse monoclonal, Ventana), CK903 (prediluted, mouse monoclonal, Cell Marque), p53 (prediluted, mouse monoclonal, Ventana), CD68 (prediluted, mouse monoclonal, Ventana), MART-1 (prediluted, mouse monoclonal, Ventana), beta-human chorionic gonadotropin (βHCG) (prediluted, rabbit monoclonal, Cell Marque), PSA (prediluted, mouse monoclonal, Cell Marque) and p16 (prediluted, mouse monoclonal, Ventana). Evaluation of the immunohistochemical staining was performed by light microscopy. An appropriately positive nuclear and/or cytoplasmic expression in 1% or more of neoplastic cells qualified as "positive (+)".

Electron microscopy

Representative tissue samples (1 mm cubes) from the urinary bladder tumor were fixed in 4F1G for 4 h, postfixed in osmium tetroxide, dehydrated in graded alcohols, and embedded in epoxy resin. The sections were stained with uranyl acetate and lead citrate and examined on a JEM 1200 transmission electron microscope.

The use of paraffin blocks for this study meets Institutional Review Board and Health Insurance Portability and Accountability Act requirements, and has been approved by the Institutional Review Board at the University of Maryland (HP-47559).

Case report

Clinical history

A 65-year-old male patient with end stage renal disease due to autosomal dominant polycystic kidney disease underwent a living related donor renal transplant in 2000. In 2012, a renal biopsy to evaluate proteinuria and rising creatinine showed no acute rejection and no evidence of BKV nephropathy. Voided urine samples sent to cytology to rule out BKV were positive for malignancy as well as decoy cells (June, 2012). Cystoscopy demonstrated a nodular mass involving the right lateral wall, adjacent to the ureteral orifice. Biopsies from the lesion sent for histologic evaluation were positive for pleomorphic giant cell carcinoma (August, 2012). A cystoprostatectomy with omental resection was performed (October, 2012).

Cytologic findings

Cytologic examination showed atypical urothelial cell clusters and isolated cells with markedly increased nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, nuclear membrane irregularities and rare prominent nucleoli. Numerous markedly atypical uninucleated and multinucleated giant cells admixed with scattered type 1 (classical) and type 2 (CMV-like) decoy cells were also noted (Fig. 1A–C).

Macroscopic findings

Macroscopic examination of the cystoprostatectomy specimen demonstrated a white-tan firm mass (4.8 cm × 4.3 cm × 2.1 cm) involving the trigone, posterior wall, dome, and right lateral wall