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Primary Malignant Melanoma of Female Urethra: A Case Report and Review of Literature

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ABSTRACT

We report a very rare case report of female diagnosed with primary malignant melanoma. A 65 years old diabetic elderly postmenopausal female presented with a history of intermittent blood spots on undergarments for few days. Genital examination revealed a single, tan colored, soft chestnut size and polypoidal non ulcerated mass lesion protruding through the urethral meatus. Mass biopsy revealed poorly differentiated epithelial malignancy and immuno-histological analysis revealed positive with HMB 45 and protein S-100 suggestive of melanoma. Metastatic work up for the malignancy was negative. Complete urethrectomy with Mitrofanoff procedure with inguinal lymph node dissection was performed. Histopathological examination was suggestive of malignant melanoma of urethra. Here we discuss the clinicopathological features and management option possible in this scenario.

1. Introduction

Primary malignant melanoma of female urethra is very uncommon tumour and constitutes 0.1 - 0.2% of all melanoma^[1-5]. Urethral melanoma can be sub classified based on its origin type into mucosal melanomas or cutaneous melanomas. Urethral melanomas are usually under reported clinically and it inherits grave prognosis with poor five year survival rates^[6]. Here we present a case of an elderly female diagnosed with primary malignant melanoma of urethra in and its surgical management at our center along with review the literature.

2. Case Report

A 65 years old diabetic elderly female came with a history of intermittent blood spots on undergarments for few days. She had no complaints of difficulty in micturition, hematuria, flank pain, lithuria. She has attained post menopause and had no history of postmenopausal syndrome. At primary center she was diagnosed with urethral mass and biopsy of mass suggestive of poorly differentiated epithelial malignancy. Immunohistological analysis revealed positive with HMB 45 and protein S-100 which were suggestive of melanoma.

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Genital examination revealed a single, tan colored, soft chestnut size and polypoidal shape non ulcerated mass lesion measuring 2 x 2 x 1 cm protruding through the urethral meatus (Figure 1). Her per vaginal and speculum examination was normal. Abdominal examination revealed no organ enlargement of no regional lymphadenopathy.



Figure 1. Urethral malignant melanoma presenting as a mass protruding from external urethral meatus on genital examination

Abdomen-pelvis contrast enhanced computed tomography (CECT) along with MRI T2W saggital sequence revealed that single enhancing lesion of 2 x 1.3 cm in urethra with not involvement of periurethral tissue, bladder, regional or distant lymphadenopathy.

Initially urethral meatus was difficult to visualize but with suprapubic pressure gush of urine flow was seen and the glide wire was passed in urethra followed by its serial dilatation up to 16 Fr. Cystourethroscopy examination revealed polypoidal reddish brown growth involving the distal urethra and urethral meatus. Bladder was unremarkable. Vaginoscopy showed compression of anterior vaginal wall with mass however no any evidence of invasion seen on inspection. Complete urethrectomy with formation of continent catheterizable stoma using the appendix (Mitrofanoff procedure) with inguinal lymph node dissection was performed. Mass was removed along with the normal appearing surrounding tissue. Frozen section of proximal urethral margin and adjacent vaginal mucosa were free of tumour.

Gross examination of specimen showed a polypoidal solid mass of 2 x 1.8 x 1.5 cm with brownish cut surface without any ulceration on surface. Histopathological analysis showed loosely cohesive nests of epitheloid cells with dusty brown melanin pigments. Malignant cells had abundant eosinophilic cytoplasm, large nuclei with promi-

nent nucleoli along with mitotic figures. No lymphovascular invasion was seen (Figure 2). Immuno-histochemical analysis of the malignant cells was positive for protein S-100 (Figure 3) and HMB-45 (Figure 4) which are markers for melanocyte differentiation.

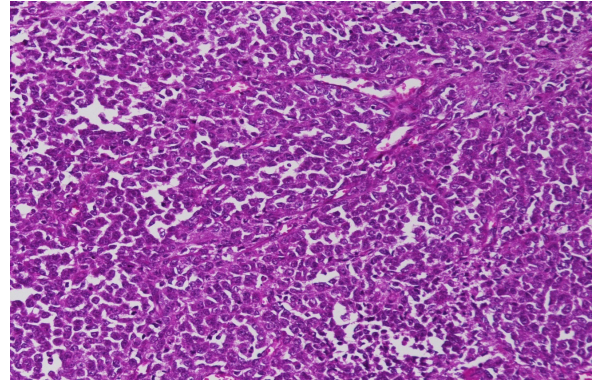


Figure 2. Microscopic findings of specimen. Large epitheloid cells with high N/C ratio. Deposition of melanin pigment could not be seen clearly

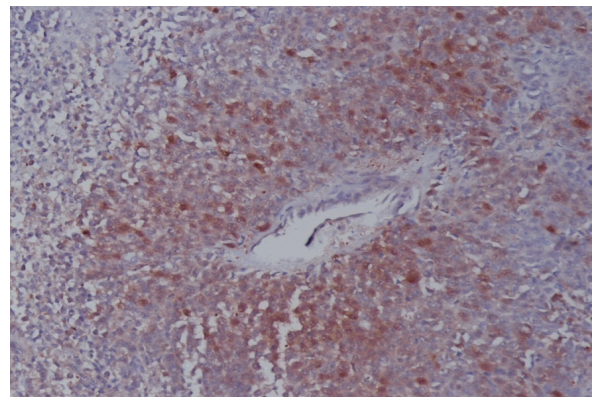


Figure 3. The immunohistochemical staining findings of the surgical specimen. The tumor cells were immunoreactive for S-100 protein

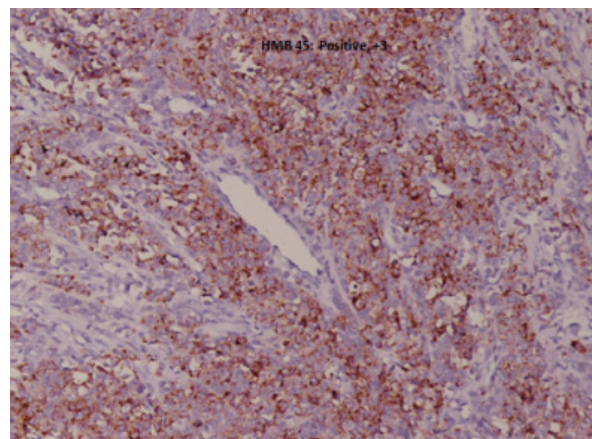


Figure 4. The immunohistochemical staining findings of the surgical specimen. The tumor cells were immunoreactive for HMB - 45

Currently the patient is asymptomatic and is doing clean intermittent catheterization through mitrofanoff and no recurrence of disease have observed yet.

3. Discussion

Malignant melanoma of urethra was first reported in a female by Reed in 1896^[7]. Median age of presentation is 68 years^[8]. Females are more commonly affected as compared to males (3:2)^[9]. Urethral melanoma risk factors are not established^[10].

Lack of visibility and non-specific symptoms causes delay in detection of urethral melanoma. Symptoms may include bleeding, urethral mass, pain, lower urinary tract symptoms. Clinically, differential diagnosis can be other malignant diseases or even benign lesions, including carcinoma, mucosal prolapse, urethral polyps^[11,12].

The diagnosis is confirmed after biopsy from the lesion. The metastatic evaluation should be done before surgical treatment for this highly invasive neoplasm. An abdominal-pelvic CECT scan provides necessary information regarding nodal involvement and metastatic foci. c-KIT mutation test is useful as it can dictate the chemotherapeutic agents^[10].

Metaplasia of squamous and glandular epithelium into pigment-producing cells is proposed mechanism for melanoma originating from mucosal surface^[13].

Like all mucosal melanomas, urethral malignant melanoma has grave prognosis than its cutaneous melanoma counterpart^[8]. This is mostly due to significant delay in diagnosis because of its inaccessible location and also due to its vertical growth phase in urethral melanomas, lymph node metastasis^[14]. Median survival in two largest series was 16 months^[4,5]. Overall survival range was from 2 months to 191 months. Few case series showed five year overall survival in 10% patients^[15-19].

Microscopic examination a wide histological spectrum like diffuse, nested, fascicular, and storiform growths of pleomorphic cells exists in case of urethral malignant melanomas^[11]. Thus the role of immunohistochemical markers for accurate diagnosis come into existence. In clinical practice most commonly used melanocytic markers are S-100 protein and HMB-45. More than 90% of melanomas react with S-100 monoclonal antibody^[20]. HMB-45, specific for melanocytic neoplasms, is less sensitive than S-100 protein for identifying melanoma^[20]. Positive test with S 100 protein and subsequent testing with HMB-45 in our case confirm definitive diagnosis of malignant melanoma.

No definitive consensus or guidelines exist for management of primary malignant urethral melanoma because of its extreme rare pathology, however it depends on the tumour staging. The definite management of primary

neoplasm is surgical excision with tumor-free margins to achieve control of local disease. Less radical surgical approaches are also mentioned in literature which include local excision; partial or total urethrectomy, with or without inguinal lymphadenectomy, and anterior pelvic exenteration, but neither has depicted improved survival advantage over other^[10]. DiMarco et al have also advocated radical surgeries. They found high rate of urethral recurrences (69%) in their cases of partial urethrectomy patients was due to inadequate surgical margins. Overall disease-specific survival observed was 39% approximately^[5].

Sentinel lymph node (SN) dissection is still controversial in primary urethral melanoma. Though the incidence of false-negative SN dissection has gone down, it is still not mandatory to perform this procedure in all cases^[21].

Role of lymphadenectomy as proposed by some authors is not properly established and is debatable in various different case scenarios. This procedure, though adds to the morbidity of the patient, has failed to improve disease-specific survival in affected individuals. So, role of radical surgery in case of inguinal lymph node involvement is not clear^[5]. In our case we performed inguinal lymph node dissection in our case.

4. Conclusion

Urethral melanoma is an uncommon neoplasm with poor prognosis. No definitive guidelines for management exist till date. All proposed treatments are based upon case series/reports. Similar neoplastic diseases also give input for its management. Surgical excision with adequate margins is gold standard treatment of urethral melanoma. There is no basis to do inguinal lymph node dissection in all cases. Adjuvant chemotherapy and immunotherapy can be prescribed based upon surgeon preferences as no proper guidelines exist in literature.

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