


## Case Report

# Localized prostate cancer with pelvic arteriovenous malformation treated with low-dose-rate brachytherapy after transcatheter embolization: Two case reports

Takuya Owari,<sup>1</sup> Nobumichi Tanaka,<sup>1</sup>  Yasushi Nakai,<sup>1</sup> Isao Asakawa,<sup>2</sup> Mitsuru Tomizawa,<sup>1</sup> Makito Miyake,<sup>1</sup> Yosuke Morizawa,<sup>1</sup> Shunta Hori,<sup>1</sup> Satoshi Anai,<sup>1</sup> Masatoshi Hasegawa<sup>2</sup> and Kiyohide Fujimoto<sup>1</sup>

Departments of <sup>1</sup>Urology, and <sup>2</sup>Radiation Oncology, Nara Medical University, Kashihara, Nara, Japan

### Abbreviations & Acronyms

ADT = androgen deprivation therapy

AS = active surveillance

AVM = arteriovenous malformation

CT = computed tomography

EBRT = extra beam radiation therapy

GS = Gleason score

IMRT = intensity-modulated radiation therapy

LDR = low-dose-rate

MRI = magnetic resonance imaging

pAVM = pelvic AVM

PSA = prostate-specific antigen

RP = radical prostatectomy

**Background:** We describe two patients who underwent low-dose-rate prostate brachytherapy after embolization for pelvic arteriovenous malformation.

**Case presentation:** Case 1: A 76-year-old man was referred for definitive treatment of intermediate-risk prostate cancer (prostate-specific antigen 8.667 ng/mL, cT2aN0M0, Gleason score 3 + 4 = 7). We planned low-dose-rate brachytherapy. However, magnetic resonance imaging and computed tomography demonstrated a large pelvic arteriovenous malformation. We performed embolization of the arteriovenous malformation before initiating treatment to lower the risk of rupture of the arteriovenous malformation during low-dose-rate brachytherapy. Case 2: A 69-year-old man was referred for the definitive treatment of high-risk prostate cancer (prostate-specific antigen 5.81 ng/mL, cT2aN0M0, Gleason score 4 + 4 = 8) with a pelvic arteriovenous malformation. Similar to Case 1, we performed embolization of the arteriovenous malformation before initiating treatment. In both cases, low-dose-rate brachytherapy could be performed without complications.

**Conclusions:** Low-dose-rate brachytherapy after transcatheter embolization of pelvic arteriovenous malformations can safely and effectively treat localized prostate cancer with pelvic arteriovenous malformations.

**Key words:** arteriovenous malformation, definitive therapy, low-dose-rate brachytherapy, prostate cancer, transcatheter embolization.

**Correspondence:** Nobumichi Tanaka M.D., Ph.D., Department of Urology, Nara Medical University, 840 Shijocho, Kashihara, Nara 634-8522, Japan. Email: sendo@naramed-u.ac.jp

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Received 24 August 2018; accepted 14 January 2019. Online publication 12 February 2019

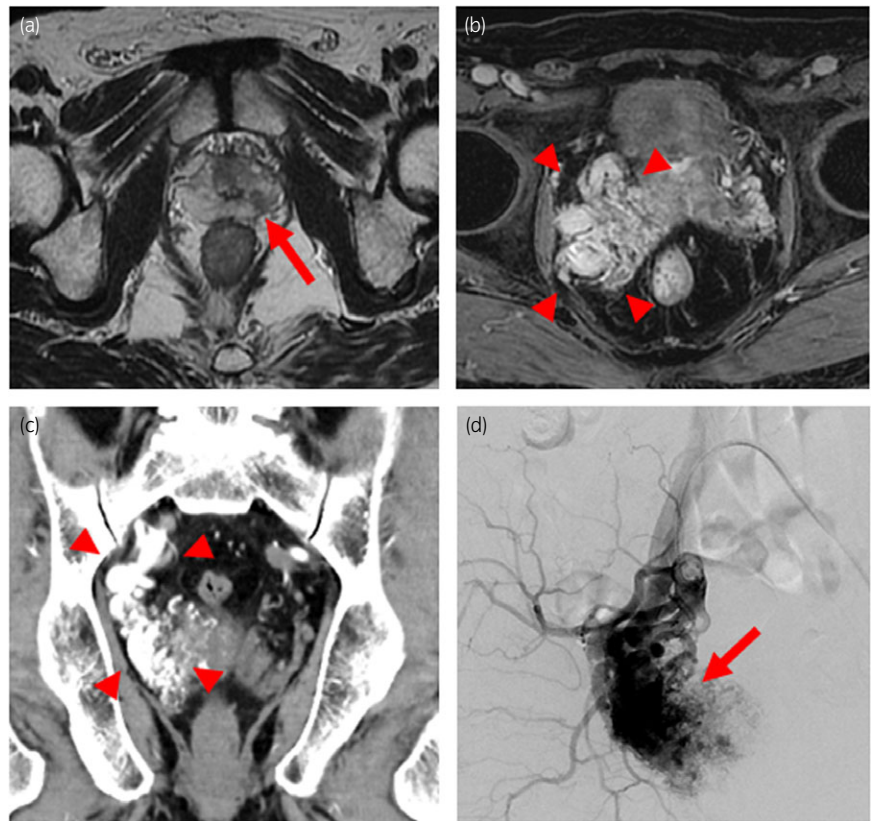
## Keynote message

Congenital pAVMs are rare in men. This is the second report describing definitive treatment for localized prostate cancer with pAVMs and the first describing brachytherapy in such patients. Brachytherapy after transcatheter embolization of pAVMs could serve as a safe and effective treatment for such patients.

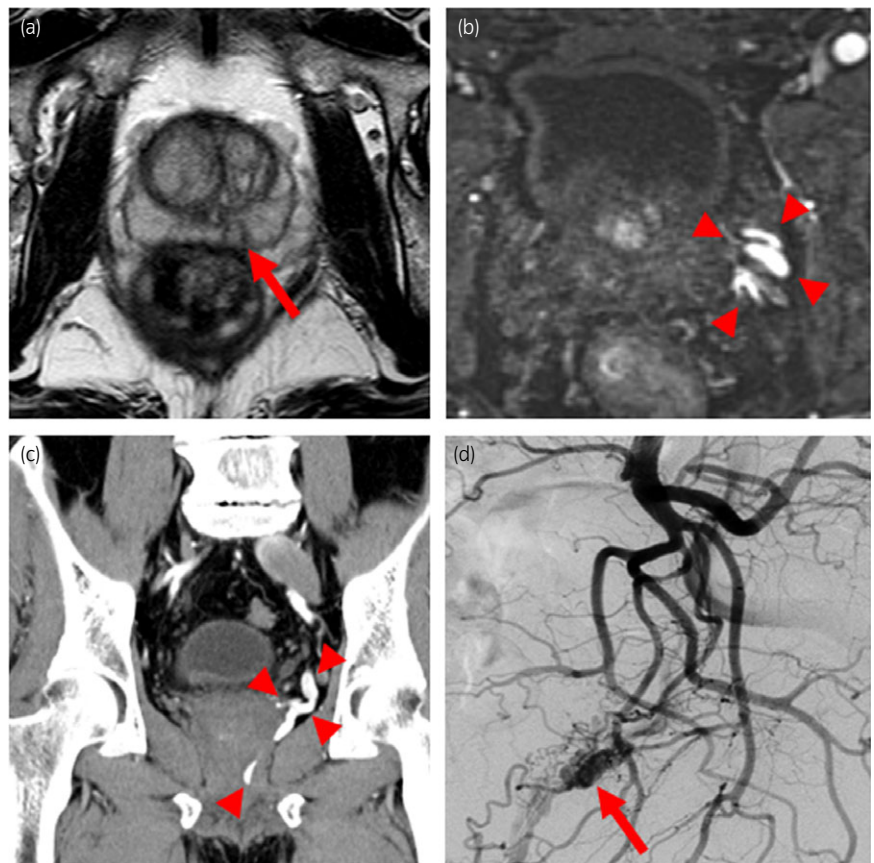
## Background

AVMs are abnormal connections between arteries and veins. AVMs are uncommon, and congenital pAVM particularly, are rare in men.<sup>1,2</sup> To our knowledge, only one report has described definitive treatment (RP) for localized prostate cancer with pAVMs.<sup>3</sup>

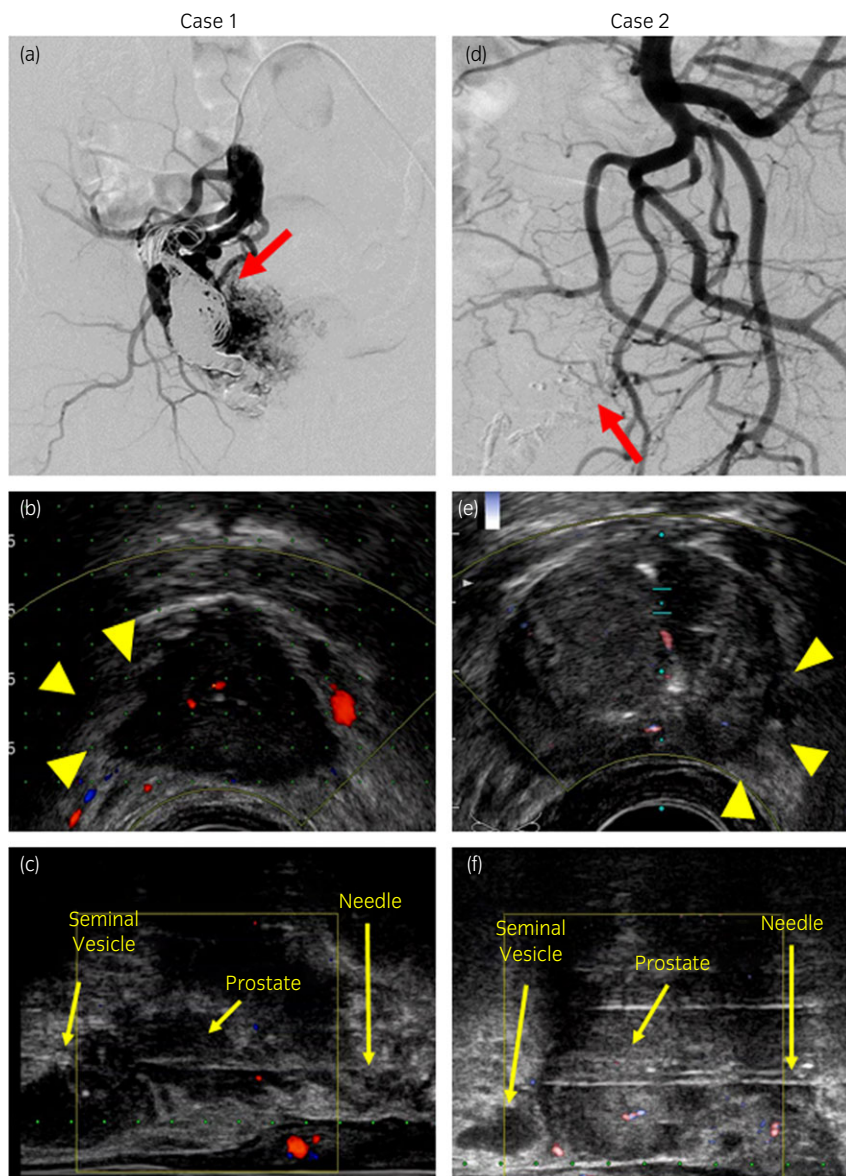
LDR brachytherapy serves as definitive treatment for localized prostate cancer alongside RP and IMRT.<sup>4–6</sup> The biochemical failure-free survival in patients with low-/intermediate-risk prostate cancer undergoing brachytherapy is significantly higher than that in patients undergoing EBRT.<sup>7,8</sup> Moreover, a randomized controlled study has shown that the biochemical failure-free survival rate in patients with high-risk prostate cancer undergoing brachytherapy combined with EBRT and ADT was significantly higher than that in patients undergoing only EBRT and ADT.<sup>9</sup>



**Fig. 1** Imaging performed in Case 1: (a, b) MRI performed before prostate needle biopsy shows an abnormal intensity in the left peripheral zone of the prostate (red arrow) and a large pAVM (red arrowheads). (c) Contrast-enhanced CT shows a large pAVM adjacent to the right side of the seminal vesicle and the prostate with a 4 cm nidus (red arrowheads). (d) Angiogram obtained before embolization of the pAVM in Case 1 (red arrow).



**Fig. 2** Imaging performed in Case 2: (a, b) MRI before a prostate needle biopsy shows an abnormal intensity in the left peripheral zone of the prostate (red arrow) and a large pAVM (red arrowheads). (c) Contrast-enhanced CT shows a pAVM adjacent to the left side of the seminal vesicle and the prostate with the 2 cm nidus (red arrowheads). (d) Angiogram obtained before embolization of the pAVM in Case 2 (red arrow).



**Fig. 3** Images showing transcatheter embolization of a pAVM performed to lower the risk of intraprocedural rupture of the pAVM in our patients: (a; Case 1 and d; Case 2) Angiogram obtained after embolization (red arrow). (b, c; Case 1 and e, f; Case 2) Color Doppler ultrasonography performed during the operation of LDR brachytherapy shows the absence of abnormal vessels in the area of pAVMs (yellow arrowheads).

We report two cases of LDR brachytherapy after transcatheter embolization in patients with localized prostate cancer concomitant with a pAVM. To our knowledge, this is the second report describing definitive treatment for localized prostate cancer with pAVMs and the first describing LDR brachytherapy in such patients.

## Case presentation

### Case 1

A 76-year-old man was admitted to another hospital with an elevated PSA level of 8.667 ng/mL. MRI demonstrated an abnormal intensity in the left peripheral zone of the prostate (Fig. 1a, red arrow). A prostate biopsy was performed, and histopathological diagnosis revealed adenocarcinoma with a GS of 3 + 3 = 6. The clinical stage of the tumor was determined to be cT2aN0M0. AS was selected as primary therapy. PSA level rose to 11.532 ng/mL 2 years after the initiation of AS, and a repeat biopsy was performed. Histopathological

diagnosis revealed adenocarcinoma with a GS of 3 + 4 = 7. We planned LDR brachytherapy; however, MRI and CT demonstrated a large pAVM adjacent to the right side of the seminal vesicle and the prostate with a 4 cm nidus fed by several branches of the internal iliac artery (Fig. 1b,c, red arrowheads). Needle manipulation of these abnormal vessels was associated with a potentially high risk of rupture. Using N-butyl-2-cyanoacrylate and lipiodol, we embolized the AVM before LDR brachytherapy to lower the risk of intraprocedural rupture of the AVM (Figs 1d and 3a, red arrow). LDR brachytherapy was performed using a prescribed dose of 160 Gy after color Doppler ultrasonography confirmed the absence of abnormal vessels in the area (Fig. 3b,c, yellow arrowheads).

### Case 2

A 69-year-old man was admitted to another hospital with an elevated PSA level of 5.1 ng/mL. MRI demonstrated an

abnormal intensity in the left peripheral zone of the prostate (Fig. 2a, red arrow). A prostate biopsy was performed, and histopathological diagnosis revealed an adenocarcinoma with a GS of 3 + 3 = 6, and the clinical stage was determined to be cT2aN0M0. AS was selected as initial therapy. A repeat prostate biopsy was performed 2 years after the initiation of AS. Histopathological diagnosis revealed an adenocarcinoma with a GS of 4 + 4 = 8. We planned LDR brachytherapy combined with EBRT (45 Gy/25 fractions) and neoadjuvant ADT. However, a pAVM adjacent to the left side of the seminal vesicle and the prostate with a 2 cm nidus fed by several branches of the internal iliac artery was detected (Fig. 2b,c, red arrowheads). We performed transcatheter embolization of the AVM before performing LDR brachytherapy (Figs 2d and 3d, red arrow). LDR brachytherapy was performed using a prescribed dose of 110 Gy confirmed the absence of abnormal vessels in the area (Fig. 3e,f, yellow arrowheads). In both cases, no perioperative complications including anemia or hematoma formation was reported.

## Discussion

pAVMs are uncommon vascular entities, which are classified as congenital or acquired which are secondary to trauma, operation, or pregnancy.<sup>1,2</sup> Both patients in this study reported no history of trauma or operation of pelvic organs; however, MRI performed before the prostate biopsy demonstrated AVMs. Thus, these lesions were classified as congenital pAVMs. pAVMs may present with pelvic pain, hematuria, dysuria, erectile dysfunction,<sup>1,2,10</sup> heart failure,<sup>11</sup> and massive bleeding during transurethral resection of the prostate.<sup>12</sup> Both patients had been asymptomatic. Transcatheter embolization is widely used for pain relief in patients with AVMs.<sup>13</sup> Although most asymptomatic AVMs do not require treatment,<sup>10</sup> transcatheter embolization was performed in our patients to reduce the risk of rupture of AVMs.

To our knowledge, only one previous report has described definitive treatment performed in a patient with localized prostate cancer concomitant with pAVMs.<sup>3</sup> That study reported laparoscopic RP after transcatheter embolization of pAVMs. However, massive intraoperative bleeding was reported from the AVM and the lateral pedicle. Therefore, RP might not be entirely safe in such patients. We also performed transcatheter embolization of the pAVM before the LDR brachytherapy. However, transcatheter embolization does not guarantee freedom from recurrence of lesions<sup>13</sup> and we observed residual AVM on the right side of the prostate in Case 1. Therefore, brachytherapy is useful because abnormal vessels could be identified intraprocedurally using color Doppler ultrasonography.

To our knowledge, no report has described definitive radiotherapy including brachytherapy and EBRT after transcatheter embolization for prostate cancer. In contrast, transcatheter embolization of pelvic vessels to control active uterine bleeding before definitive radiotherapy must be performed cautiously in women with cervical cancer because embolization-induced reduction in intra-tumoral oxygenation and increased radioresistance are known to occur.<sup>14</sup> Although we performed transcatheter embolization to secure safety, we

were concerned regarding radioresistance. However, the dose delivered in brachytherapy is reported to be high enough to overcome the increased radioresistance caused by hypoxia.<sup>15</sup> Moreover, the partial pressure of oxygen and perfusion were increased in the tumor microenvironment after LDR brachytherapy.<sup>16</sup> These mechanisms explain the efficacy of brachytherapy in precipitating tumor hypoxia. Thus, brachytherapy can be considered useful and safe treatment in hypoxia-mediated radioresistance following embolization of pelvic vessels as was observed in our patients.

## Conclusion

This case report shows that LDR brachytherapy after transcatheter embolization of pAVMs could serve as safe and effective treatment for localized prostate cancer with pAVMs. This is the first report to describe LDR brachytherapy after embolization of pelvic vessels for prostate cancer. Long-term follow-up is warranted to assess oncological effectiveness.

## Acknowledgment

The authors thank all members of the Department of Radiology, Nara Medical University, who performed transcatheter embolization of pAVMs.

## Conflict of interest

The authors declare no conflict of interest.

## References

- 1 Addo EA, Emtage J, Massis K, Hernandez DJ. A congenital high flow arteriovenous malformation of the bladder presenting with polypoid cysts and ureteral obstruction. *Urol. Case Rep.* 2015; **3**: 181–4.
- 2 Hammad FT, Shawish F, Kazim E. Congenital pelvic arteriovenous malformation presenting with urinary retention: a case report. *Med. Princ. Pract.* 2011; **20**: 294–6.
- 3 Richards AJ, Hatrick A, Eden CG. Large pelvic arteriovenous malformation complicating laparoscopic radical prostatectomy. *Urology* 2008; **72**: 1359–61.
- 4 Tanaka N, Asakawa I, Hasegawa M *et al.* The biochemical recurrence-free rate in patients who underwent prostate low-dose-rate brachytherapy, using two different definitions. *Radiat. Oncol.* 2014; **9**: 107.
- 5 Tanaka N, Asakawa I, Nakai Y *et al.* Comparison of PSA value at last follow-up of patients who underwent low-dose rate brachytherapy and intensity-modulated radiation therapy for prostate cancer. *BMC Cancer* 2017; **17**: 573.
- 6 Grimm P, Billiet I, Bostwick D *et al.* Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate, and high-risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group. *BJU Int.* 2012; **109**: 22–9.
- 7 Zelefsky MJ, Yamada Y, Pei X *et al.* Comparison of tumor control and toxicity outcomes of high-dose intensity-modulated radiotherapy and brachytherapy for patients with favorable risk prostate cancer. *Urology* 2011; **77**: 986–90.
- 8 Smith GD, Pickles T, Crook J *et al.* Brachytherapy improves biochemical failure-free survival in low- and intermediate-risk prostate cancer compared with conventionally fractionated external beam radiation therapy: a propensity score matched analysis. *Int. J. Radiat. Oncol. Biol. Phys.* 2015; **91**: 505–16.
- 9 Morris J, Tyldesley S, Rodda S *et al.* Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the ASCENDE-RT Trial): an analysis of survival endpoints for a randomized trial comparing a low-dose-rate brachytherapy boost to a dose-escalated external beam boost for high- and intermediate-risk prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2017; **98**: 275–85.

- 10 Game X, Berlizot P, Hassan T *et al.* Congenital pelvic arteriovenous malformation in male patients: a rare cause of urological symptoms and role of embolization. *Eur. Urol.* 2002; **42**: 407–12.
- 11 Bekci T, Yucel S, Turgut E, Soylu AI. Giant congenital pelvic AVM causing cardiac failure, diplegia, and neurogenic bladder. *Pol. J. Radiol.* 2015; **80**: 388–90.
- 12 Touyama H, Hatano T, Ogawa Y. Massive prostate bleeding after transurethral resection of prostate in a patient with a congenital pelvic arteriovenous malformation. *J. Urol.* 1998; **160**: 1803.
- 13 Jacobowitz GR, Rosen RJ, Rockman CB *et al.* Transcatheter embolization of complex pelvic vascular malformations; Results and long-term follow-up. *J. Vasc. Surg.* 2001; **33**: 51–5.
- 14 Kapp KS, Poschauko J, Tauss J *et al.* Analysis of the prognostic impact of tumor embolization before definitive radiotherapy for cervical carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.* 2005; **62**: 1399–404.
- 15 Lindblom E, Dasu A, Beskow C, Toma-Dasu I. High brachytherapy doses can counteract hypoxia in cervical cancer—a modelling study. *Phys. Med. Biol.* 2017; **62**: 560–72.
- 16 Cron G, Berghein N, Crokart N *et al.* Changes in the tumor microenvironment during low-dose-rate permanent seed implantation Iodine-125 brachytherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2005; **63**: 1245–51.