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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 Jia [b], David Vaughn [c], Christopher Miller [d], Franz Fogt [e], R. Caleb Kovell [a]

[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

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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 orchiectomy 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 orchiectomy 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 scar over the right hemi-scrotum that was found to be scrotal 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 left 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,

Abbreviations: RT, Radiation therapy; TC, Testicular cancer; SNM, Secondary malignant neoplasm; SCC, Squamous cell carcinoma; GU, Genitourinary.

* Corresponding author. Division of Urology, Department of Surgery, University of Pennsylvania Health System, Perelman Center for Advanced Medicine, West Pavilion, 3rd Floor, 3400 Civic Center Blvd, Philadelphia, PA, 19104, USA.
E-mail address: Daniel.roberson@pennmedicine.upenn.edu (D. Roberson).

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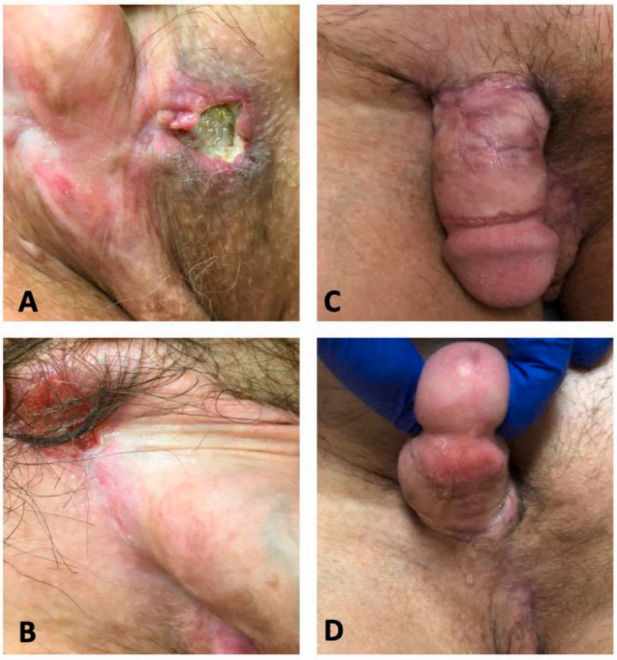

Fig. 1. Images A and B represent the preoperative assessment of multifocal GU SCC lesions that were recurrent following wide local excision, an excisional biopsy, and a course of radiation and chemotherapy. Images C and D demonstrate physical exam 14 weeks following Mohs Micrographic Resection and urologic local reconstruction of the penis and scrotum which included placement of the left testicle in a medial thigh pouch.

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.[1]

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.[2] 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.[3] 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.[4]

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.[5] 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

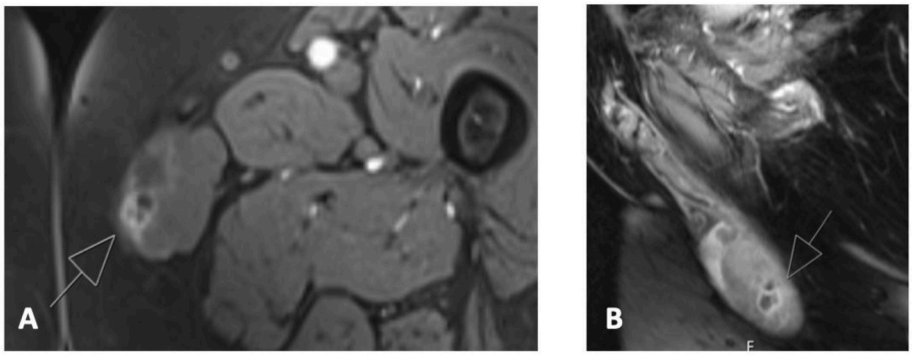

Fig. 2. MRI showing multiseptated and enhancing 1.5cm × 1.1cm x 1.2 cm complex cystic lesion in the medial aspect of the left testicle which was transplanted into a left medial thigh pouch during a prior operation. Image A is an axial T1 cross section and image B is a sagittal T1 cross section. The lesion was noted to have grown in all dimensions with a growth rate of 6mm over the span of 6 months.

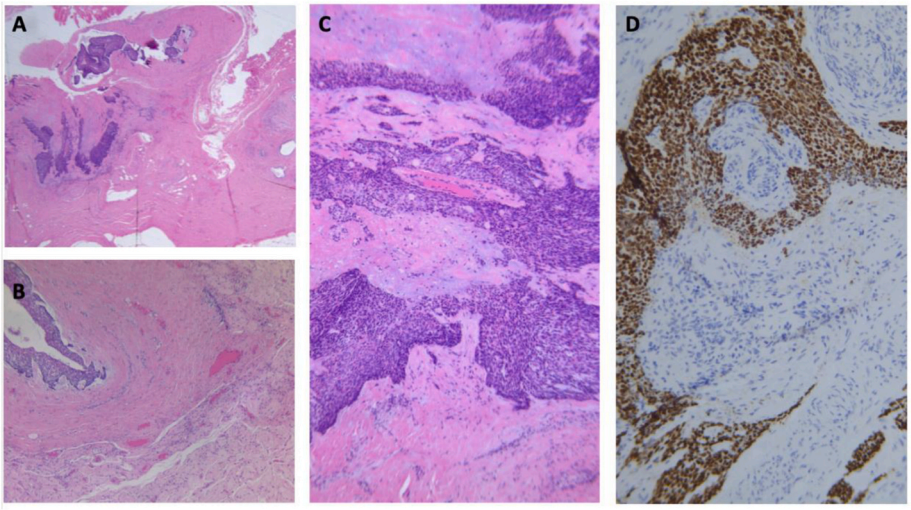

Fig. 3. Histologic findings from 2021 radical orchiectomy of the solitary, left testicle. Panel A demonstrates squamous cell carcinoma in the soft tissue of the testicle with standard H and E staining. Squamous cell carcinoma and radiation injury to tissue both in and outside the testicle can be appreciated in panel B. A high-power image of squamous cell carcinoma within the tissue of the testicle is demonstrated in panel C. Panel D shows specimen positivity for squamous markers with a P40 immunohistochemical stain. The tissue stained positive for MLH1 and PMS2, and negative for MSH6 and MSH2 (not pictured).

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.

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Declaration of competing interest

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