Urology Case Reports 2 (2014) 73–74

Contents lists available at ScienceDirect

Urology Case Reports

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

Oncology

Adenoma-carcinoma Sequence in the Bladder After Augmentation Cystoplasty

Akihiro Naito [a], Taketo Kawai [a,*], Tetsuya Fujimura [a], Teppei Morikawa [b], Haruki Kume [a], Yukio Homma [a]

[a] Department of Urology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
[b] Department of Pathology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

ARTICLE INFO

Article history:
Received 25 January 2014
Accepted 31 January 2014
Available online 28 February 2014

Keywords:
Augmentation cystoplasty
Tubulovillous adenoma
Adenoma-carcinoma sequence
Multistep carcinogenesis

ABSTRACT

We present a case of a 64-year-old woman showing multistep progression from adenoma to adenocarcinoma in the bladder 46 years after augmentation ileocystoplasty. She underwent augmentation ileocystoplasty for tuberculous contracted bladder at 18 years. After 44 years, tubulovillous adenomas were found and resected at the ileovesical anastomosis site. After 2 more years, bladder tumors recurred and revealed adenocarcinomas. Finally, radical cystectomy was required because of frequent recurrence and tumor extensiveness. To our knowledge, this is the first case demonstrating adenoma-carcinoma sequence histopathologically in the bladder after augmentation cystoplasty, indicating multistep carcinogenesis similar to intestinal carcinogenesis.

Introduction

Augmentation cystoplasty using an intestinal tract is indicated for patients with a deterioration of bladder storage function resistant to pharmacologic or other conservative interventions. For example, patients with neurogenic bladder caused by spinal cord injury, contracted bladder caused by urogenital tuberculosis, or interstitial cystitis are candidates for augmentation cystoplasty. Malignant transformation of primary or substitutional bladder epithelium after augmentation cystoplasty is rare and needs a long postoperative period.[1] However, these malignant tumors are frequently aggressive and associated with a poor prognosis,[2] and the mechanisms of carcinogenesis are unclear.

We previously reported a case of a 62-year-old woman with tubulovillous adenoma that developed 44 years after ileocystoplasty.[3] Two more years later, she developed bladder adenocarcinoma. The adenoma-carcinoma sequence has been implicated in the multistep processes of intestinal carcinogenesis in colon cancer.[4] To the best of our knowledge, this is the first case report to provide histopathologic evidence of the adenoma-carcinoma sequence in the bladder after augmentation cystoplasty.

Case presentation

A 16-year-old female patient underwent right nephrectomy for renal tuberculosis. Augmentation ileocystoplasty for tuberculosis contracted bladder was performed at 18 years. Left nephrostomy was required at 38 years because of hydronephrosis and repeated pyelonephritis.

In March 2005, 44 years after ileocystoplasty, the patient presented at our hospital with gross hematuria. Cystoscopy revealed multiple papillary tumors in the region of the ileovesical anastomosis. Transurethral resection of the bladder tumor (TURBT) was performed. Histopathologic examination revealed tubulovillous adenoma (Fig. 1A). The tumor recurred 4 times, necessitating repeated TURBT in April 2005, November 2007, March 2008, and October 2008. Histopathologic diagnosis was tubulovillous adenoma at the second TURBT in 2005, but the diagnosis of well-differentiated adenocarcinoma, pTa, (Fig. 1B) was made at the third TURBT in 2007, 46 years after ileocystoplasty. The fourth and fifth TURBT also revealed well-differentiated adenocarcinoma.

In January 2009, radical cystectomy with ileal conduit diversion was performed because of incomplete resection during the fifth TURBT. Macroscopic findings (Fig. 2A) and histologic examination (Fig. 2B) revealed that the tumor developed around the region of ileovesical anastomosis. Histopathologic diagnosis was well-differentiated adenocarcinoma, pTa, u-rt0, u-lt0, ur0, ew0, ly0, v0, pN0 (Fig. 2B). The postoperative course was uneventful, and the left nephrostomy catheter was removed. She has been recurrence and metastasis free until December 2013.

* Corresponding author. Tel.: +81-3-5800-8753; fax: +81-3-5800-8917.
E-mail address: taketokawai@yahoo.co.jp (T. Kawai).

2214-4420/
http://dx.doi.org/10.1016/j.eucr.2014.01.009

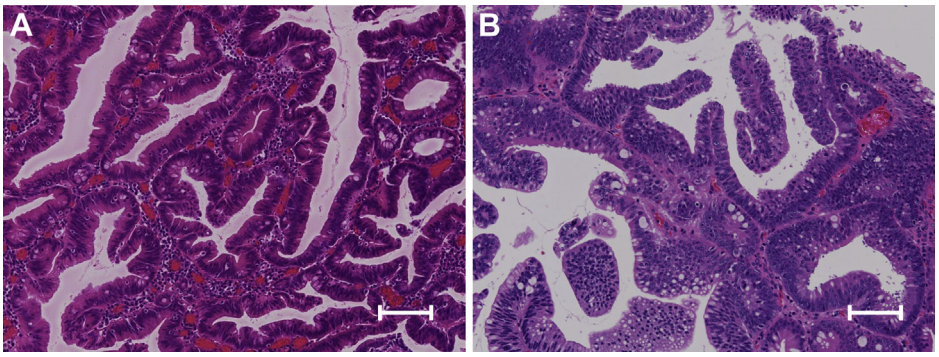

Figure 1. Histopathologic findings showing adenoma-carcinoma sequence (hematoxylin and eosin stain). **(A)** Tubulovillous adenoma identified during the first transurethral resection of the bladder tumor in 2005. Cells with minimum nuclear atypicality formed in glandular and villiform structure. **(B)** Well-differentiated adenocarcinoma identified during the third transurethral resection of the bladder tumor in 2007. Atypical tumor cells formed in the glandular structure. Tumor stage was pTa. Scale bars represent 50 μm.

Discussion

Malignant transformation of primary or substitutional bladder epithelium is relatively rare, with an approximate risk of 1.2% in patients treated with augmentation cystoplasty.[1] Malignant tumors may develop over long periods, usually more than 10 years, in augmented bladders.[1] However, these malignant tumors are frequently aggressive and cause the death in nearly 50% of patients.[2]

Bladder tumors after augmentation cystoplasty are generally adenocarcinoma most commonly located in the region of enterovesical anastomosis,[5] in which urothelial cells at the site of the anastomosis may be susceptible to intestinal metaplasia. Previous reports have shown that urothelial cells at the enterovesical junction acquire characteristic of the enteric epithelium in an experimental canine model of augmentation cystoplasty.[6] Furthermore, a variety of gene aberrations have been found in the region of enterovesical anastomosis in patients treated with ileocystoplasty, such as chromosomal numerical abnormalities in chromosomes 18, 9, and 8,[7] and *p53* mutations.[8] These findings suggest that multiple factors are involved in the bladder carcinogenesis after cystoplasty.

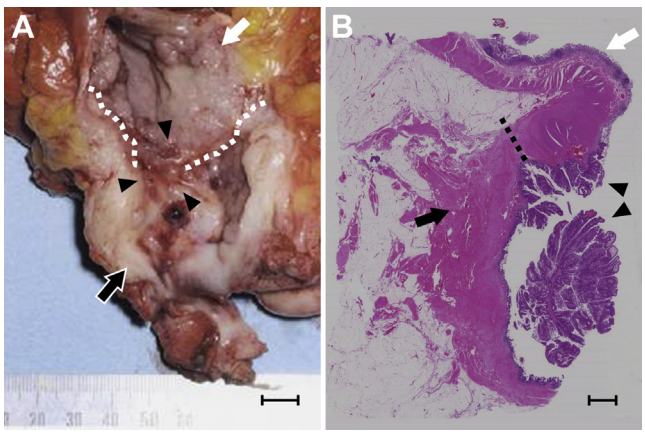

Figure 2. Macroscopic and histopathologic findings after total cystectomy. **(A)** Macroscopic findings of the isolated preparation. Multiple tumors (arrowheads) were found in the region of the anastomosis (broken line) of primary bladder (black arrow) and substituted bladder by the ileal segment (white arrow). Scale bars represent 1 cm. **(B)** Histopathologic findings (hematoxylin and eosin stain). The tumor (arrowheads) was located around the site of anastomosis (broken line) of primary bladder (black arrow) and in the ileal segment (white arrow). Histopathologic diagnosis was well-differentiated adenocarcinoma, pTa, u-rt0, u-lt0, ur0, ew0, ly0, v0, pN0. Scale bars represent 1 mm.

Intestinal carcinogenesis is known to be a multistep process called adenoma-carcinoma sequence, progressing from adenoma to adenocarcinoma, involving various oncogenic factors.[4] Our case newly demonstrated adenoma-carcinoma sequence histopathologically in the bladder after augmentation cystoplasty. Our findings suggest that multistep carcinogenesis develops in the region of enterovesical anastomosis after cystoplasty as the intestinal carcinogenesis.

Late diagnosis of the diseases at an advanced stage accounts for the poor prognosis of patients with malignancies after cystoplasty.[2] In our case, the malignancy was fortunately discovered at the stage of tubulovillous adenoma, and a good prognosis was achieved. Our experience in the current case suggests that detection at the early stage of carcinogenesis improves patient prognosis in malignancies after augmentation cystoplasty.

Conclusion

Carcinogenesis in the bladder after augmentation cystoplasty may be a multistep process, progressing adenoma to adenocarcinoma, and detection at the early stage of carcinogenesis would be important for patient prognosis.

Conflict of interest

The authors of this article have no conflict of interest.

References

1. Soergel TM, Cain MP, Misseri R, Gardner TA, Koch MO, Rink RC. Transitional cell carcinoma of the bladder following augmentation cystoplasty for the neuropathic bladder. *J Urol*. 2004;172:1649–1651; discussion 51–2.
2. Filmer RB, Spencer JR. Malignancies in bladder augmentations and intestinal conduits. *J Urol*. 1990;143:671–678.
3. Yamada Y, Fujimura T, Takahashi S, Takeuchi T, Takazawa Y, Kitamura T. Tubulovillous adenoma developing after urinary reconstruction using ileal segments. *Int J Urol*. 2006;13:1134–1135.
4. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell*. 1990;61:759–767.
5. Nurse DE, Mundy AR. Assessment of the malignant potential of cystoplasty. *Br J Urol*. 1989;64:489–492.
6. Gitlin JS, Wu XR, Sun TT, Ritchey ML, Shapiro E. New concepts of histological changes in experimental augmentation cystoplasty: insights into the development of neoplastic transformation at the enterovesical and gastrovesical anastomosis. *J Urol*. 1999;162:1096–1100.
7. Ivil KD, Doak SH, Jenkins SA, et al. Fluorescence in-situ hybridisation on biopsies from clam ileocystoplasties and on a clam cancer. *Br J Cancer*. 2006;94:891–895.
8. Ivil KD, Jenkins SA, Doak SH, et al. Identification of early p53 mutations in clam ileocystoplasties using restriction site mutation assay. *Urology*. 2007;70:905–909.