Female Urethral Melanoma: 2 Year Follow-Up with Bladder Sparing Approach

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Introduction and Background

Genitourinary malignant melanoma is a rare form of melanoma that includes mucosal melanomas of the urethra. Urethral melanoma accounts for the majority of cases of genitourinary melanoma and is associated with a poor prognosis in comparison to cutaneous melanomas [1, 2]. Being a rare disease, diagnostic and treatment recommendations are not clearly defined in the literature and as a result treatment decisions may be difficult in regards to providing adequate oncologic control while preserving genitourinary function. For example, the decision to perform a radical extirpative surgery, lymphadenectomy, and possible urinary diversion must be weighed against the treatment’s benefit and patient’s quality of life. Herein we present a case of malignant urethral melanoma with a synchronous cervical lesion in a patient where local disease control was achieved while preserving urinary function.

Case Presentation

The patient is a 68-year-old woman with a chief complaint of pelvic floor pressure and pain, dysuria, and strangury. Several weeks prior to referral she noticed blood on her undergarments and began using 1-2 sanitary pads daily. She did not have any additional complaints, and her past urologic, gynecological, and social history was noncontributory. Her past medical history was significant for Non-Hodgkins lymphoma involving the nasopharynx, and had been in remission for fifteen years after chemotherapy. Physical examination was remarkable for anephphotic, pedunculated soft tissue mass emanating from the urethral meatus (Figure 1). The lesion was darkly pigmented, and did not involve the bladder neck. On pelvic examination there was a flat pigmented lesion found at the cervical so, and no remaining mucosal lesions in the vagina. There was no palpable lymphadenopathy and the remainder of the exam was unremarkable. Laboratory tests were unremarkable including complete metabolic panel, complete blood count, urinalysis, and urine cytology and urine culture. Cystourethroscopy revealed no more proximal urethral involvement of the pigmented mass and there were no urothelial lesions in the lower urinary tract. A biopsy of the urethral mass was performed and the patient was referred to gynecology for further evaluation of the cervical lesion. The urethral biopsy revealed positive Immunohistochemical staining for HMB-45 and S-100, and possessed typical histologic findings consistent with malignant melanoma. Evaluation by dermatology and ophthalmology revealed no evidence of ocular or cutaneous primary lesions. CT of the chest, abdomen, and pelvis was unremarkable, and MRI of the pelvis demonstrated an enhancing mass confined to the periurethral fascia not involving the bladder neck. A PET scan was performed prior to intervention and significant for hyperactivity confined to the cervix and the distal urethra.

The patient underwent an uneventful cervical biopsy under anesthesia and distal urethrectomy. Distal urethrectomy was performed with an approximately 1 cm urethral margin with no evidence of disease on frozen section of the anterior vagina (Figure 2). Final pathology demonstrated malignant melanoma in situ (Tis) with negative proximal urethral margins (Figure 3). Additionally, cervical biopsies also demonstrated malignant melanoma and she underwent a subsequent radical hysterectomy, bilateral salpingo-oophorectomy with proximal vaginectomy. The final specimen demonstrated malignant melanoma confined to the cervix with less than 1cm invasion, no ulceration, and negative vaginal margins (T1). The postoperative...
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The extent of local invasion and metastatic disease is often underestimated with clinical staging. For example, DiMarco et al. found over 70% of the patients in their series were upstaged from clinical T2 urethral melanoma to pT3 in their series [2]. As a result, wide local excision, often involving anterior exenteration to provide local control of disease is recommended. Our approach relied upon diagnostic imaging modalities to assess the patient’s eligibility for bladder preservation. In addition to utilizing CT for metastatic evaluation, we used MRI to assess local tumor spread to periurethral tissue and the bladder neck. Similar to the workup of cutaneous melanoma, obtaining a PET/CT scan was useful in determining disease localization in our patient to the distal urethra and uterine cervix and also for the purposes of follow up.

The mainstay of treatment for distal female urethral lesions without bladder neck involvement is distal urethrectomy [1, 2, 3]. In our case the patient desired to remain continent and based on the preoperative workup performed, the lesion was confined to the distal third of the urethra. Likewise, radical hysterectomy is indicated in the management of localized cervical melanoma. The value of inguinal lymph node dissection has not been defined for urethral melanoma, with one series concluding no difference in outcomes [2]. In this case, there was no evidence of clinical or radiographic lymph node metastasis and therefore lymphadenectomy was deferred.

Despite an absence of clinical evidence to support the routine use of adjuvant chemotherapy, published reports have demonstrated high recurrence and progression of disease despite adequate local resection. Various chemotherapy regimens have been adapted from the management of advanced cutaneous melanoma. For example, high dose beta-interferon immunochemotherapy, systemic chemotherapy (vincaalklaoids, alkylating agents), and BRAF protooncogene inhibitors have been utilized in the adjuvant setting with variable efficacy [1]. More recently, cisplatin based regimens have been investigated and shown efficacy in the management of advanced melanoma [5]. Our choice of chemotherapy was based on a recent clinical trial, where 189 patients underwent melanoma resection for stage 2 and 3 disease was randomized to observation, high dose interferon, and tenzolamide/cisplatin. Approximately 25% of the lesions were genitourinary and the overall survival was more than double in the tenzolamide/cisplatin group versus observation (20v 48.7 months). Furthermore, overall survival was greater and patients had a longer recurrence free survival compared to interferon [5].

In conclusion, bladder preservation is possible in the setting of urethral melanoma with and isolated cervical lesion. Furthermore, we propose an algorithm to guide the initial management of patients with urethral melanoma (Figure 4). An extensive preoperative workup to assess local invasion of the primary lesion, detection of distant metastases, and presence of

Discussion

Urethral malignant melanoma was first reported over a century ago with approximately 150 cases reported to date [1, 3]. The etiology of urethral and mucosal melanomas remains inconclusive with no clear environmental or genetic risk factors elucidated. Urethral melanoma is more common in women, and the mean age is approximately 64 years of age [1]. Presenting symptoms can include obstructive or irritative lower urinary tract symptoms, hematuria, perineal pain, and vaginal/urethral bleeding [3]. On physical exam the lesion may grow in a nodular, polypous, or papillary pattern and the color may range from amelanotic to dark pigmented lesions [2, 3]. Urethral melanoma is classically associated with a poor prognosis, owing to its early dissemination via the urethra’s rich vascular and lymphatic supply. Additionally, delayed patient presentation and misdiagnosis for similar appearing urethral lesions (urethral prolapse, caruncle, and polyps) contribute to advanced disease upon diagnosis[2].Thus the initial step in the workup of our patient included establishing a tissue diagnosis and proceeding with a thorough evaluation for metastatic disease.

The course was uneventful and she received six cycles of adjuvant cisplatin and temozolomide. Postoperatively, she was followed with routine pelvic examinations, cystoscopy, and PET imaging. At 2 years follow-up she has normal urinary function without incontinence. Furthermore, she has no evidence of disease on physical exam, cystoscopy (every 6-9 months), or PET/CT scan (performed annually).

Figure 2: Distal Urethrectomy specimen.

Figure 3: Malignant Melanoma. Melanocytic cells with high mitotic rate are demonstrated. Immunohistochemical staining (not shown) was positive for S-100 and HMB-45.

lymphadenopathy is critical. For lesions localized to the distal urethra without bladder neck invasion, distal urethrectomy may be offered while management of female reproductive organs is best managed with radical excision. Adjuvant chemotherapy with cisplatin and temozolomide may represent promising agents for patients at high risk of disease recurrence as in urethral melanoma. Finally, routine follow-up is critical and use of PET scan should be considered.

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**References**


