Cancer/Radiothérapie 25 (2021) 480–483

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Clinical case

Radiotherapy is effective in the management of rare penile metastases: Two case reports

Métastases péniennes : deux cas rares pris en charge efficacement par radiothérapie

B. Detti[a,*], A. Sardaro[b], V. Maragna[a], M. Mariotti[a], G. Stocchi[a], M. Roghi[a], M.A. Teriaca[a], G. Francolini[a], B. Guerrieri[a], L. Livi[a]

[a] *Radiation Oncology Unit, Azienda Ospedaliero Universitaria Careggi, l.go Brambilla 3, 50144 Florence, Italy*
[b] *Interdisciplinary Department of Medicine, Nuclear Medicine Unit and Section of Radiology and Radiation Oncology, University of Bari Aldo-Moro, Bari, Italy*

ARTICLE INFO

Article history:
Received 13 November 2020
Received in revised form 10 March 2021
Accepted 28 March 2021

Keywords:
Chemotherapy
Metastasis
Oncology

ABSTRACT

Penile metastasization is an uncommon condition, mostly derived from primitive advanced abdominal cancers, with disabling symptoms. Palliative treatment, in reason of poor prognosis patients, is frequently surgical with destructive management. We report two cases of penile metastasis, from primitive prostatic adenocarcinoma and primitive urothelial carcinoma, effectively managed with radiation treatment at our institution. A three-dimensional conformal radiation therapy with 42 Gy to the planning target volume in 14 fractions was delivered. Radiation treatment was safely delivered, with low toxicity profile and achieved adequate symptoms control without compromising genitourinary functions. Radiation therapy should be considered in management of rare penile metastases.

Mots clés :
Chimiothérapie
Métastase
Oncologie

RÉSUMÉ

La métastase pénienne est une affection rare, principalement dérivée de cancers abdominaux évolués primitifs, avec des symptômes invalidants. Le traitement palliatif, en raison du pronostic défavorable, est souvent chirurgical avec une prise en charge destructive. Nous rapportons deux cas de métastases péniennes, d'adénocarcinome prostatique primitif et de carcinome urothélial primitif, gérées efficacement par radiothérapie dans notre établissement. Une radiothérapie conformationnelle tridimensionnelle de 42 Gy dans le volume cible prévisionnel en 14 fractions a été délivrée. La radiothérapie a été administrée en toute sécurité, avec un faible profil de toxicité et a permis un contrôle adéquat des symptômes sans compromettre les fonctions génito-urinaires. La radiothérapie doit être envisagée dans la prise en charge des rares métastases péniennes.

1. Introduction

Penile metastases are an uncommon clinical condition, as only 460 cases are reported in literature since the first report in 1870 [1]. They mostly origin from advanced pelvic primary cancers, spreading via hematogenous and lymphatic patterns [2]. Retrograde venous spreading seems to be the most common cause, due to the communication between penile dorsal system and pelvic venous plexus: this could explain the frequent involvement of corpora cavernosa from primary prostatic, urothelial and rectosigmoid cancers [1]. Bladder cancer and prostatic adenocarcinoma account for about 30% of penile metastases each, rectal cancer for about 12%

* Corresponding author.
E-mail address: bdetti@unifi.it (B. Detti).

https://doi.org/10.1016/j.canrad.2021.03.004

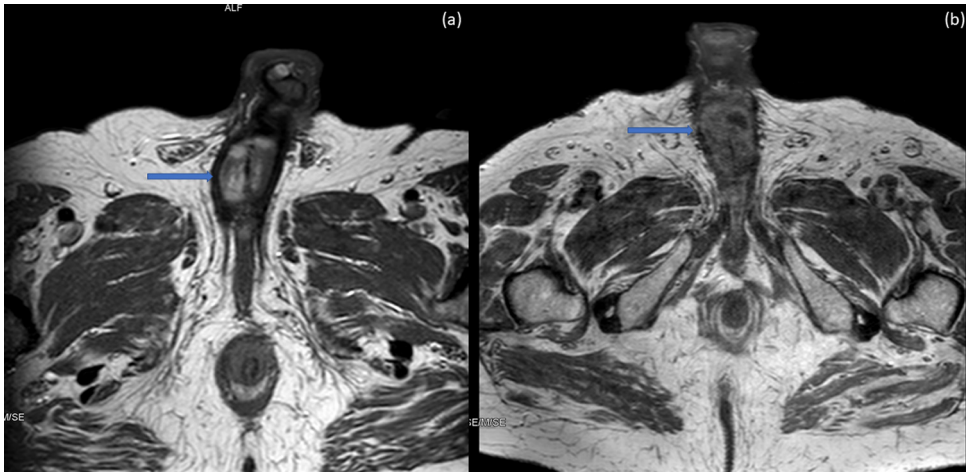

Fig. 1. MRI, axial view showing a penile metastasis in a patient with prostatic adenocarcinoma (case 1).

and renal cancer, lung cancer and lymphomatous entities account for about 6-7% overall [3]. Symptoms of presentation vary from penile nodes to malignant priapism [4], obstructive urinary deflux and, less frequently, superficial skin involvement. Penile localization often appears in an advanced setting of disease and goes with a poor prognosis: palliation of symptoms to preserve acceptable quality of life is the main goal of the management. Radiotherapy could be helpful and less invasive than surgery, besides reducing psychological impact of treatment.

Herein, we report two rare cases of penile metastases successfully treated with radiation in our Radiation Oncology Unit, AOU Careggi, Florence, Italy.

2. Patients and methods

2.1. Case 1

A 89-year-old patient with a history of cardiovascular disease was diagnosed in 2004 with prostatic adenocarcinoma, Gleason score (GS) 3 + 3, and was subsequently treated with flutamide inhibitor. In August 2018, the patient presented a PSA elevation of 5.5 ng/mL. Staging exams were performed, including computer tomography (CT) scan that demonstrated metastatic spread of disease to lumbar vertebrae L5 and to the left fibula. The patient was then directed to stereotactic radiation therapy (SBRT), which was delivered with CyberKnife® in 3 fractions, for a total dose of 27 Gy at 70% IDL (isodose line) to L5. The fibula localization was treated with 3-dimensional conformal radiation therapy (3DCRT), for a total dose of 30 Gy in 10 fractions. Leuprorelin, gonadotropin-releasing hormone analogue (GnRH) was started as systemic therapy. Three months later, biochemical analysis showed a rise of PSA up to 17.7 ng/mL, and physical examination revealed a suspicion of penile corpora cavernosa infiltration. Patient reported severe urinary impairment with weakened and alternating urinary jet in addition to penile pain and hardening of the penis, mostly localized to the base. Contrast-enhanced magnetic resonance imaging (MRI) was performed and the presence of penile metastasis was confirmed Fig. 1. The patient was subsequently sent to the Emergency Department for urological evaluation and suprapubic cystostomy was performed. The patient was then treated to the infiltrating penile localization, with 3DCRT employing 2 radiation fields, for a total dose of 42 Gy to the planning target volume (PTV) in 14 fractions. The PTV was defined as an isotropic expansion of 8 mm from clinical target volume (CTV) comprising the entire penis Fig. 2. The treatment was overall well tolerated; a penile and scrotal G1 oedema according to the CTCAE v. 4.03 was reported as the main side-effect one week after the conclusion of radiotherapy [5]. In the frame of metastatic castration resistant prostate cancer (mCRPC), patient started enzalutamide treatment after thorough cardiological evaluation. One month after the conclusion of radiotherapy, the previously reported edema was resolved and the patient was able to proceed with cystostomy removal. Physical examination demonstrated softened consistency of irradiated tissues. At the last follow up (18.8 months after radiotherapy), biochemical analysis showed PSA nadir of 0.02 ng/mL. The patient was still receiving enzalutamide treatment, with biochemical disease control and subjective clinical improvement. No local recurrence was detected after 20 months from radiotherapy.

2.2. Case 2

A 76-year-old patient was treated in May 2018 with radical cystoprostatectomy for a high grade, stage III urothelial carcinoma. He presented to our centre in February 2019 for gluteal and ischiatic discomfort and penile pain. Abdominal MRI revealed the presence of multiple skeletal dissemination and a corpora cavernosa localization. The patient had mild symptoms with obstructive urinary manifestations, moderate pain to the penis and erectile deficiency. At physical examination a mass in the penile body was found. The patient was considered for palliative radiation treatment and was treated with 3DCRT. A total dose of 42 Gy in 14 fractions to the PTV was delivered; the PTV was obtained from an 8 mm isotropic expansion of the CTV, comprehending the entire penis. The patient completed the radiotherapy with optimal tolerance, no onset of side effects was reported and a subjective clinical benefit in terms of pain control was achieved. At the first clinical evaluation after radiotherapy, the patient was asymptomatic and was not on medications for pain relief; furthermore, he reported recovery of erectile function. Afterwards, the patient started chemotherapy with carboplatin and gemcitabine for six cycles. After 7 months, a CT-scan showed progressive bone disease. Subsequently, a II line of treatment was started with an anti-programmed death-ligand 1 (PDL-1) antibody. No local penile recurrence was detected at 26.4 months after radiotherapy. The patient is currently still receiving maintenance anti PDL-1 treatment with stable disease.

3. Results

In the first presented case, the patient experienced rapid resolution of obstructive urinary symptoms and was able to remove cystostomy in less than a month. Notably, despite the elderly age and the presence of multiple cardiovascular comorbidities, we were

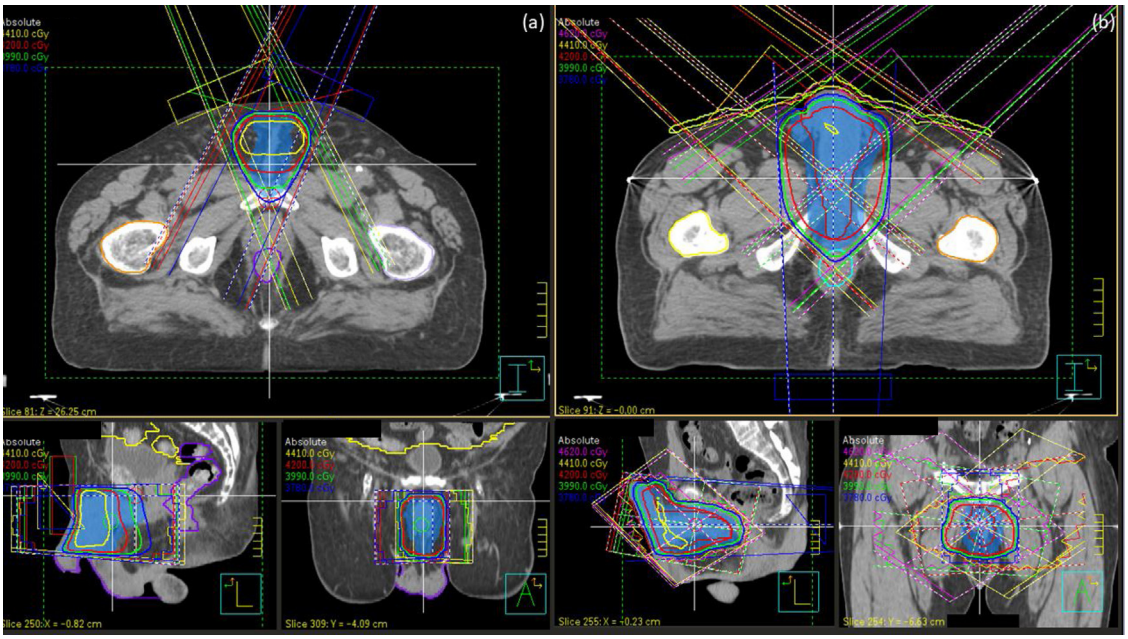

Fig. 2. Three-dimensional conformal radiation therapy for penile metastasis in a patient with prostatic adenocarcinoma: isodoses with target and organs at risk (case 1).

Table 1
Cases of patients treated with radiotherapy reported in the literature.

Author	Primary	Dose	Local response	Follow up
Zhang K et al.	Lung cancer	Unknown	Unknown	6 months
Kumar PP et al.	Rectal carcinoma	Unknown	Unknown	Died
	Prostate cancer	4000 rads in 20 fractions	CR	1 year
Nunes B et al.	Rectal carcinoma	30 Gy in 10 fractions	CR	1 year
McGuinness LA et al.	Rectal carcinoma	30 Gy in 10 fractions	CR	3 months
Mansbridge MM et al.	Prostate cancer	30 Gy in 10 fractions	PR	5 months

able to achieve a persistent local control with a non-invasive treatment. In the second presented case, erectile function was restored shortly after radiotherapy, with a sensible improvement of quality of life, a good clinical outcome and acceptable toxicity profile. No treatment interruptions were recorded. Only one adverse effect was reported: G1 scrotal oedema in clinical case 1 recovered a month after the end of radiotherapy and was the only noteworthy toxicity.

4. Discussion

Our single-centre experience in the treatment of penile metastases revealed that radiotherapy is an effective, tolerable and quality of life preserving treatment. The first known attempt to resume literature about this rare condition dates back to 1961 by Abeshouse [5]. Since then, other systematic reviews and small series have been carried on [1,6,7]. Mearini and colleagues underlined a very poor outcome of penile metastases requiring non-invasive palliative management: an average of 47 weeks of survival irrespective from treatment choice was reported for genitourinary primary malignancies, while metastatic prostate cancers record a slightly better survival [3]. All treatment options were explored and discussed, including surgical treatments (local excision, penectomy), radiotherapy (external beam radiotherapy or brachytherapy) and chemotherapy, but none of them proved to be superior.

Due to the rarity of this particular localization of disease and consequent low expertise, palliative treatments (including radiotherapy) lack the support of solid scientific evidence. On these grounds, we proposed a 3DCRT for a total dose of 42 Gy in 14 fractions, assuming an alfa/beta of 3 for prostate cancer and an alfa/beta of 10 for bladder cancer, resulting in a biologically effective dose (BED) of respectively 84 Gy and 54.6 Gy. Cante et al. reported a case of penile metastasis from prostate cancer treated with hormone therapy and external beam RT (35 Gy/14 fractions 2.5 daily); this experience provided a description of the successful use of hypofractionation in this setting and opens the way for more similar treatments in the future [8].

Indication of radiation treatments in this setting of patients is not well addressed in literature and no validated guidelines are currently available. Kumar and Newman in 1980 obtained priapism resolution after 4000 Rads (Table 1) in 20 fractions over 60 days using 18 meV electrons in a patient affected by penile metastasis from prostate cancer [9]. More recently, a 3DCRT treatment for a total dose of 30 Gy in 10 fractions was used in association with capecitabine in a penile localization from rectal cancer, with a complete response consisting in a resolution of the penile lesion [10]. In another experience from 2015, a radiotherapy course of 30 Gy in 10 fractions was delivered with adjuvant intent after circumcision and modified glansectomy to prevent local recurrence in rectal adenocarcinoma histology proven metastasis: despite patient poor outcome because of overall burden of disease, six months after palliative treatment no local recurrence was noted [11]. Masbridge et al. reported the early detection of a case of penile metastasis from prostate cancer thanks to the use of PSMA-PET/CT [12]. The impact of this incidental finding on survival is not known, but the authors underline the positive effect on local management of the disease; furthermore, the treatment of a penile metastatic site before clinical manifestation could translate in a survival benefit.

Our experience in this rare condition revealed radiotherapy is cost effective: with an adequate radiation plan we can successfully

treat disabling symptoms, obtaining a local complete response, without compromising organ function.

Literature describes this uncommon localization as expression of advanced disease and consequently considers penile metastasis as a poor prognostic sign; therefore, adequate balance between aggressive surgical treatments and quality of life needs to be taken into account. Moreover, in our experience patients were still alive and in active oncological therapy at 18 and 26 months after treatment respectively.

5. Conclusion

The chronicization of metastatic disease is common in some histologies, for instance prostatic adenocarcinoma, and long term survivors are frequent: thus, preservation of the quality of life has to be a priority. In selected cases, radiation treatment should be considered as a valid option for penile metastasis in order to palliate symptoms and to improve local control of disease. Multidisciplinary tumour board including radiologists, oncologists, radiotherapists and urologists, must be encouraged in order to define the best treatment option for patients affected by this rare condition.

Contribution

BD: project administration, supervision, writing original draft, review and editing; AS, GF, LL: review and editing; VM, MR, MAT: writing original draft; MMD, BG, GS: data curation; formal analysis.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Chaux A, Amin M, Cubilla AL, Young RH. Metastatic tumors to the penis: a report of 17 cases and review of the literature. Int J Surg Pathol 2011;19:597–606, http://dx.doi.org/10.1177/1066896909350468.
[2] Osther PJ, Løntoft E. Metastasis to the penis. Case reports and review of the literature. Int Urol Nephrol 1991;23:161–7.
[3] Mearini L, Colella R, Zucchi A, Nunzi E, Porrozzi C, Porena M. A review of penile metastasis. Oncol Rev 2012;6:e10.
[4] Cocci A, Hakenberg OW, Cai T, Nesi G, Livi L, Getti B, et al. Prognosis of men with penile metastasis and malignant priapism: a systematic review. Oncotarget 2017;9:2923–30, http://dx.doi.org/10.18632/oncotarget.23366.
[5] US Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE) version 4.03. 2010. USA: National Institutes of Health, National Cancer Institute; 2016.
[6] Abeshouse BS, Abeshouse GA. Metastatic tumors of the penis: a review of the literature and a report of two cases. J Urol 1961;86:99–112.
[7] Zhang K, Da J, Yao HJ, heng DC, Cai ZK, Jiang YQ, et al. Metastatic tumors of the penis: a report of 8 cases and review of the literature. Medicine (Baltimore) 2015;94:e132.
[8] Mansbridge MM, Strahan A, Parker J, Rhee H. PSMA-PET/CT-avid metastatic prostate cancer to the penis. BMJ Case Rep 2020;13:e233522, http://dx.doi.org/10.1136/bcr-2019-233522.
[9] Zhu YP, Yao XD, Zhang HL, Shen YJ, Huang D, Ye DW. Penile metastasis from primary bladder cancer: a study of 8 cases and review of the literature. Onkologie 2012;35:196–9.
[10] Kumar PP, Newland JR. Metastatic carcinoma of the penis. J Natl Med Assoc 1980;72:55–8.
[11] Nunes B, Matias M, Alves A, Jorge M. Metastasis to the glans penis: an unusual site of rectal cancer recurrence. Acta Med Port 2015;28:525–7.
[12] McGuinness LA, Floyd Jr MS, Lucky M, Parr NJ. Penile metastases treated with partial glansectomy and adjuvant radiotherapy 5 years after an initial diagnosis of rectal cancer. BMJ Case Rep 2013;2013 [bcr2013200829].