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PRIMARY MALIGNANT MELANOMA OF FEMALE URETHRA: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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We report herein one case of malignant melanoma with a survival period of more than four years, refer to its recent conception on histopathological and ultrastructural problems and its treatment, and review the literature.

Key words: Malignant melanoma, Female urethral tumor, Fine structure

INTRODUCTION

Melanocytes synthesize specialized pigmented organelles, called melanosomes, and these particles are transferred to keratinocytes of the skin by means of dendritic processes. Though cutaneous malignant melanoma is frequently reported, primary malignant melanoma of the female urethra is extremely rare. Among 3,305 cases of malignant melanoma in females, Ariel reported only 3% of the genitourinary melanoma, but none from the urethra.

Katz and Grabstald reviewed 44 cases of primary malignant melanoma of the female urethra.

We found ten other cases, and referred to histopathological and ultrastructural problems, and its treatment.

CASE

On July 2, 1980, a 76-year-old Japanese woman was seen for urethral pain and mild dysuria for the past five months. Examination revealed a dark black, round new growth approximately 15 by 15 mm in diameter at the external urethral meatus. Brittle and hemorrhagic tumor resected by electrode under local anesthesia, was diagnosed as malignant melanoma histopathologically. On her next consultation day, patchy formed and black coloured pigmentation was observed in the restricted proximal urethra and vesical neck cystoscopically (Fig. 1).

After admission, she was examined for the presence of other tumors; chest plain X-ray, excretory urogram, 99mTc-citrate whole body lymph scanning through toes, etc.

No abnormalities were detected. On August 13, 1980, cystourethrectomy with regional lymphnode dissection and cutaneous bilateral ureterostomy were performed. Postoperatively the patient was suffering from severe paralytic ileus and stercoral fistula and underwent hyperalimentation therapy for 6 weeks until recovery. Postcare for malignancy could not be administered because the patient's family refused it. No melanogen was detected in urine postoperatively. Up to the present, there has been no detectable tumor recurrence.

HISTOPATHOLOGY

The primary site of external meatal tumor was filled with melanotic cells; forming nest, pleomorphic variety of nuclear size and its density, mitotic figures, and pulverized melanin granule deposition (Fig. 2).

In the proximal urethra and vesical neck, tumor infiltration was observed at the muscle layer, occasionally with a
Fig. 1. Shows black pigmented tumor, penetrating in patchy form on entire urethra and vesical neck.

Fig. 2. High power view of nest formation of melanotic cells with pleomorphism. H. & E. Reduced from \( \times \) 200.

DISCUSSION

Primary malignant melanoma of female urethra was first reported by Reed (1896)\(^3\). Since then several reviews have been written 14 cases by Long\(^4\) (1946), 34 cases by Block\(^5\) (1971), and 37 cases by Katz\(^2\) (1976). Another 11 cases including reports in Japan and the present case are shown in the Table.

As with other primary cancers of the female urethra, primary malignant melanoma of the female urethra seems to arise from distal urethra or just external urethral orifice\(^12\).

In the previously reported cases of primary malignant melanoma of the female urethra the details of histopathological and ultrastructural problems as recommended were hardly mentioned.

Normal epidermis contains dendric cells at the dermo-epidermal junction, usually are dopa-positive, and contain melanin granules in pigmented skin. And melanocytes contribute melanin granules to the
Fig. 3, 4. Penetration of pigmented cells from mucosa to muscle layer observed with characteristics of pigmented acinar lining of the so-called Brunn’s nest (arrow) in the vesical neck. H. & E. Reduced from ×100 in Fig. 3 and ×63 in Fig. 4.

Fig. 5. Melanoma cells with numerous melanosomes. Uranyl acetate & Lead citrate staining. Reduced from ×4500

epidermal keratinizing hair cells. Primary cutaneous malignant melanoma, in general, are clinically considered to have three theoretical origins: 1) epithelial tissue, 2) mesodermal tissue, and 3) nervous tissue. But it is still difficult to clarify the carcinogenesis and/or malignant transformation to change malignant melanoma in various kinds of the pigmentary disorders. Besides, the histopathological classification designated on the invasive malignant melanoma by McGovern et al., the Pigment Cell Subcommittee of the Organizing Committee of the International Cancer Conference (1972) recommended to make reports on other unknown parameters to better recognize malignant melanoma; histologic system, level of invasion, cell type, infiltration system and etc.

Our case belongs to group 4, malignant melanoma, invasive without adjacent intraepidermal component; and others of parameters were described in histopathology.
Table. Primary malignant melanoma of female urethra

<table>
<thead>
<tr>
<th>No</th>
<th>Reporter</th>
<th>Age (yrs.)</th>
<th>Presenting Symptom</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Reed</td>
<td>(1896)</td>
<td>Not stated</td>
<td>Urethrectomy</td>
</tr>
<tr>
<td>2</td>
<td>Mundell</td>
<td>(1901)</td>
<td>46</td>
<td>Local excision</td>
</tr>
<tr>
<td>3</td>
<td>Kustner</td>
<td>(1917)</td>
<td>N.S.</td>
<td>Not stated</td>
</tr>
<tr>
<td>4</td>
<td>Herrmann</td>
<td>(1917)</td>
<td>58</td>
<td>N.S.</td>
</tr>
<tr>
<td>5</td>
<td>Kauffman</td>
<td>(1922)</td>
<td>55</td>
<td>N.S.</td>
</tr>
<tr>
<td>6</td>
<td>Basler</td>
<td>(1922)</td>
<td>55</td>
<td>N.S.</td>
</tr>
<tr>
<td>7</td>
<td>Saenger</td>
<td>(1926)</td>
<td>72</td>
<td>Roentgen therapy, excision</td>
</tr>
<tr>
<td>8</td>
<td>Koerner</td>
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<td>75</td>
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</tr>
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<td>(1931)</td>
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</tr>
<tr>
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<td>(1927)</td>
<td>75</td>
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<td>11</td>
<td>Newell</td>
<td>(1938)</td>
<td>64</td>
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<tr>
<td>12</td>
<td>Naegan</td>
<td>(1940)</td>
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<td>13</td>
<td>Kyrie</td>
<td>(1945)</td>
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<td>14</td>
<td>Savran</td>
<td>(1948)</td>
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<td>15</td>
<td>Glenn</td>
<td>(1953)</td>
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<td>16</td>
<td>McBurney</td>
<td>(1953)</td>
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<td>(1955)</td>
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<td>18</td>
<td>Limburg</td>
<td>(1956)</td>
<td>68</td>
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<td>Abeshouse</td>
<td>(1958)</td>
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<td>Woodruff</td>
<td>(1958)</td>
<td>60</td>
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<tr>
<td>21</td>
<td>Letszerukov</td>
<td>(1962)</td>
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<td>22</td>
<td>Sokal</td>
<td>(1962)</td>
<td>58</td>
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</tr>
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<td>23</td>
<td>Rabot</td>
<td>(1964)</td>
<td>60</td>
<td>None</td>
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<tr>
<td>24</td>
<td>Gupta</td>
<td>(1965)</td>
<td>65</td>
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<tr>
<td>25</td>
<td>Maeda</td>
<td>(1967)</td>
<td>64</td>
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<tr>
<td>26</td>
<td>Gillenwater</td>
<td>(1968)</td>
<td>56</td>
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</tr>
<tr>
<td>27</td>
<td>Block</td>
<td>(1971)</td>
<td>54</td>
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</table>
Ultrastructural differences in human malignant melanoma have been well analyzed by Klug and Günther. Two different forms were referred to as just “nevocytic” and “melanocytic.” They characterized the melanocytic melanoma as containing only spherical melanosomes, whereas the premelanosomes show no internal fibrillar structure. The mitochondria mostly appear spherical, and their matrix is slightly electron dense.

Occasionally there are non-pigmented types of malignant melanoma which may be helpful to examine by stain for activated tyrosinase or dioxypyphenyl alanine (DOPA) oxidase, and by fine structure electron microscopically. The fine structure of the primary malignant melanoma of female urethra has been presented in only one case, which was unique to make its definition clear clinically, but was not so typical in its fine structure.

In our case, irregular shaped tumor cells contained abundant spherical melanosomes, a few mitochondrias with several criste, and bizarre-shaped nucleus with nucleoli, which were characteristic and corresponded to melanoma (Fig. 5).

On review of primary malignant melanoma of the female urethra, therapy in most of the first half was limited in local excision and/or irradiation palliatively. Herbut suggested that melanomas are notoriously resistant to irradiation. It is interesting to note that there are reports of cases of radio-effective and/or spontaneously regressive series.

As already reported, there have been no recurrences or deaths among 22 patients who underwent combined chemo-immunotherapy with dimethyl triazeno imidazole carboxamide (DTIC) and bacillus Calmette-Guerin (BCG), which were significantly superior treatments to both the immunotherapy and chemotherapy alone. On the other hand, Yamano et al. reported a patient alive with no recurrence over 36 months after combined therapy of cryosurgery, topical administrations of Bleomycin, and active immunotherapy with BCG and a Streptococcal agent.
Excenteric surgery of urethrocystectomy with lymphnode dissection has been performed in only 5 cases of primary malignant melanoma of female urethra, of which only 3 cases were certified in reviews of all cases as cases of more than five years survival.

Concerning the prognosis, primary malignant melanoma of the female urethra is uniformly unfortunate, and has been predicated to be causative of early recurrence and wide spread metastasis.

In these respects we should recognize the stage of primary malignancy of female urethra and prognosis, needless to say, early recognition of the disease.

We believe that wide exenteration operation with lymphnode dissection and combined immuno-chemotherapy might be a desirable method for prevention and improvement of the survival rate of primary malignant melanoma of the female urethra.

REFERENCES


(Accepted for publication April 25, 1985)
原発性女子尿道悪性黑色腫
—症例および文献的考察—

日本医科大学附属病院泌尿器科（主任：秋元成大教授）

吉田 和 弘
坪井 成 美
秋元 成 太

女子尿道に発生した原発性悪性黑色腫の報告はきわめて少ない。皮膚色素異常症の中で悪性黑色腫は細胞形態および新生物として十分に検討されているが、その発生要因についての解明は十分になされていない。今回われわれは76歳で尿道痛・排尿困難を主訴とした悪性黑色腫症例に対し尿道膀胱全摘除術および所属リンパ節療清術を施行した。4年経過にて再発の徵候を認めていない。本症例の病理組織学的および超微形態学的検討を行うとともに、内外文献にみる治療法を中心に考察を加え報告した。