Surgical Management of Primary Scrotal Cancer

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KEYWORDS

• Scrotal cancer • Squamous cell carcinoma • Extramammary Paget's disease • Sarcoma
• Basal cell carcinoma • Melanoma • Adnexal skin tumor

KEY POINTS

- Wide surgical excision is recommended for localized scrotal cancer.
- Reconstruction of the defect can be performed with primary closure, skin grafts, or flaps.
- High-risk scrotal cancer has a poor prognosis, with a decreased overall survival compared with penile cancer.

INTRODUCTION

Percival Pott, the 18th-century English surgeon, is credited as the first to associate an occupational exposure to the ensuing development of disease.[1] Cases of squamous cell carcinoma of the scrotum, known colloquially as chimney sweep's carcinoma, were seen almost exclusively in England among young men who worked as chimney sweepers.[2] Sweeps, as they were called, were forced to work in dirty conditions and many times worked while naked to fit into tight spaces. This led to the overexposure of coal on the genitals and the subsequent development of soot warts and cancer, if left untreated. More recently, polycyclic aromatic hydrocarbons in the soot were discovered to be the causative agent of this disease and steps were taken to protect workers.[3] As occupational exposure has decreased, so has the incidence of scrotal cancer, which makes studying this virulent malignancy much more difficult.

Primary scrotal cancers are rare, with the majority of the literature being composed of small case series. Johnson and colleagues[4] evaluated the Surveillance, Epidemiology, and End Results database for scrotal cancer patients and found that histologies included squamous cell carcinoma (35.1%), extramammary Paget's disease (21.9%), sarcoma (20.4%), basal cell carcinoma (16.7%), melanoma (3.3%), and adnexal skin tumors (2.6%). The median (95% CI) overall survival for localized low-risk scrotal cancers (basal cell carcinoma, extramammary Paget's disease, sarcoma) and localized high-risk scrotal cancers (melanoma, squamous cell carcinoma, adnexal skin tumors) was 166 (145–188) and 118 (101–135) months, respectively. Patients with regional and distant disease are reported to have worse overall survival.[5,6]

Diagnosis requires an excisional biopsy of the lesions to determine the underlying histology of the scrotal cancer. Evaluation of nonlocalized disease and metastases can be performed through careful physical examination and cross-sectional imaging modalities such as computed tomography scanning or MRI. PET should be regarded as investigational. Treatment for all histologies requires surgical removal of the malignancy. Adjuvant treatments, including radiation and chemotherapy may be warranted. Owing to the small number of reported cases, details in management and overall prognosis are limited. We discuss surgical management of primary scrotal cancers based on National Comprehensive Cancer Network guidelines, if present, and also expert opinion (**Box 1**).

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Box 1
Indications and contraindications

Indications for Surgery

Localized, resectable disease

Contraindications to Surgery

Nonmalignancy after biopsy

Metastatic disease

Comorbid conditions with poor prognosis

TECHNIQUE/PROCEDURE

Preparation

Scrotal anatomy

The skin of the scrotum can be divided into an anterior and a posterior aspect, each with distinct neurovasculature. The anterior scrotum is supplied by the deep external pudendal arteries, which branch off the femoral artery and course medially into the scrotum. The posterior scrotum is supplied by the perineal arteries, which branch off the pudendal arteries. The vessels do not cross the median raphe and this allows for a relatively bloodless incision.

The anterior scrotal skin and the posterior scrotal skin have their own dedicated venous drainage that course along with their respective arterial supplies. The anterior surface is drained via the external pudendal veins and the posterior surface by the scrotal branches of the perineal vessels. The lymphatic drainage of the scrotum is supplied by the superficial inguinal lymph nodes for both the anterior and posterior sides. This differs from testicular lymphatics, which drain into the paraortic lymph nodes. The innervation of the scrotal skin is provided by the anterior scrotal nerves, which are branches of the ilioinguinal nerve, and the posterior scrotal nerves, which are branches of the perineal nerve.

Preoperative prophylactic antibiotic and infection management

The American Urologic Association best practice policy guidelines on surgical antimicrobial prophylaxis of the scrotum recommends a single dose of preoperative antibiotics, particularly in patients with certain risk factors for infection (**Table 1**).[7] This is owing, in part, to the scrotal surgical infection rate being comparatively low, ranging from 0% to 10%. The recommended prophylactic antibiotic of choice is a first-generation cephalosporin or clindamycin as an alternative.

Traditionally, hair has been removed preoperatively to reduce the risk of surgical site infections, although recent studies indicated that this may not be necessary. A recent analysis of randomized, controlled trials compared hair removal with no removal, the different methods of hair removal, as well as the different times of hair removal before surgery.[8] No significant difference in surgical site infections was found among patients who had their hair removed and those who did not. In circumstances when removal of hair is necessary, using clippers instead of a razor is associated with fewer surgical site infections.

Patient Positioning

1. The patient should be placed in the exaggerated dorsal lithotomy position to provide visualization of the entire scrotum and adjacent regions, including the penis, suprapubic/inguinal regions, medial thigh, and perineum/perianal regions.

Table 1
Factors and results

Factor	Result
Impaired natural defense mechanism	
Advanced age Anatomic anomalies of the urinary tract Poor nutritional status Smoking Chronic corticosteroid use Immunodeficiency	Decreased natural defense mechanisms of the urinary tract and immune system
Increase local bacterial concentration and/or spectrum of flora	
Externalized catheters Colonized endogenous/exogenous material Distant coexistent infection Prolonged hospitalization	Increased local bacterial concentration and/or spectrum

2. Betadine scrub and paint can be used to widely prepare the scrotum and adjacent regions.
3. Towels should be placed in a triangular manner around the scrotum. The penis can be reflected cephalad, covered by the towel over the suprapubic region. During the case, the towels can be adjusted to access adjacent region, if necessary. Standard cystoscopy drapes can be used.

Approach

General thoughts regarding surgical excision

- Scrotal cancer most often presents superficially. The skin and dartos of the scrotum is thicker than the respective tissue in the penis, which contributes to the superficial nature of this disease
- As with any surgery for resectable malignancy, the goal is to remove the disease with clear margins (both peripheral and deep). Mohs surgery and frozen sections can be used to ensure adequate margins.

General thoughts regarding reconstruction

- The scrotal skin is extremely elastic, which helps to provide coverage for reconstruction. Factors that contribute to a larger scrotum include older age and men with hydroceles.
- Approximately 60% of the scrotal skin can be removed with adequate tissue remaining for primary closure. Primary closure is preferred over skin grafts or flaps when possible.
- Closed suction drains can be considered to prevent the development of fluids collections, such as seromas and hematomas.

Technique and Procedure (Detailed Steps)

The goal of surgical treatment for scrotal cancer is excision of the disease. We present steps in management for the various histologic subtypes of scrotal cancer. We also present a case of scrotal cancer diagnosed at our institution, along with pictures taken during the surgery and reconstruction.

Squamous cell carcinoma

1. Biopsy-proven lesions should be excised with 4- to 6-mm clinical margins. Mohs surgery can alternatively be performed.[9]
2. Margins should be assessed. If positive, surgical reexcision should be performed. If unable to obtain a negative margin, which would be rare, radiation therapy is recommended.
3. Fine needle aspiration or core biopsy should be performed for palpable regional lymph nodes or abnormal lymph nodes identified on imaging. If positive and operable, regional lymph node dissection should be performed. Radiation therapy should be considered if multiple lymph nodes are involved or if extracapsular extension is present. If regional lymph nodes are positive and inoperable, radiation therapy with or without systemic therapy is recommended.
4. Excision site can be managed with tension-free primary approximation, skin graft, or flap and, seldom, with healing by secondary intention.
5. Nonsurgical candidates should receive radiation therapy.
6. Minimal evidence is available regarding systemic therapy for metastatic disease.

Extramammary Paget's disease

1. Biopsy-proven lesions should be excised with a wide surgical margin and intraoperative frozen section to ensure complete resection.[10]
2. The excision site can be managed with primary closure. A simultaneous reconstructive procedure, including a skin graft or flap, can be performed if the defect is unable to be closed primarily.
3. Imiquimod cream, 5-fluorouracil cream, and CO_2 laser have been used with variable results. Photodynamic therapy has been used for palliative results.
4. Of note, traditionally extramammary Paget's disease was thought to represent adenocarcinoma in situ, arising from the epidermis. However, more advanced disease, including deeper invasion, nodal disease, and metastatic disease have been reported, with 1 large series reporting up to 16.6% of patients with regional or distant disease.[5] Although the role of radiation therapy and chemotherapy is not entirely clear, these modalities have been applied as primary treatment, as adjuvant therapy, and for nonsurgical candidates. It is important to assess for other malignancies, because there may be an association with other underlying malignancies in patients with extramammary Paget's disease.

Sarcoma

1. Biopsy-proven lesions are treated according to stage.[11]
   A. For stage I sarcoma, wide local excisional surgery should be performed to obtain adequate negative oncologic margins. Although an adequate margin size is not specified, close margins may be necessary to preserve critical neurovascular and musculoskeletal structures. Failure to obtain adequate oncologic margins can be

managed by re-resection or radiation therapy.
   B. For stage IIA sarcoma that is resectable with functional outcomes, surgery, surgery with adjuvant radiation, or neoadjuvant radiation therapy with surgery can be performed.
   C. For stage IIB and III sarcomas that are resectable with functional outcomes, surgery, neoadjuvant radiation therapy and surgery, neoadjuvant chemoradiation and surgery, or neoadjuvant chemotherapy and surgery can be performed. Adjuvant radiation therapy with or without chemotherapy can be given.
   D. For stage II and III sarcomas that are resectable with adverse functional outcomes or unresectable disease, radiation therapy, chemoradiation, chemotherapy, or regional limb therapy can be performed. If the lesion is subsequently resectable with acceptable functional outcomes, surgery should be performed. Adjuvant radiation therapy with or without chemotherapy can be performed.
   E. For nodal involvement, regional lymph node dissection should be performed with or without radiation and chemotherapy.
   F. For metastatic disease to a single organ and limited tumor bulk that is amenable to local therapy, metastasectomy with or without radiation and preoperative or postoperative chemotherapy can be performed. A marginal efficacy has been reported for the use of chemotherapy in localized resectable soft tissue sarcoma with respect to local recurrence, distant recurrence, overall recurrence, and overall survival.[12] Ablation procedures, embolization procedures, stereotactic body radiation therapy, or observation can also be considered.
   G. For disseminated metastatic disease, palliation should be considered. Options include chemotherapy, radiation therapy, surgery, observation, supportive care, ablation procedures, or embolization procedures.
2. The excision site can be managed with tension-free primary approximation, skin graft, or flap; it is seldom healed by secondary intention.
3. For spermatic cord sarcoma, a radical inguinal orchiectomy with high ligation of the spermatic cord is recommended. Wide circumferential margins may be difficult to obtain because of anatomic constraints. Partial scrotectomy and resection of the surrounding tissues may be necessary. The major pattern of failure for spermatic cord sarcoma is local recurrence. Combined surgery and radiation may be considered in patients who are at high risk (lesions >5 cm) for local failure.[13]

Basal cell carcinoma

1. Biopsy-proven lesions should be excised with 4-mm clinical margins. Mohs surgery can be performed alternatively.[14]
2. Margins should be assessed. If positive, surgical reexcision should be performed. If unable to obtain a negative margin, radiation therapy is recommended. If margins are negative but extensive perineural or large nerve involvement is present, radiation therapy is recommended.
3. No guidelines from the National Comprehensive Cancer Network are available for regional lymphadenopathy for basal cell carcinoma. Surgical management can be extrapolated from treatment of regional lymphadenopathy in squamous cell carcinoma. Fine needle aspiration or core biopsy should be performed for palpable regional lymph nodes or abnormal lymph nodes identified on imaging. If positive and operable, regional lymph node dissection should be performed. Radiation therapy should be considered if multiple lymph nodes are involved or if extracapsular extension is present. If regional lymph nodes are positive and inoperable, radiation therapy with or without systemic therapy is recommended.
4. The excision site can be managed with tension-free primary approximation, skin graft, or flap; it is seldom healed by secondary intention.
5. Nonsurgical candidates should receive radiation therapy.
6. Recent developments in systemic therapy, such as Hedgehog pathway inhibitor, may be an option for metastatic disease. Minimal evidence is available regarding chemotherapy.

Melanoma

1. Biopsy-proven lesions are treated according to stage. Scrotal melanoma management can be guided by the profusion of data on other skin melanoma sites, because no data specifically exist for scrotal-only melanomas.[15]
   A. For stage 0 or IA and IB (<0.75 mm thick), wide excision should be performed based on tumor thickness.
   B. For stage IA (0.76–1.00 mm thick), wide excision should be performed and consider sentinel lymph node biopsy. If sentinel lymph node biopsy is positive, see stage III.
   C. For stage IB (0.76–1.00 mm thick) or stage II (>1.00 mm thick), wide excision should be performed and consider sentinel lymph

node biopsy. If sentinel lymph node biopsy is positive, see stage III. If sentinel lymph node biopsy is negative, adjuvant therapy such as clinical trials, observation, or possibly interferon alfa can be considered.

D. For stage III (positive sentinel node), perform complete lymph node dissection. Adjuvant therapy clinical trials, observation, interferon alfa, or high-dose ipilimumab can be considered. Newer immunotherapy agents, including PD-1 inhibitors such nivolumab and pembrolizumab, are currently being evaluated. They have preliminarily been shown to improve overall survival.[16]

E. For stage IV (metastatic disease) that is resectable, surgical resection should be performed. Systemic therapy can also be considered. For metastatic disease that is unresectable, options include systemic therapy, clinical trials, intralesional injection, or palliative resection with or without radiation therapy.

2. Excision site can be managed with tension-free primary approximation, skin graft, or flap and seldom, with healing by secondary intention (Table 2).

Adnexal tumors

1. Biopsy-proven lesions should be excised with a wide margin. Owing to the rarity of these tumors, adequate margins have not been evaluated in clinical trials or observational studies. In general, 1- to 2-cm clinical margins are recommended.[17]
2. No guidelines from the National Comprehensive Cancer Network are available for regional lymphadenopathy in adnexal tumors. However, because the staging of malignant cutaneous adnexal tumors is consolidated with the staging for cutaneous squamous cell carcinoma, surgical management of regional lymphadenopathy is likely similar. Fine needle aspiration or core biopsy should be performed for palpable regional lymph nodes or abnormal lymph nodes identified on imaging. If positive and operable, regional lymph node dissection should be performed. Radiation therapy should be considered if multiple lymph nodes are involved or if extracapsular extension is present. If regional lymph nodes are positive and inoperable, radiation therapy with or without systemic therapy is recommended.
3. The excision site can be managed with tension-free primary approximation, skin graft, or flap and seldom, with healing by secondary intention.
4. Nonsurgical candidates should receive radiation therapy.
5. Minimal evidence is available regarding treatment of metastatic disease.

Table 2
Wide excision surgical margins for melanoma

Tumor Thickness (mm)	Recommended Clinical Margins (cm)
In situ	0.5–1.0
≤1.00	1.0
1.01–2.00	1.0–2.0
2.01–4.00	2.0
>4.00	2.0

Case report

A 67-year-old Caucasian male presented with scrotal ulceration for 6 years. He had a previous scrotal exploration and incision and drainage 8 years prior for scrotal abscesses. He stated that the surgical incision dehisced and had never healed. The wound had worsened over time, constantly draining foul-smelling discharge. He reported a 25-pound weight loss over the past 6 months. His history was significant for an 80 pack-year smoking history. He did not report any chemical exposure, significant sun exposure, or other malignancies.

On examination, there is a 10-cm ulcerated condylomatous lesion involving the majority of his scrotum. The lesion spares the perineum and extends to the base of the ventral penis. Serous drainage is noted. The testes are palpable and involvement is unclear. There are palpable bilateral enlarged, freely mobile inguinal nodes.

Computed tomography scan of the chest, abdomen, and pelvis revealed enlarged bilateral external iliac chain lymph nodes, measuring up to 1.2 cm. There are also enlarged bilateral inguinal lymph nodes, measuring up to 1.8 cm. Nodular skin thickening and ulceration is noted involving the scrotum, which is abutting and inseparable from bilateral testicles. No hilar, mediastinal, retroperitoneal lymph nodes, or osseous lesions are reported.

Excisional biopsy of the lesion revealed invasive well-differentiated squamous cell carcinoma. The patient was consented for and taken to the operating room for cystoscopy, radical scrotectomy, bilateral simple orchiectomy, and reconstruction as a joint case with plastic surgery. Intraoperative photographs are presented (Figs. 1–10).

The patient had an uncomplicated postoperative course. Pathology revealed well-differentiated

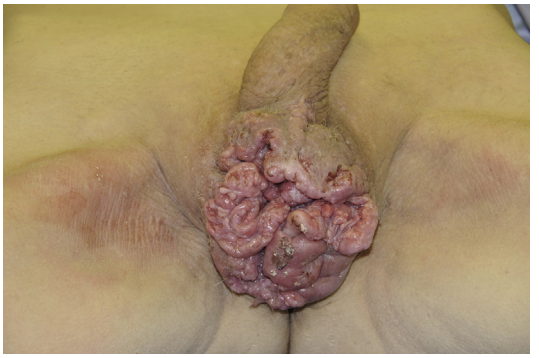

Fig. 1. The patient had a 10 cm ulcerating, condylomatous lesion on his scrotum. The penis and adjacent regions do not seem to be involved.

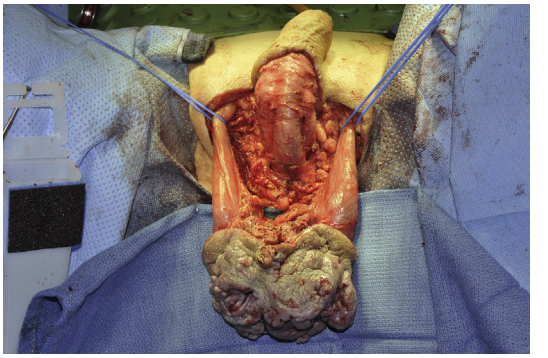

Fig. 4. The incision was carried through the skin, subcutaneous tissue, and dartos. The lesions seemed to involve the bilateral testes. The spermatic cords were isolated with vessel loops.

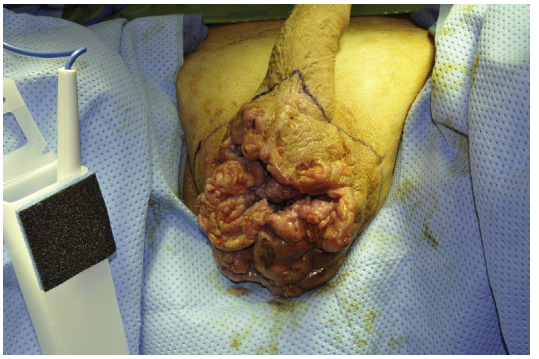

Fig. 2. He was placed in the exaggerated dorsal lithotomy position, widely prepped, and draped. The superior aspect of the lesion was circumferentially marked with clear clinical margins.

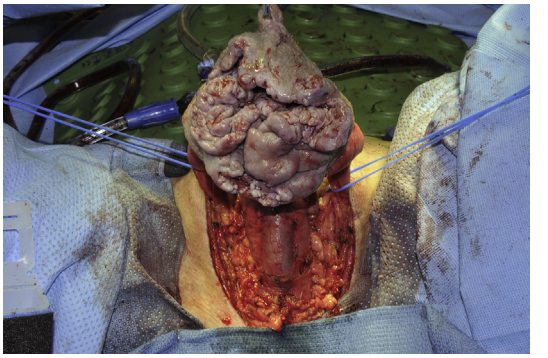

Fig. 5. The lesion did not involve the perineum or medial thighs.

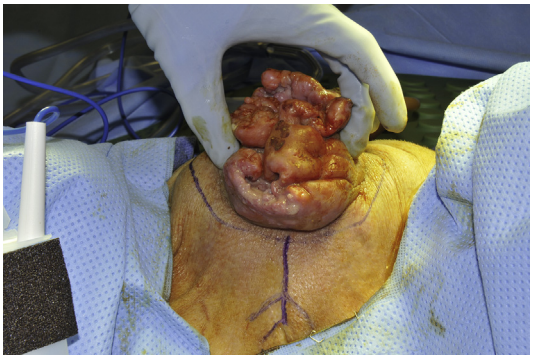

Fig. 3. The inferior aspect of the lesions was marked circumferentially with clear clinical margins.

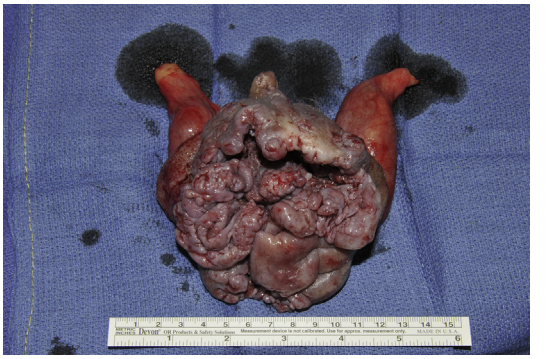

Fig. 6. The spermatic cords were ligated and the specimen was passed of the operating field.

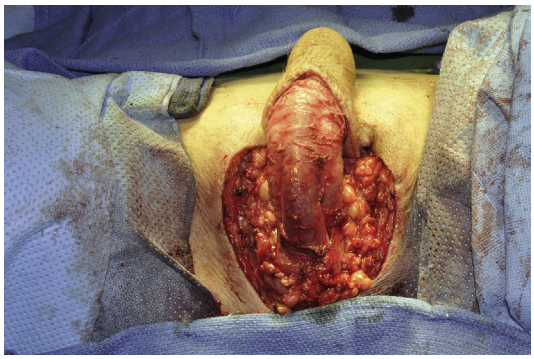

Fig. 7. The lesion did not involve the corporal tissues of the penis.

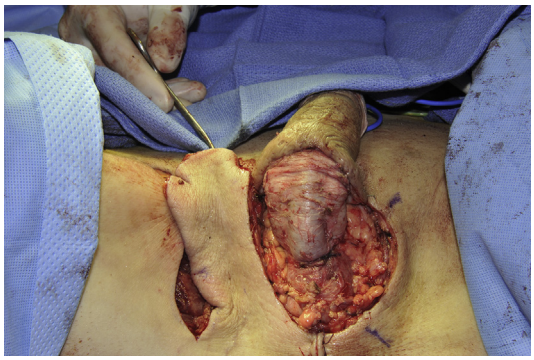

Fig. 8. A rotational skin and fascial flap was developed from the right medial thigh.

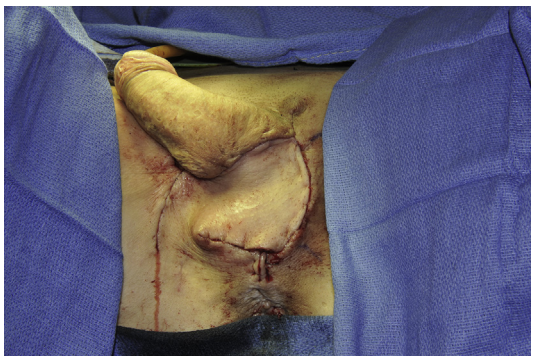

Fig. 9. The rotational flap provided adequate coverage for closure of the defect.

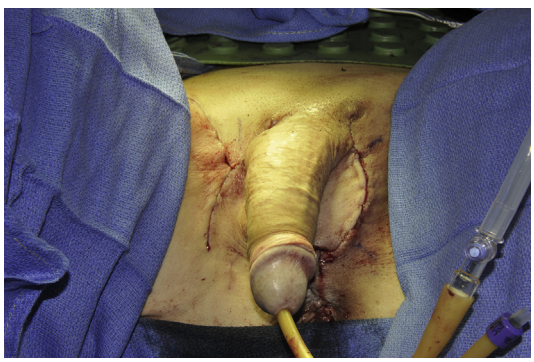

Fig. 10. The reconstructed region was viable at the end of the case.

Table 3
Complications and management

Complications	Management
Wound infection	• Antibiotics • May require opening the incision and drainage if abscess is present
Hematoma	• Resolution with time • Scrotal support • Drainage if infected
Pain	• Nonsteroidal anti-inflammatory drugs • Ice • Scrotal support

squamous cell carcinoma, extending to the deep dermal soft tissues. The testes were not involved. All margins were negative, with the closest margin measuring 0.3 cm. The patient was discussed at tumor board and the consensus was that no additional surgery, radiation, or chemotherapy was necessary. His follow-up PET scan was negative for residual or metastatic disease. His serial imaging has been negative and he is alive without evidence of disease (Table 3).

POSTOPERATIVE CARE

- Surgical removal of scrotal cancer can usually be performed as outpatient surgery.
- Nonsteroidal anti-inflammatory drugs, ice, scrotal support, and narcotics as needed are recommended for pain control and swelling.

Table 4
Stage and description

Stage	Description
A1	Localized to the scrotal wall
A2	Locally extensive tumor invading adjacent structure (testis, spermatic cord, penis, pubis, perineum)
B	Metastatic disease involving inguinal lymph node
C	Metastatic disease involving pelvic lymph nodes without evidence of distance spread
D	Metastatic disease beyond the pelvic lymph nodes involving distant organs

Adapted from Lowe FC. Squamous cell carcinoma of the scrotum. J Urol 1983;423–7; with permission.

Table 5
Follow-up time frame for evaluation and recurrence location and treatment

	Follow-up Time Frame and Evaluation	Recurrence Location and Treatment
Squamous cell carcinoma[9]	Local disease: • History and physical, including complete skin examination, every 3–12 mo for 2 y, then every 6–12 mo for 3 y, then annually for life • Patient education regarding sun protection and examination of skin Regional disease: • History and physical, including complete skin examination, every 1–3 mo for 1 y, then every 2–4 mo for 1 y, then every 4–6 mo for 3 y, then every 6–12 mo annually for life • Patient education regarding sun protection and examination of skin	Local: • Local excision New regional disease: • Regional lymph node dissection Regional recurrence or distant metastases: • Multidisciplinary tumor board consultation
Extramammary Paget's disease[10,19]	Close monitoring for long periods is recommended because recurrences are common because of subclinical disease; no recommended schedule is available	• Wide local excision • Adjuvant neodymium:YAG laser and topical 5-fluorouracil
Sarcoma[11]	Stage 1 disease: • History and physical, including complete skin examination, every 3–6 mo for 2–3 y, then annually for life • Chest imaging every 6–12 mo • Consider obtaining postoperative baseline and periodic imaging of primary site based on risk of locoregional recurrence • Evaluation for rehabilitation Stage II, III, and IV disease: • History and physical, including complete skin examination, and chest imaging every 3–6 mo for 2–3 y, then every 6 mo for 2 y, then annually for life • Consider obtaining postoperative baseline and periodic imaging of primary site based on risk of locoregional recurrence • Evaluation for rehabilitation	Local: • Local excision and treatment based on stage I, II, or III Isolated regional disease or nodes: • Regional node dissection with or without radiation and chemotherapy • Metastasectomy with or without radiation and preoperative or postoperative chemotherapy can be performed • Stereotactic body radiation therapy • Isolated limb perfusion Single organ and limited tumor bulk that is amenable to local therapy: • Metastasectomy with or without radiation and preoperative or postoperative chemotherapy can be performed • Ablation procedures • Embolization procedures • Stereotactic body radiation therapy Disseminated metastases: • Palliation, including chemotherapy, radiation therapy, surgery, observation, ablation procedures, embolization procedures
Basal cell carcinoma[14]	• History and physical, including complete skin examination, every 6–12 mo for life • Patient education regarding sun protection and examination of skin	Local: • Local excision Nodal or distant metastases: • Surgery and/or radiation therapy • Multidisciplinary tumor board consultation

(*continued on next page*)

Table 5
(*continued*)

	Follow-up Time Frame and Evaluation	Recurrence Location and Treatment
Melanoma[15]	Stage 0: • Annual complete skin examination for life • Education about regular self-skin and lymph node examination Stage IA-IIA NED: • History and physical, including complete skin examination, every 6–12 mo for 5 y, then annually as clinically indicated • Education about regular self -skin examination and lymph node examination • Routine radiologic imaging for asymptomatic recurrent/metastatic disease is not recommended Stage IIB-IV NED: • History and physical, including complete skin examination, every 3–6 mo for 2 y, then every 3–12 mo for 3 y, then annually as clinically indicated • Consider chest radiograph, CT, brain MRI, and/or PET/CT scans every 3–12 mo to screen for recurrent/metastatic disease • Routine radiologic imaging for asymptomatic recurrent/metastatic disease is not recommended after 3–5 y • Education about regular self-skin examination and lymph node examination	Persistent disease or local scar recurrence: • Reexcision to appropriate margins Local, satellite, and/or in-transit recurrence: • Clinical trial (preferred) • Local therapy, such as surgical excision, intralesional injection, ablation, topical imiquimod, radiation therapy • Regional therapy • Systemic therapy Nodal: • If no previous dissection, perform complete lymph node dissection and then adjuvant treatment • If previous dissection, perform complete lymph node dissection if possible and then adjuvant treatment • If unresectable, systemic therapy is preferred; can consider clinical trial, palliative radiation therapy, or intralesional injection Metastatic disease: • Follow treatment for stage IV (metastatic disease) melanoma
Adnexal skin tumors[17]	Routine follow-up is recommended as local recurrence rates range from 10%–50% among patients treated with wide local excision. No recommended schedule is available.	• Wide excision for local recurrence • Radiation therapy if surgical margins are positive • Metastatic disease is treated on a case by case basis

Abbreviations: CT, computed tomography; NED, no evidence of disease.

- Bacitracin ointment can be applied to surgical incision for 1 to 2 weeks.
- Showering is encouraged after 24 hours.
- Minimal exertion for 1 to 2 weeks.
- Postoperative follow-up in 1 to 2 weeks for evaluations and drain removal, if present.

REPORTING, FOLLOW-UP, AND CLINICAL IMPLICATIONS

The staging for scrotal cancer, reported by Lowe,[18] is shown in **Table 4**. However, because of the various histologic subtypes of scrotal cancer (ie, sarcoma and melanoma), many reports use the cancer staging system developed by the American Joint Committee on Cancer. Additionally, many reports do not provide sufficient information to determine staging (**Table 5**).

OUTCOMES

Because scrotal cancer is a rare disease and comprises multiple histologies, data regarding outcomes are limited. In an analysis of the Surveillance, Epidemiology, and End Results database for scrotal cancers, Johnson and colleagues[4] reported that the 6 histologic subtypes of scrotal cancers can be divided into 2 subgroups, with a higher and lower overall survival. Patients with basal cell carcinoma, extramammary Paget's

Table 6
SCC comorbidities, staging, surgical findings, and outcomes

	Comorbidities	Staging	Surgical Findings	Outcomes
Matoso et al,[20] 2014 (n = 29, median follow-up 37 mo)	Condylomas Other skin cancers Immunocompromised state (HIV, kidney transplantation) Leukemia/lymphoma Infection/inflammatory conditions Tanning bed use	In situ (19/29) Invasive (10/29) Inguinal lymphadenopathy (3/29)	Positive margins (13/29) Recurrence (3/29)	18 NED 3 alive with disease 3 deaths not from SCC 5 not available
Andrews et al,[6] 1991 (n = 14, mean follow-up 84 mo)	Psoriasis treated with coal tar and arsenic Human papillomavirus Cutaneous epitheliomas	Stage A1 (8/14) Stage B (3/14) Stage C (3/14)	Unknown	11 NED 3 deaths from SCC
Parys & Hutton,[21] 1991 (n = 11, median follow-up unknown)	Industrial exposure to machine oils and tar	Stage A1 (9/11) Stage B (1/11) Stage C (1/11)	Unknown	2 deaths from SCC 4 deaths not from SCC

Abbreviations: HIV, human immunodeficiency virus; NED, no evidence of disease; SCC, squamous cell carcinoma.

Table 7
Extramammary Paget's disease comorbidities, staging, surgical findings, and outcomes

	Comorbidities	Staging	Surgical Findings	Outcomes
Qi et al,[22] 2014 (n = 14, median follow-up 63 mo)	Other cancers	Lymph node metastasis (3/14) Distant metastasis (1/14)	Positive margins (5/14) Recurrence (1/14)	9 NED 2 alive with disease 2 deaths from EMPD 1 lost to follow-up
Park et al,[10] 2001 (n = 5, median follow-up 14 mo)	Unknown	Lymph node metastasis (1/5)	Unknown	5 NED
Chen et al,[23] 2013 (n = 30, mean follow-up 64.9 mo)	Unknown	Epidermis only (15/30) Epidermis with visceral or adnexal carcinoma (9/30) Lymph node metastasis (6/30)	Positive margins (2/30) Recurrence (8/30)	22 NED 5 deaths from EMPD
Zhang et al,[24] 2010 (n = 25, mean follow-up 119 mo)	Unknown	Stage A1 (10/25) Stage A2 (13/25) Stage B (1/25) Stage D (1/25)	Positive margins (5/25) Recurrence (7/25)	1 death from metastatic EMPD 6 deaths not from EMPD
Yang et al,[25] 2005 (n = 36, median follow-up 36 mo)	Unknown	Unknown	Positive margins (18/36) Recurrence (9/36)	1 death from metastatic EMPD
Koh et al,[26] 2015 (n = 5, median follow-up unknown)	Unknown	Dermis invasion (1/5) Dartos invasion (1/5) Inguinal lymph node metastasis (5/5) Pelvic lymph node metastasis (2/5) Distant metastasis (1/5)	Positive margins (1/5) Recurrence (3/5)	2 NED 3 alive with disease
Lai et al,[27] 2003 (n = 31, median follow-up unknown)	Unknown	Epidermis (14/31) Involving adnexal glands (10/31) Adnexal carcinoma (7/31)	Recurrence (6/31)	3 deaths from metastatic EMPD

Abbreviations: EMPD, extramammary paget's disease; NED, no evidence of disease.

Table 8
Sarcoma comorbidities, staging, surgical findings, and outcomes

	Comorbidities	Staging	Surgical Findings	Outcomes
Matoso et al,[28] 2014 (n = 5, median follow-up 6.5 mo)	Unknown	Infiltrative borders (0/5)	Positive margin (2/4, 1 not available) Recurrence (0/2, 3 not available)	2 NED 3 not available
Boland et al,[29] 2010 (n = 2, median follow-up 35 mo)	Unknown	Unknown	Unknown	2 NED
Froehner et al,[30] 2000 (n = 11, median follow-up 49 mo)	Unknown	Stage 1 (5/11) Stage 2 (4/11) Stage 3 (1/11) Stage 4 (1/11)	Recurrence (2/11)	10 NED 1 alive with disease
Ballo et al,[13] 2001 (n = 32, median follow-up 108 mo)	Unknown	T1 (≤5 cm) (15/32) T2 (>5 cm) (17/32)	Recurrence (12/32)	23 NED 9 deaths from sarcoma

Abbreviation: NED, no evidence of disease.

disease, and sarcoma were noted to have a higher overall survival, with median (95% CI) survival of 143 (116–180), 165 (139–190), and 180 (141–219) months, respectively. Patients with melanoma, squamous cell carcinoma, and adnexal tumors were noted to have a lower overall survival, with a median (95% CI) survival of 136 (70–203), 115 (97–133), and 114 (55–174) months, respectively. The 5-year overall survival for low-risk risk scrotal cancers (sarcoma, extramammary Paget's disease, basal cell carcinoma) and high-risk scrotal cancers (melanoma, squamous cell carcinoma, adnexal tumors) are about 75% and 55%, respectively. An extensive review of the literature was performed to assess outcomes from the various histologic subtypes of scrotal cancer. Outcomes from case series on squamous cell carcinoma, extramammary Paget's disease, sarcoma, basal cell carcinoma, and melanoma, based on histology, are provided in **Tables 6–10**. Outcomes from case reports were not included. No case series are available for adnexal tumors.

CURRENT CONTROVERSIES AND FUTURE CONSIDERATIONS

- Rare nature and small case series of scrotal cancers limits results regarding outcomes.
- Pooling of multiinstitutional data and the use of a scrotal cancer registry can improve knowledge of this disease and help develop treatment algorithms.

Table 9
Basal cell carcinoma comorbidities, staging, surgical findings, and outcomes

	Comorbidities	Staging	Surgical Findings	Outcomes
Dai et al,[31] 2012 (n = 10, mean follow-up 47 mo)	None	Reticular dermis (7/10) Subcutaneous tissue (1/10) Extending down to the Dartos muscle (2/10)	Positive margins (0/5) Recurrence (2/5)	8 NED

Abbreviation: NED, no evidence of disease.

Table 10
Melanoma comorbidities, staging, surgical findings, and outcomes

	Comorbidities	Staging	Surgical Findings	Outcomes
Sanchez-Ortiz et al,[32] 2005 (n = 6, median follow-up 39 mo)	Unknown	Inguinal metastasis (2/6)	Recurrence (3/6)	4 deaths from melanoma

SUMMARY

Primary scrotal cancer is a rare urologic malignancy. Pathologic assessment is necessary to determine the histologic subtype of this disease. The management for localized disease is surgical excision of the cancer with wide margins, because subclinical disease is often present. Lymph node metastases can also be managed with a regional lymph node dissection, although no trials have formally examined the usefulness of regional lymphadenectomy. Treatment for distant metastases is not as clear, with the use of various modalities in case reports.

Outcomes are also limited for this disease, with most data being reported in case series. Based on their analysis of the Surveillance, Epidemiology, and End Results database, Johnson and colleagues[4] noted that the 5-year overall survival for low-risk and high-risk scrotal cancers is about 75% and 55%, respectively. Interestingly, the 5-year relative survival for patients with penile cancer is reported to be 69%.[33] As such, high-risk scrotal cancers seem to have a worse prognosis and low-risk scrotal cancer may have comparable prognosis with penile cancer, a cutaneous urologic cancer in an adjacent region.

Occupational exposure to aromatic hydrocarbons is not as prevalent today, contributing to the decrease in scrotal cancers and limited data regarding this disease. Further work, including obtaining larger cohorts and the use of a database, can improve the management and information regarding long-term outcomes for scrotal cancer.

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