Primary Malignant Melanoma of Female Urethra

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Primary malignant melanoma of the female urethra is a rare tumor with great agressivity and poor prognosis. We reported the case of 65-year-old woman with polypoid tumor on the external meatus of the urethra. Tumor was localy resected, and immunohistochemistry revealed diagnosis of malignant melanoma. After three months distal urethrectomy was performed with tumor-free margin, and the patient is still alive during more than five years follow up period.

Key words: female urethra, local excision, malignant melanoma

INTRODUCTION

Primary malignant melanoma is one of the rarest tumors of the female urethra. It occurs in 0.2% of all melanomas (1). However, the urethra is the most common site of origin in primary malignant melanoma of the genitourinary tract (2). Reed (3) reported the first authentic case of primary melanoepithelioma of the female urethra in 1896. Urethral melanoma shows its peak incidence in the older age group, the average patient age being 64 years (4). The majority of the lesions have been located at the meatus or in the distal urethra. As a rule, melanoma of the anterior female urethra has a generally better prognosis than the posterior or entire urethral melanoma (5). Because primary malignant melanoma of the female uretha tends to metastasize at the early stage to adjecent areas, regional lymph nodes, and occasionally distant sites by the hematogenous route, the prognosis is poor. Size of the tumor, depth of invasion (6), and the presence of involved lymph nodes are the main prognostic factors for the disease (7). Treatment of urethral malignant melanoma remains an unsolved problem. Surgery, radiation and chemotherapy has been uniformly ineffective. The relative radioresistence of malignant melanoma and the failure of chemotherapy must be recognized. Only eleven patients have been reported so far who lived for 4 years or more (table 1.). In this report we describe an additional case who is alive and well after 5 years.

CASE REPORT

A 65-year-old woman was refered by a gynaecologist due to a urethral mass with a gross appearance of a caruncle. Upon examination a 3-cm wide, pedunculated, black pigmented, friable and hemorrhagic polyp was found at the posterior wall of the urethral meatus. The tumor was removed by a local excision. The removed polyp appeared to be partly ulcerated, covered with stratified squamous epithelium and urothelial cells. Most of the specimen was infiltrated with tumor tissue arranged in solid nests of non-cohesive atypic melanocytes with large hyperchromatic nuclei, prominent nucleoli and numerous mitoses up to 10 per high power field. Proliferating cells showed foci of fine intracytoplasmic melanin granules (figure 1.). In addition, HMB-45 antigen immunohistochemical stains were positive for malignant cells, confirming that it was a malignant melanoma (figure 2). Three months after local excision, in another institution was performed low third resection of distal urethra with no evidence of tumor, and the patient was uneventful during 5-year-followup period.

DISCUSSION

The histogenesis of melanomas arising in mucous membranes still remains in dispute and several theories have been proposed. In some animals, such as amphibians, birds, mice and rats, it has been clearly demonstrated that melanoblats originating from the neural rests may subsequently migrate with mesodermal cells to sites, where they usually do not exist. A possible alternative mechansm is the so-called "melanogenic metaplasia" of the epithelium, in other words metaplasia of squamous and glandular epithelium into pigment-producing cells. Finally, neural crest elements may be transformed into melancytes and nevus cells.

Melanomas occuring in unexpected sites, such as mucous membranes, can be accepted as a primary tumor only if no evidence of any other concurrent or previously excised tumor exists. The presence of junctional activity in the area adjecent to the lesion is of primary impotance in this determination.

Symptoms of urethral melanomas rapidly develop and are not distinctive. They include urethal mass, nonspecific perineal pain, dysuria, frequency, incontinence, hematuria or local bleeding (2). Serosanguineous vaginal discharge is often associated with this tumor. In 75% of cases the tumor arises at the anterior wall of the urethra and may sometimes prolapse through the exterior urethral meatus with edema or even partial necrosis.

TABLE 1
Reported cases of primary malignant melanoma of female urethra with survival of 4 or more years

Author (ref)	Age (yrs)	Location	Depth/ Stage	Treatment	Recurrence			Follow up	
					Time (mos)	Location	Treatment	Total time (mos)	Status
Geisler	71	Urethral meatus	4.6 mm A	Anterior pelvic exenteration+ lymphadenectomy (-)				78	AW
Kim	59	Urethral meatus	A	Total urethrectomy+ lymphadenectomy (-) Chemo + interferon				60	AW
Mayer	?	Distal urethra	A	Partial uretherectomy+ vulvectomy				180	AW
Rikaniadis	80	Distal urethra	7mm A	Distal urethrectomy+ lymphadenectomy (-)	64	Lung	Chemo+ interferon	84	DOD
Block	54	Distal urethra	A	Cystourethrectomy	16	Left groin	LND+ chemo	77	DOD
					40	Right vaginal mass	Excision		
Katz	61	Distal urethra+ bladder neck	C	Anterior exenteration+ RT+ lymphadenectomy (-)				120	AW
Gleen	45	Urethral meatus	D	Subtotal urethrectomy		Inguinal lymph nodes	Excision	150	AW
Das Gupta	65	Urethral meatus extending to bladder neck	D	Palliative				60	DOD
Pointon	?	Distal urethra	?	Anteror pelvic exenteration+ vulvectomy				156	AW
Sharma	70	Urethral meatus	?	Excision+ lymphadenectomy (+) +RT	18	Local recurrence		48	AWD
Yoshida	76	Urethral meatus, vesical neck	?	Cystourethrectomy+ Lymphadenectomy (-)				48	AW

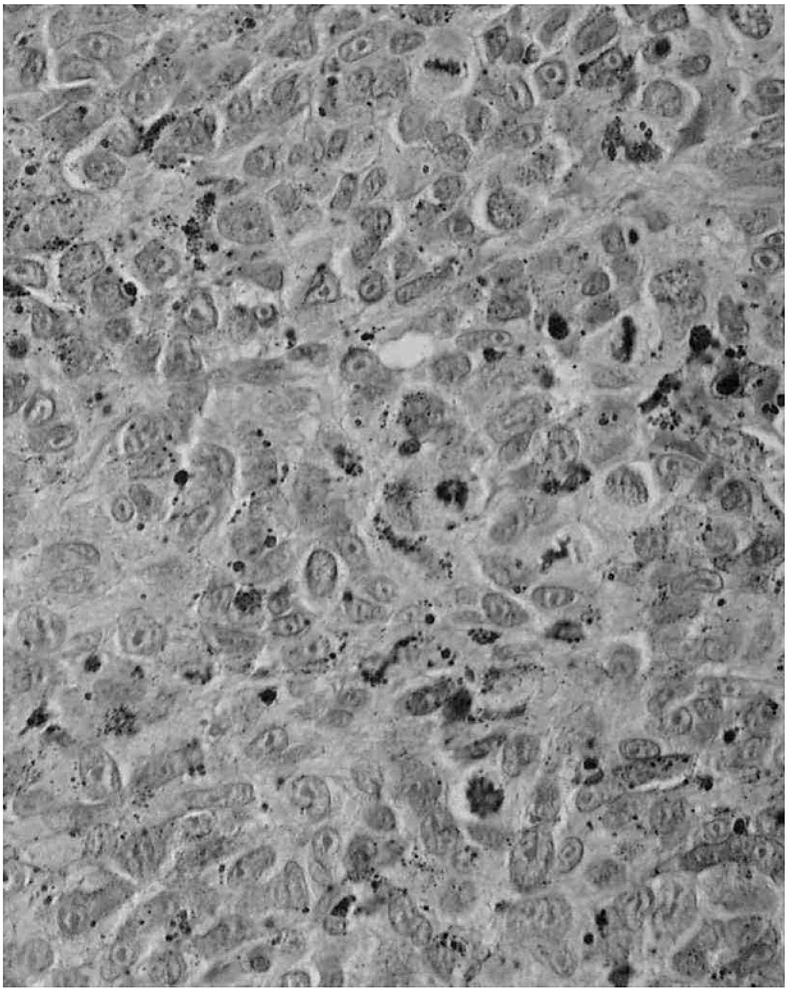
RT - radiation therapy; Chemo - chemotherapy; LND - lymph node dissection; AW - alive and well; AWD - alive with disease; DOD - died of disease

TABLICA 1.
Prikaz slučajeva primarnog malignog melanoma ženske mokraćne cijevi s preživljavanjem u periodu od 4 i više godina

Autor (ref)	Dob (god.)	Lokacija	Dubina/ stadij	Liječenje	Recidiv			Kontrolno razdoblje	
					vrijeme (mjesec)	lokacija	liječenje	ukupno vrijeme (mjeseci)	status
Geisler	71	Meatus uretre	4.6 mm A	Prednja zdjelična egzenteracija+ limfadenektomija(-)				78	AW
Kim	59	Meatus uretre	A	totalna uretrektomija+ limfadenektomija(-)				60	AW
Mayer	?	Distalna uretra	A	djelomična uretrektomija+ vulvektomija				180	AW
Rikaniadis	80	Distalna uretra	7mm A	distalna uretrektomija+ limfadenektomija(-)	64	pluća	kemoterapija+ interferon	84	DOD
Block	54	Distalna uretra	A	cistouretrektomija	16	lijeva prepona	LND+ kemoterapija	77	DOD
					40	vaginalna masa, desno	ekscizija		
Katz	61	Distalna uretra+ vrat mjehura	C	prednja egzenteracija+ RT+limfadenektomija (-)				120	AW
Gleen	45	Meatus uretre	D	djelomična uretrektomija		preponski limfni čvorovi	ekscizija	150	AW
Das Gupta	65	Meatus uretre, proteže se do vrata mjehura	D	palijativno				60	DOD
Pointon	?	Distalna uretra	?	prednja zdjelična egzentracija				156	AW
Sharma	70	Meatus uretre	?	ekscizija+ limfadenektomija(+) +RT	18	lokalni recidiv		48	AWD
Yoshida	76	Meatus uretre, vrat mjehura	?	cistouretrektomija+ limfadenektomija(-)				48	AW

RT - radiation therapy / terapija zračenjem; Chemo - chemotherapy / kemoterapija; LND - lymph node dissection / disekcija limfnih čvorova; AW - alive and well / živ i dobro se osjeća/izliječen; AWD - alive with disease / živ, ali prisutna bolest; DOD - died of disease / umro usljed bolesti

FIGURE 1.
Light microscopic view of melanoma cells with intense cytoplasmic melanin pigment. HE. X 200.
SLIKA 1.
Svjetlosno mikroskopski prikaz stanica melanoma s izraženim zrncima pigmenta melanina u citoplazmi. HE x 200.



Grossly, the tumor may be easily confused with a caruncle, having an identical appearance. The color varies from black to blue or brown.

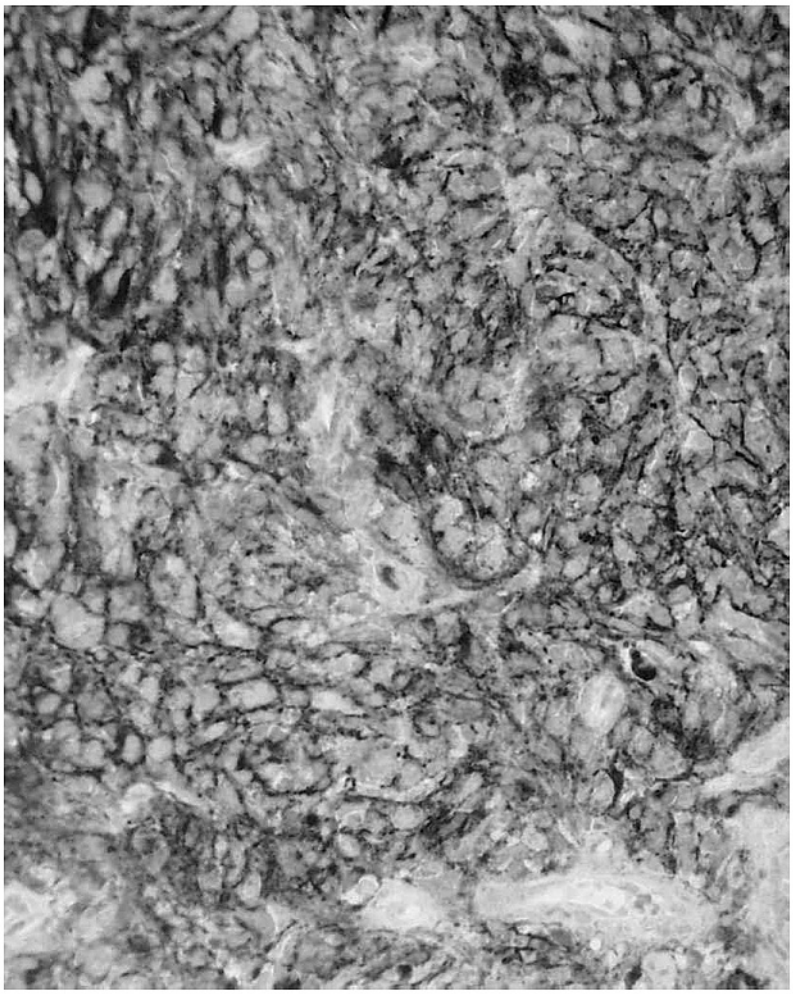
The thickness of the tumor and the mitotic index have to be taken into account on microscopic examination, since tumors more than 1.5 mm thick and with more than one mitotic figure in every high power field carry a worse prognosis (8).

Urethral melanoma spreads to the vulva and the vaginal wall via the superficial lymphatics and to the inguinal lymph nodes by means of the deep lymphatics as well as hematogenously to distant sites, such as lung, liver, bone and brain. Metastases to the inguinal lymph nodes occur early in the course of the disease, in 50% of the cases being already present at the time of the diagnosis. Rapid dissemination renders treatment very difficult and the prognosis very poor in spite of an early diagnosis.

Despite the location that allows easy examintion, and ready acces to biopsy and imprint cytology (9) a rate of curability is low. This tumor usually occur in postmenopausal women and its rarity precludes the formulation of standardized and definitive treatment. Two problems in planning the treatment should be recognized: local control and prevention of systemic disease. The local control is primarily surgical. Before any decision of a type of surgery, urethrocystoscopy should explore possible tumor extension though the urethra toward the bladder neck. Treatment options include local excision, urethrectomy and anterior pelvic exenteration, all with or without inguinal lymph node dissection. The operative treatments used in long-term survivors showed no uniform tendency (table). Nissenkorn et al (10) and Yoshida et al (11) recommended extensive operative procedures, but despite extensive resection, only two of seven patients treated wih cystourethrectomy and anterior pelvic exenteration survived 5 years. Kim et al (5) suggested that total urethrectomy with bilateral inguinal lymph node dissection should be the initial treatment in patients without evident distant metastases.

Despite conservative treatment, our patient is still alive after 4 years. We believe that local surgical excison can be an option in selected patients as it retains quality of life.

FIGURE 2.
Cytoplasmic HMB-45 positivity on immunohistochemical staining. Fast red. X 200.
SLIKA 2.
Pozitivno imunohistokemijsko bojenje na citoplazmatski HMB-45. Povećanje x 200



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PRIMARNI MALIGNI MELANOM ŽENSKE MOKRAĆNE CIJEVI

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SAŽETAK

Primarni maligni melanom ženske mokraćne cijevi vrlo je rijedak i agresivan tumor s lošom prognozom. Prikazali smo slučaj 65-godišnje žene s polipoidnim tumorom na vanjskom ušću mokraćne cijevi. Tumor je lokalno odstranjen i imunohistokemijski je potvrđena dijagnoza malignoga melanoma. Poslije tri mjeseca učinjena je donja uretrektomija. Rub je bio negativan na tumor i bolesnica je živa nakon više od pet godina praćenja.

Ključne riječi: lokalno odstranjenje, maligni melanom, ženska mokraćna cijev