

Usefulness of multi-parametric MRI for diagnosis of invasive urothelial cancer: Case reports of bladder and ureteral cancer

SENJI HOSHI^{1,2}, KEIJI HORIO³, KENJI NUMAHATA², KIYOTSUGU HOSHI¹,
VLADIMIR BILIM⁴ and ISOJI SASAGAWA¹

¹Department of Urology, Yamagata Tokushukai Hospital, Yamagata, Yamagata 990-0834; ²Department of Urology, Yamagata Prefectural Central Hospital, Yamagata, Yamagata 990-2292; ³Department of Radiology, Yamagata Tokushukai Hospital, Yamagata, Yamagata 990-0834; ⁴Department of Urology, Kameda Daiichi Hospital, Niigata, Niigata 950-0165, Japan

Received January 6, 2018; Accepted July 31, 2018

DOI: 10.3892/mco.2018.1713

Abstract. The presence or absence of metastasis has critical implications for therapeutic decision-making in urothelial cancer (UC). Conventional magnetic resonance imaging (MRI) utilizing anatomic T1- and T2-weighted images has modest efficacy in detecting lymph node and distant metastases in UC. However, incorporation of functional techniques including diffusion weighted imaging and dynamic contrast-enhanced imaging, may improve the accuracy of lesion detection and staging. Multiparametric (mp)MRI is widely used in the imaging of prostate and breast cancers, though its usefulness in UC has yet to be fully elucidated. The present study reports on mpMRI in the context of two cases of bladder and ureteral cancer, and imaging results with pathological diagnosis.

Introduction

Conventional magnetic resonance imaging (MRI) has limited value in the diagnosis of lymph node or distant metastasis in patients with urothelial cancer. Multiparametric (mp)MRI is widely used in the imaging of prostate cancer (1). mpMRI is also gaining ground for detecting and diagnosing breast cancer (2). However, there are scanty reports on the use of mpMRI in urothelial cancer (UC) (3). In the present study we describe the

visualization of primary tumors and lymph node metastasis in two cases of UC. It is expected that mpMRI can improve the sensitivity and specificity of UC imaging. MRI requires no X-ray exposure and thus may be repeated frequently during follow-up while maintaining minimal radiation exposure to patient. MRI is becoming increasingly available, and the cost of mpMRI is only 1.5 times higher than that of contrast-enhanced computed tomography (CT) in Japan, and thus it does not result in a markedly higher financial burden for patients or for the medical insurance system in general.

Case reports

Written informed consent was obtained from all of the patients and their families. Case 1 was a 78-year-old male who underwent transurethral resection (TUR) for a bladder tumor in February 2016 at Yamagata Tokushukai Hospital. Pathological diagnosis was UC, pT1, low-grade. The surgery was followed by intravesical instillation of farmorubicin. In June 2016, intravesical recurrence was suspected based on results of cystoscopy and urinary cytology (class V). In June 2016, CT identified an 8 mm left internal iliac lymph node (Fig. 1A). Imaging diagnosis of metastasis was not performed because of the shape and size of the lymph node. Dynamic contrast-enhanced MRI (DCE) revealed a highly enhanced lesion and a diagnosis of lymph node metastasis was made (Fig. 2A-C). The same CT revealed whole bladder wall thickness (Fig. 1B) but did not provide enough data to confirm the diagnosis of residual tumor. On the other hand, mpMRI revealed residual bladder cancer (Fig. 2D-G).

Peritoneum preserving retrograde radical cystectomy (4) with pelvic lymph node dissection and bilateral ureterocutaneostomy was performed in June 2016. Pathological diagnosis was UC, high-grade muscle-invasive bladder cancer (pT2) and left internal iliac lymph node metastasis (Fig. 3A). The patient received six courses of adjuvant chemotherapy with gemcitabine and carboplatin (5) and was of 'no evidence of disease' 23 months after radical cystectomy.

Case 2 was a 65-year-old male. In August 2016, TURBT was performed for a bladder tumor located around the left ureteral orifice at Yamagata Tokushukai Hospital; and the left ureter orifice was deeply resected. In September 2016, CT revealed left terminal ureter dilatation (Fig. 1C) and left hydro-

Correspondence to: Dr Senji Hoshi, Department of Urology, Yamagata Tokushukai Hospital, 2-3-51 Kiyosumi-cho, Yamagata, Yamagata 990-0834, Japan
E-mail: senjihoshi47@yahoo.co.jp

Abbreviations: UC, urothelial cancer; MRI, magnetic resonance imaging; mpMRI, multi-parametric magnetic resonance imaging; CT, computed tomography; TURBT, transurethral resection of bladder tumor; FNAB, fine needle aspiration biopsy; NMIBC, non-muscle invasive bladder cancer; MIBC, muscle invasive bladder cancer; T2W, T2 weighted imaging; PWI, perfusion-weighted imaging; DTI, diffusion tensor imaging

Key words: multi-parametric magnetic resonance imaging, urothelial cancer, bladder cancer, ureter cancer

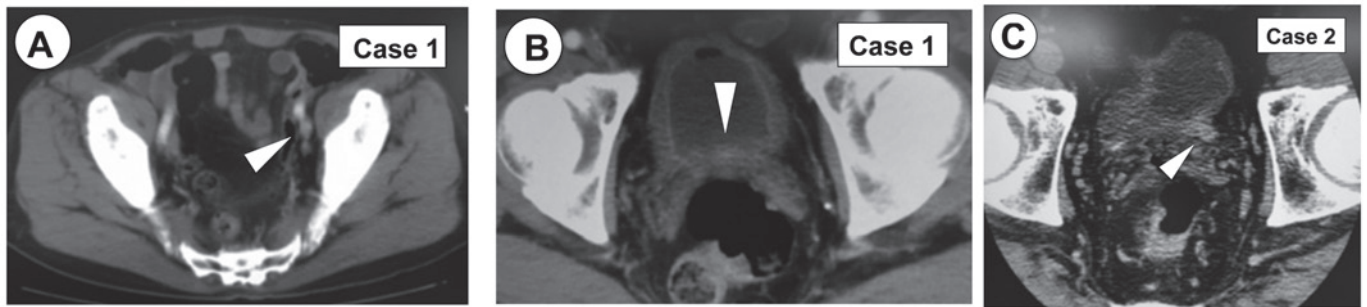


Figure 1. (A and B) CT of case 1 performed on May 20th, 2016: (A) A left external iliac node (arrowhead) was detected; however, cancer metastasis could not be diagnosed based on the CT image. (B) Bladder wall thickening was observed (arrowhead). (C) CT of case 2 performed on September 6th, 2016. Left distal ureter enhancement on contrast CT was detected (arrowhead); however, differential diagnosis between inflammation and cancer was not possible. CT, computed tomography.

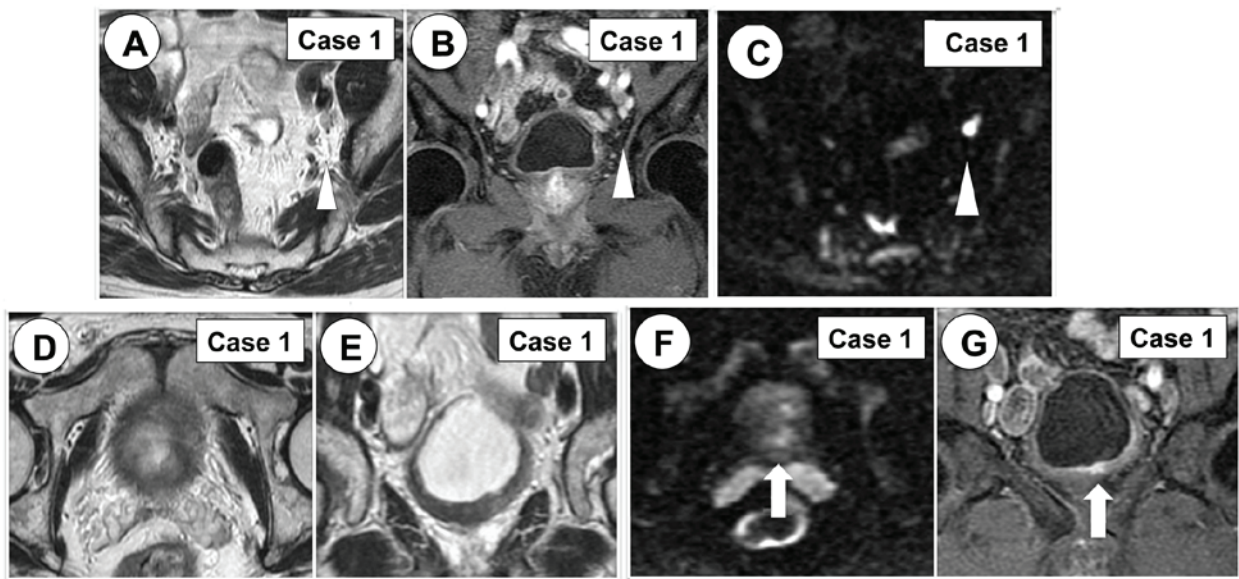


Figure 2. Lymph node metastasis (white arrowhead) and residual bladder tumor (white arrow) were diagnosed by mpMRI. (A) T2W MRI, axial view. (B) DCE MRI, coronal view. (C) DW MRI, axial view, b-value=1,000 s/mm². (D) T2W MRI, axial view. (E) T2W MRI, coronal view. (F) DW MRI, axial view, b-value=1,000 s/mm². (G) DCE MRI, coronal view. MRI, magnetic resonance imaging; mpMRI, multi-parametric magnetic resonance imaging; T2W, T2-weighted; DCE, dynamic contrast-enhanced; DW, diffusion-weighted.

nephrosis. The inflammatory changes of the left ureter were diagnosed following deep incision of the left ureteral orifice. In November 2016, ultrasound revealed disappearance of the left hydronephrosis. In January 2017, MRI revealed a left lower ureter tumor (Fig. 4). In February 2017, partial resection of the left terminal ureter was performed and the pathological diagnosis was UC, high-grade, pT2 (Fig. 3B-D).

Discussion

mpMRI in prostate and breast cancers improves diagnostic accuracy, eliminates the need for biopsies, and enables improved assessment, image-guided biopsy targeting and prediction of response to neoadjuvant therapy (1,2). In bladder cancer patients, staging and postoperative follow-up depends on CT scan data. However, the sensitivity and specificity of CT imaging in detecting lymph node metastasis are relatively low, and regular CT scans result in an accumulation of radiation. Lymph node metastasis not resulting in significant lymph node enlargement typically results in false-negative results while enlarged

non-metastatic lymph nodes lead to false-positive results in CT scanning. For early diagnosis of pelvic lymph node metastasis in bladder cancer, our group has previously performed bipedal lymphography and percutaneous fine needle aspiration biopsy (FNAB) of pelvic lymph nodes. In a series of 200 bladder cancer patients at Yamagata Prefectural Central Hospital, a diagnosis of metastasis to the pelvic lymph nodes was determined by this method in 34 patients (17%). Of these 34 patients, only 12 (35%) were positive or suspected of having pelvic lymph node metastasis by CT scan. A total of 16 patients (47%) exhibited positive or highly suspected positive lymphogram and 18 patients (53%) exhibited normal lymphogram. A total of 78 cases, including 8 FNAB-positive cases, were treated by radical cystectomy and regional lymph node dissection. The sensitivity, specificity, positive predictive value and negative predictive value of FNAB were 57, 100, 100 and 91%, respectively (6). With FNAB, cytopathological diagnosis is possible; however, this technique is complex, time consuming and exposes patients to ionizing radiation. On the other hand, bipedal lymphography could not visualize obturator or internal iliac lymph nodes. mpMRI may

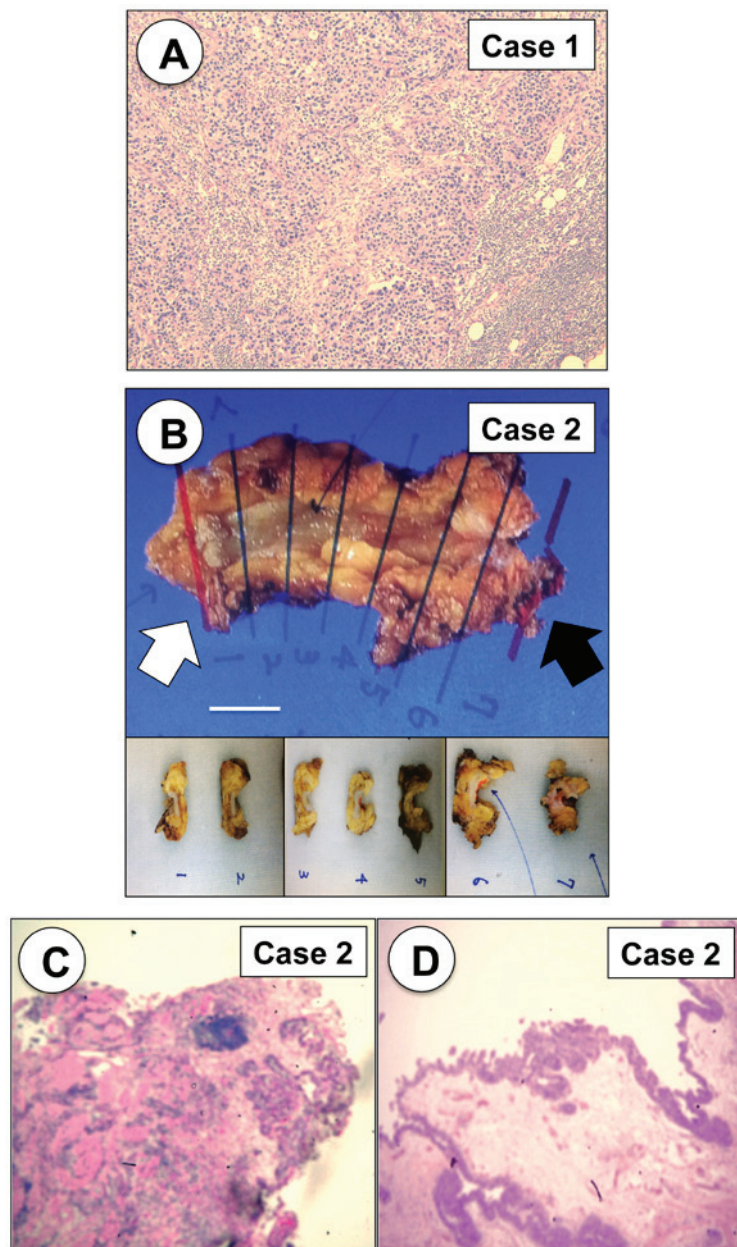


Figure 3. (A) Pathological detection of lymph node metastasis via low magnification (magnification, x40) H&E staining: ~80% of the lymph node was occupied by cancer cells. (B) Macroscopic (scale bar, 1 cm) and (C and D) microscopic H&E staining images (magnification, x100) of the resected lower ureter. The white arrow on the left indicates the cranial side and the black arrow on the right indicates the caudal side of the ureter. Tumor cells had invaded into the muscle layer of the ureter. Pathological diagnosis was urothelial cancer, pT2, high-grade. H&E, hematoxylin and eosin.

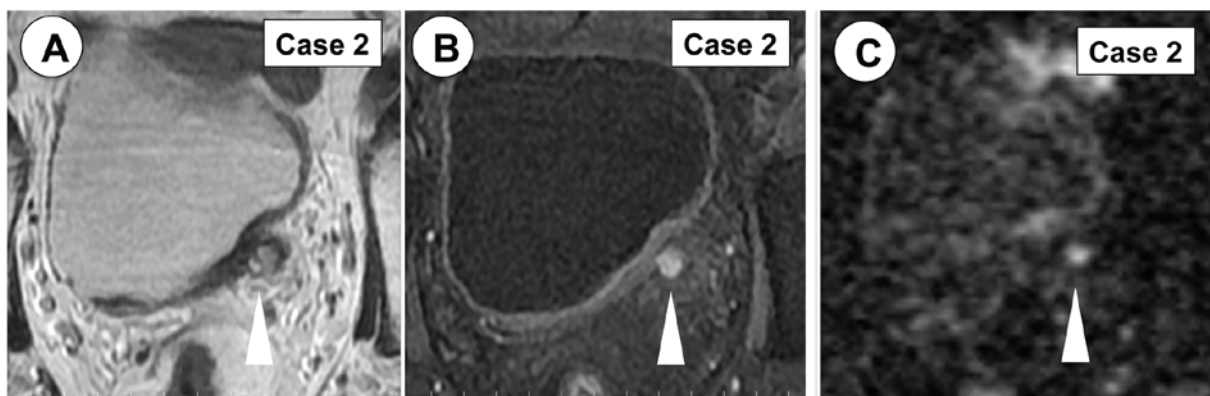


Figure 4. Multi-parametric MRI detected left lower ureteral tumor (arrowhead). (A) T2-weighted MRI. (B) Dynamic contrast-enhanced MRI. (C) Diffusion-weighted MRI, b-value=1,000 s/mm². MRI, magnetic resonance imaging.

improve the accuracy of tumor detection and staging without the risk of exposure to ionizing radiation. Additionally, mpMRI is a more feasible technique than FNAsB for the pelvic lymph node and may be performed regularly on an out-patient basis.

For high-grade non-muscle invasive bladder cancer (NMIBC) and muscle invasive bladder cancer (MIBC), MRI may detect and stage tumors with high sensitivity and specificity (7). mpMRI has demonstrated high diagnostic accuracy in differentiating NMIBC from MIBC and organ-confined disease from non-organ confined disease (8); exceeding that of T2 weighted imaging (T2W) or diffusion weighted imaging (DWI)-MRI used alone (8). Compared with CT, MRI offers improved soft-tissue resolution, making it easy to distinguish between NMIBC and MIBC. It has even been proven to be superior to CT in identifying bladder-wall invasion (7). There are a number of reports on the usefulness of mpMRI for the detection of tumor recurrence (9) and differentiation of non-muscle invasive UC from muscle-invasive UC (10,11). Afifi *et al* (8) reported on the usefulness of mpMRI in detecting metastatic lymph nodes. The largest size of the metastatic lymph nodes detected was 42 mm, and lymph nodes with low apparent diffusion coefficient values were considered positive (8). However, in general, data on lymph node staging from mpMRI remains limited.

Both patients reported presently underwent mpMRI prior to tumor resection. A total of 4 MRI sets T2W + perfusion-weighted imaging (PWI), T2W + DWI, T2W + DWI + PWI and T2W + DWI + PWI + diffusion tensor imaging (DTI) were interpreted qualitatively. PWI, DWI and DTI were also analyzed quantitatively. Accuracy was determined using histopathology as the reference standard. Thus, mpMRI may provide qualitative and quantitative information on the tumor microenvironment beyond traditional tumor size measures and/or morphological assessments.

pMRI was useful for the diagnosis of pelvic lymph node metastasis of bladder cancer and invasive lower ureteral tumor. mpMRI with DWI and DTI has the potential to become a reliable staging tool for invasive bladder cancer and lower ureteral cancer, and to diagnose metastasis of pelvic lymph nodes when the lymph node is not significantly enlarged.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The raw data used during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SH participated in data acquisition, developed the concept of the manuscript and was a major contributor in writing the manuscript. KH analyzed and interpreted MRI images. KN participated in data acquisition and critically revised the content of the manuscript. KH was involved in data acquisi-

tion and analysis. VB was involved in drafting the manuscript and revising it critically for important intellectual content. IS participated in data acquisition, and also provided administrative support and supervision. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patients and their families.

Patient consent for publication

Written informed consent was obtained from the patients and their families.

Competing interests

The authors declare that they have no competing interests.

References

1. Christidis D, McGrath S, Leaney B, O'Sullivan R and Lawrentschuk N: Interpreting prostate multiparametric magnetic resonance imaging: Urologists' guide including prostate imaging reporting and data system. *Urology* 111: 136-138, 2018.
2. Pinker K, Helbich HT and Morris AE: The potential of multiparametric MRI of the breast. *Br J Radiol* 90: 20160715, 2017.
3. Bouchelouche K, Turkbey B and Choyke PL: PET/CT and MRI in bladder cancer. *J Cancer Sci Ther* S14: pii: 7692, 2012.
4. Hoshi S, Yamamuro T, Ogata Y, Numahata K and Sugano O: 948 Peritoneum preserving retrograde radical cystectomy for elderly and high risk bladder cancer patients. *J Urol* 183: e369, 2010.
5. Hoshi S, Ohyama C, Ono K, Takeda A, Yamashita S, Yamato T, Itoh A, Satoh M, Saito S, Okada Y, *et al*: Gemcitabine plus carboplatin; and gemcitabine, docetaxel, and carboplatin combined chemotherapy regimens in patients with metastatic urothelial carcinoma previously treated with a platinum-based regimen: Preliminary report. *Int J Clin Oncol* 9: 125-129, 2004.
6. Hoshi S, Orikasa S, Suzuki KI, Takahashi T, Ohyama C, Sato K and Ono K: Diagnosis and treatment of pelvic lymph node metastasis in bladder cancer. *Int J Urol* 6: 400-407, 1999.
7. Bagheri MH, Ahlman MA, Lindenberg L, Turkbey B, Lin J, Cahid Civelek A, Malayeri AA, Agarwal PK, Choyke PL, Folio LR and Apolo AB: Advances in medical imaging for the diagnosis and management of common genitourinary cancers. *Urol Oncol* 35: 473-491, 2017.
8. Afifi AH, Abdel Maksoud TAS, El-noueam KI, Ataa MA and Abdallah DM: Multiparametric-MRI as a comprehensive study in evaluation, characterization & local staging of urinary bladder carcinomas. *Egyptian J Radiol Nuclear Med* 48: 493-507, 2017.
9. Wang HJ, Pui MH, Guo Y, Yang D, Pan BT and Zhou XH: Diffusion-weighted MRI in bladder carcinoma: The differentiation between tumor recurrence and benign changes after resection. *Abdom Imaging* 39: 135-141, 2014.
10. Panebianco V, De Berardinis E, Barchetti G, Simone G, Leonardo C, Grompone MD, Del Monte M, Carano D, Gallucci M, Catto J and Catalano C: An evaluation of morphological and functional multi-parametric MRI sequences in classifying non-muscle and muscle invasive bladder cancer. *Eur Radiol* 27: 3759-3766, 2017.
11. Wang HJ, Pui MH, Guo Y, Li SR, Guan J, Zhang XL and Cai HS: Multiparametric 3-T MRI for differentiating low-versus high-grade and category T1 versus T2 bladder urothelial carcinoma. *AJR Am J Roentgenol* 204: 330-334, 2015.