

Oncology

Neoadjuvant chemotherapy for penile cancer enabling organ preservation: A case of individualized management for bilateral lymph node metastasis and a bulky primary tumor

Aeen M. Asghar, Andrew G. McIntosh, Alexander Kutikov, David YT. Chen, Daniel M. Geynisman*

Fox Chase Cancer Center, Temple University Health System, 333 Cottman Ave, Philadelphia, PA 19111, United States

Introduction

Penile cancer, most commonly squamous cell carcinoma (SCC), is rare in the United States and Europe but has an aggressive natural history. Due to disease rarity, randomized clinical trials demonstrating efficacious multimodal therapies for advanced disease are lacking. Multi-agent cisplatin-based neoadjuvant chemotherapy (NAC) utilizing the “TIP” regimen (paclitaxel, ifosfamide, and cisplatin) has demonstrated good clinical response rates in T_xN₂₋₃ disease.¹ Clinical responders to NAC who undergo consolidative surgery show improved overall survival and time to progression. We present a case of invasive SCC of the penis with a bulky primary tumor and bilateral lymphadenopathy in a patient who refused initial penectomy. We discuss the role of NAC in this setting and our results employing multimodal therapy to facilitate a limited local excision.

Case presentation

A 46-year-old man presented with biopsy proven invasive keratinizing SCC of the penis, with clinical and radiographic evidence of concurrent inguinal lymphadenopathy. He sought a second opinion after being advised he would require a complete penectomy and perineal urethrostomy by an outside provider—he was unwilling to consider treatment that would demand loss of his penis. Physical examination revealed a large, draining, ulcerated and nearly circumferential penile mass, covering the bulk of the ventral and lateral surfaces (Fig. 1). Multiple left-sided (largest 2cm) inguinal lymph nodes (LNs) and shoddy, non-specific right-sided LNs were palpable. Evaluation by F₁₈-FDG PET/CT was performed, and the primary tumor and bilateral inguinal LNs were positive; needle biopsy of the left inguinal LN confirmed metastatic SCC (Fig. 1). Per National Comprehensive Cancer Network guidelines for AJCC Stage IIIb disease (cT1N2M0; Grade 2), NAC was offered,² with deferral of treatment of the primary tumor. Four cycles of TIP were administered and well tolerated with minimal toxicity, and we observed a complete response in the LNs on

repeat F₁₈-FDG PET/CT (Fig. 2). Additionally, NAC resulted in a profound primary tumor response with significant regression (Fig. 2). Subsequently, he proceeded with consolidative surgery and the residual penile mass was removed by wide local excision with the surgical defect reconstructed by use of full thickness skin graft; he also underwent bilateral inguinal LN dissection to obtain complete pathologic staging. No gross invasion of the corpora or spongiosum was noted intra-operatively (Fig. 3). Final surgical pathology demonstrated no residual cancer in 16 inguinal LNs and a 2.8 cm residual superficial invasive carcinoma of the penis (AJCC Stage 1: ypT1aN0M0, Grade 2). He has fully recovered, retaining his baseline voiding function, and he reports no change in sexual function. MRI of the pelvis performed 8 months post-operative reveals no evidence of disease.

Discussion

We present a case of invasive bulky penile SCC with synchronous bilateral inguinal LN metastases. At the time of presentation, given the extent of local disease, initial penile sparing resection of the primary tumor was not possible. Given his confirmed inguinal LN metastases, he received NAC, per NCCN guidelines.² This resulted in complete regression of his LN disease as well as a marked reduction in the primary tumor burden, allowing penile sparing consolidative surgery and an otherwise unachievable final cosmetic and functional outcome.

While radical oncologic surgery is recognized to often have an impact on patient quality of life, partial or total penectomy may have a particularly profound psychological effect, beyond the direct impact on sexual and urinary function. Alternative organ preserving treatments have been developed for patients with penile cancer, such as application of brachytherapy; however, patients with large penile tumors usually warrant partial or total penectomy as the treatment with the greatest potential for cure. Additionally, utilization of NAC is recommended for N₂₋₃ disease per NCCN guidelines² but NAC has limited described utility in clinically node negative patients with organ-confined penile SCC. Such patients are typically offered radical definitive

* Corresponding author.

E-mail address: daniel.geynisman@fccc.edu (D.M. Geynisman).

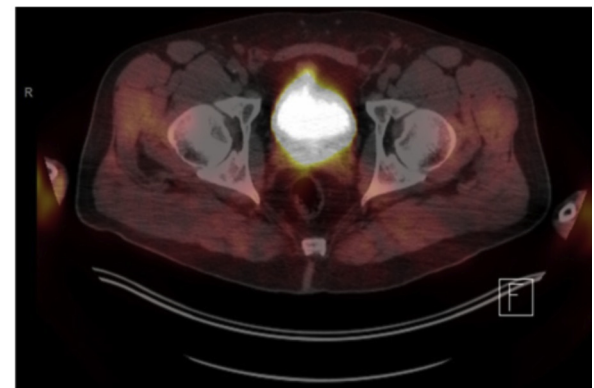
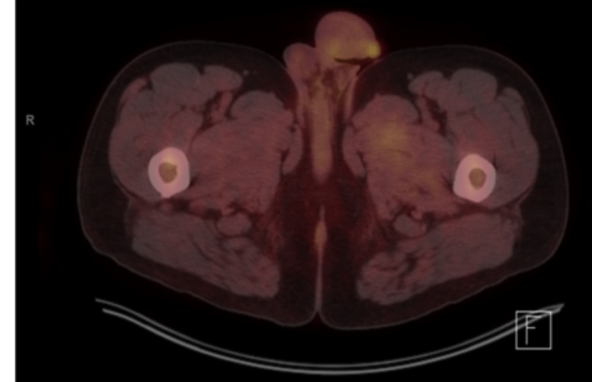
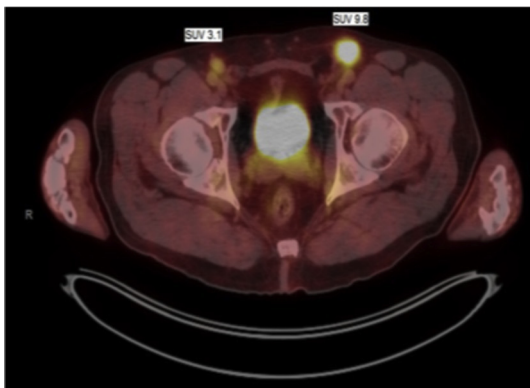
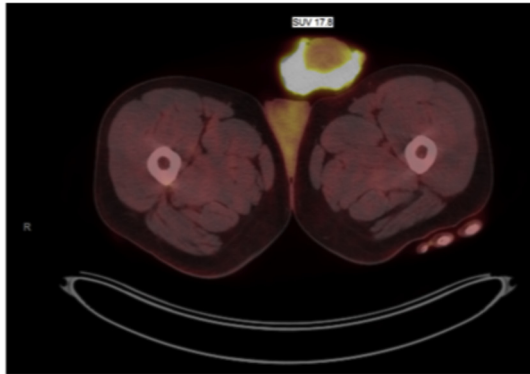


Fig. 1. Primary tumor and lymphadenopathy at time of diagnosis (Photo and PET Scan).

resection up front. Necchi et al. compared the use of NAC v. adjuvant chemotherapy v. both in patients with T3-4Nx and TxN1-3 and found no significant difference regarding the timing of perioperative chemotherapy in overall survival.³ These findings suggest a potential role for NAC in locally advanced but organ-confined disease to shrink and downstage the primary tumor, and without a negative impact on patient survival.

This case not only illustrates the efficacy of NAC in confirmed LN metastatic SCC, but also the dramatic impact of NAC on the primary tumor, which can facilitate an organ-preserving resection. In a small cohort of patients with advanced primary tumors ± LN metastasis (T3-4N0-3), Lejte et al. showed that the majority of patients respond to NAC and with consolidative surgery are long-term survivors.⁴ Our case differs from the majority of current literature regarding NAC as the primary tumor was bulky in size, but biopsy revealed an early stage tumor (cT1 Grade 2 SCC).

In patients with penile SCC facing partial or complete penectomy who desire organ preservation, NAC has the potential to result in significant tumor regression and to facilitate a limited resection. This case

Fig. 2. Primary tumor and lymphadenopathy after NAC (Photo and PET Scan).

suggests that NAC could be considered in selected patients without concurrent metastatic disease. Being able to identify patients who will maximally respond to NAC would be an important advance, prior to universally applying such an approach.

Conclusion

This case demonstrates the successful application of NAC to treat penile SCC with a bulky primary tumor and bilateral inguinal LN metastasis. We highlight the importance of shared decision making to individualize treatment and demonstrate the potential efficacy of NAC when prescribed according to NCCN guidelines for N2-3 disease. NAC has potential benefit for patients with bulky tumors who desire penile-sparing surgery and may facilitate minimizing the degree of organ and function typically lost with standard resection of the primary tumor by partial or total penectomy.

Funding

This research did not receive any specific grant from funding



Fig. 3. Intra-operative and post-operative outcome (Photos).

agencies in the public, commercial, or not-for-profit sectors.

References

1. Pagliaro LC, et al. Neoadjuvant paclitaxel, ifosfamide, and cisplatin chemotherapy for metastatic penile cancer: a phase II study. *J Clin Oncol.* 2010;28(24):3851–3857.

2. Clark, P.E.S., P. E; Agarwal, N., et al NCCN guidelines: penile cancer. NCCN Clinical Practice Guidelines in Oncology [Report] 2017 3/10/2017 [cited 2017 12/10/2017]; 2.2017:[Available from: https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf].
3. Necchi A, et al. Clinical outcomes of perioperative chemotherapy in patients with locally advanced penile squamous-cell carcinoma: results of a multicenter analysis. *Clin Genitourin Canc.* 2017;15(5):548–555 e3.
4. Leijte JA, et al. Neoadjuvant chemotherapy in advanced penile carcinoma. *Eur Urol.* 2007;52(2):488–494.