Effective control of recurrent and metastatic GU SCC by employing a multimodal approach in a patient with a history of radiation and transscrotal surgery for stage I seminoma

Daniel Roberson*a, Hanna Jiab, David Vaughnc, Christopher Millerd, Franz Fogte, R. Caleb Kovella

a Division of Urology, Department of Surgery, University of Pennsylvania Health System, Philadelphia, PA, USA
b Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
c Division of Hematology and Oncology, Department of Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA
d Department of Dermatology, University of Pennsylvania Health System, Philadelphia, PA, USA
e Department of Pathology and Laboratory Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA

ARTICLE INFO

Keywords:
Secondary malignant neoplasm
Squamous cell carcinoma of the scrotum
Mohs micrographic surgery of scrotal cutaneous malignancy
Multimodal therapy for genitourinary metastatic squamous cell carcinoma

ABSTRACT

This 68-year-old male, with a history of treated testicular seminoma, developed scrotal SCC 30 years later, with a metastatic SCC recurrence following another interval of 10 years. He exhibited good response to multimodal therapy, though subsequently underwent orchiectomy, revealing SCC invading his solitary testicle. This case presents a unique danger of adjuvant radiation in testicular cancer survivors, demonstrates the efficacy of multimodal therapy with GU SCC, and describes a highly unusual histologic finding.

1. Introduction

Scrotal violation at the time of orchietomy for malignancy confers a risk of cancer upstaging, a risk which remains purely theoretical given all available data.1 Additionally, adjuvant radiation therapy (RT) is no longer standard of care for testicular cancer (TC) patients in the settings of scrotal violation or for adjuvant treatment for stage I seminoma.1 While it is known that patients with testicular cancer and those who have undergone radiation therapy are at a higher risk of secondary malignant neoplasm (SMN), there is no association with squamous cell carcinoma (SCC) and either of these factors.2 Metastatic SCC of the genitourinary (GU) organs can be challenging to treat, with varying success when undergoing multimodal therapy.3 To our knowledge, metastatic SCC of the GU skin has never been described to recur in the para-testicular tissue with testicular invasion following adequate locoregional control resulting in remission.

2. Case presentation

We herein present the case of a 68-year-old male with a noncontributory past medical history, including no predisposing occupational or lifestyle risk factors for SCC. In 1978, he underwent a right scrotal orchietomy for a testicular mass ultimately proving to be seminoma. He had no evidence of disease outside of the testicle. He received 10 fractions of adjuvant radiation in a dog leg pattern with inclusion of the scrotal scar. Following a period of 30 years, he represented with a non-healing scrotal ulcer that was found to be SCC following wide local excision. He continued on surveillance and in 2018 he had a non-healing ulcerated wound develop on his scrotum which returned as SCC on excisional biopsy. He was also found to have inguinal adenopathy, which was biopsy proven to be SCC. Following multidisciplinary discussion at our institutional genitourinary tumor board, he received 20 Gy in five fractions of palliative radiation to the midline anterior scrotal wound for severe bleeding and six cycles of carboplatin/paclitaxel. Disease burden responded exceedingly well,
with almost complete resolution of primary tumor and nodal metastases. He then underwent Mohs resection in 2019 with excision of nearly his entire scrotum and positioning of his solitary left testicle in a left medial thigh pouch (Fig. 1).

On surveillance imaging in 2021, a mass in his solitary left testicle was noted. It was seen to be intratesticular, 1.5cm in diameter, and comprised of complex structure with enhancement of septations and internal vascularity (Fig. 2). The mass demonstrated growth of 6mm in 6 months. Testicular cancer tumor markers were within normal limits. We performed a radical inguinal orchiectomy. Final pathology showed moderately differentiated SCC originating from para-testicular tissue and invading into the testicle. The spermatic cord was free of tumor and there were sclerotic changes consistent with radiation in the specimen (Fig. 3). He is maintained on supplemental testosterone therapy as he was hypogonadal prior to this most recent orchiectomy. The case was again discussed at our university based, multidisciplinary GU oncology board, with a final consensus for close surveillance including physical exam and imaging over short intervals.

3. Discussion

This case illustrates a rare and complex scenario of SMN following a remote history of treatment for stage I testicular seminoma. With this patient initially undergoing a scrotal orchiectomy for what turned out to be malignancy, the scrotal violation would theoretically upstage the cancer, though is highly unlikely to have contributed to his scrotal SCC. A meta-analysis from 1995 showed no significantly worse prognosis in those with scrotal violation during orchiectomy for malignancy, and presented data to argue against adjuvant local therapy (radiation or surgery) for scrotal violation.

It is well known that testicular cancer survivors carry an elevated risk of developing a SMN, which is further elevated in those treated with RT following orchiectomy. An international population-based study of 40,576 TC survivors, found a 2.7-fold increased solid cancer risk in infra-diaphragmatic locations within the RT field, which persists for 35 years following initial therapy. However, they did not find an increased risk for skin cancers in the RT field which has been corroborated by other studies.

To date there is no evidence that RT increases the risk of cancers of the skin. We hypothesize, however, that adjuvant RT may have contributed to poor wound healing, which could have subsequently contributed to the development of SCC.

Another unique aspect of this case was this patient’s excellent response to palliative RT, chemotherapy, and resection at the time of SCC metastasis, demonstrating a subsequent 2-year period with no evidence of disease. Metastatic scrotal SCC historically confers a very poor prognosis, with median survival of 6 months and no survival benefit with radiation therapy. While combination bleomycin, methotrexate, and cisplatin has been found to be effective in 72% of cases, the median response rate in this study was 6 months, and 14% of patients experienced a complete response.

To our knowledge, only one prior case report has demonstrated a strong response of metastatic scrotal SCC to multimodal therapy, showing a 22-month recurrence free survival after treatment with a similar regimen as our patient. Our findings continue to support that multimodal therapy is effective in management of metastatic scrotal SCC. Our patient did develop recurrence of SCC in his contralateral testicle which brings up another unique finding of this case. To our knowledge, this is the first report of metastatic scrotal SCC recurrence developing in para-testicular tissue and invading into the adjacent testicle.

4. Conclusion

This complicated case raises several important points in regard to GU malignancy. It demonstrates a unique danger of adjuvant radiation
following trans scrotal testicular cancer excision, with development of scrotal cutaneous malignancy possibly through contribution from impaired wound healing. This case demonstrates high efficacy of multimodal treatment of metastatic scrotal SCC. We finally see a previously undescribed histologic finding of para-testicular SCC invading into testicular tissue in the setting of metastatic scrotal SCC previously in a state of remission.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review upon request.

Financial statement

There are no directly relevant conflicts of interest to declare from any author.

Funding

The authors report no funding.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

Acknowledgements

The authors have no acknowledgements.

References

1. Capelouto C, Clark P, Ransil BJ, Loughlin KR. A review of scrotal violation in testicular cancer: is adjuvant local therapy necessary? J Urol. 1995;153(3):981–985.
2. Travis LB, Fossá SD, Schonfeld SJ, et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. J Natl Cancer Inst. 2005;97(18):1354–1365. https://doi.org/10.1093/JNCI/DJI278.
3. Johnson TV, Hsiao W, Delman KA, Canter DJ, Master VA. Scrotal cancer survival is influenced by histology: a SEER study. World J Urol. 2013;31(3):585–590. https://doi.org/10.1007/S00345-012-0834-0/FIGURES/3.
4. Dexeus FH, Logothetis CJ, Sella A, et al. Combination chemotherapy with methotrexate, bleomycin and cisplatin for advanced squamous cell carcinoma of the male genital tract. J Urol. 1991;146(5):1284–1287. https://doi.org/10.1016/S0022-5347(17)38069-2.
5. Arai Y, Kinouchi T, Kuruda M, Usami M, Kotake T. A case of scrotal cancer with inguinal lymph node metastasis treated by multidisciplinary modalities including chemotherapy with methotrexate, bleomycin and cisplatin. Hinyokika Kiyo. 1997;43(9):683–685.