CASE REPORT

Malignant melanoma of the female urethra

Tadashi Terada*

Departments of Pathology, Shizuoka General Hospital, Shizuoka, Japan

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ABSTRACT

Backgrounds: Malignant melanoma (MM) of urethra is extremely rare; only 84 cases have been reported in PubMed search.
Case: An 84-year-old woman presented dysuria. Physical and endoscopic examination revealed a polypoid tumor in proximal urethra, and endoscopic tumorectomy was performed. The tumor could not be seen in outer genitalia. Grossly, the tumor is brownish soft tumor measuring 15 mm × 26 mm × 23 mm. Multiple sections were made and immunohistochemical procedures were performed. Microscopically, malignant epithelioid cells with brown pigment were seen to proliferate and invade. The size of tumor was circa 13 mm × 21 mm × 18 mm. The depth of invasion was 10 mm (pT4), but it was not clear whether the marginal tissue status is positive or negative. Lymphovascular permeation seen, yet no obvious vascular invasion was noted. The brown pigment was found to be melanin by Masson-Fontana stain. Immunohistochemical study showed tumor cells were positive for vimentin, S100 protein, HMB45, Melan A, p53, and Ki67 (labeling = 85%), KIT and PDGFRA, while they were negative for cytokeratins. Genetic analysis of paraffin-embedded tumor tissue identified no mutations in hot spots of KIT and PDGFRA genes. No apparent metastatic lesions were seen after the diagnosis. The outcome of the patient is unknown because the patient was referred to a large hospital specializing in cancer treatment.
Conclusions: The author presented a very rare case of MM of the proximal urethra. The MM showed typical histochemical and immunohistochemical features. No mutations of KIT and PDGFRA were seen.

Key Words: Urethra, Female, Melanoma

1. INTRODUCTION

Malignant melanoma (MM) is relatively rare in Japan, the author's country. MM is more prevalent in Caucasian than Mongoloid and Negroid.[1] MM is a malignant tumor derived from melanocytes, cells producing melanin. Although MM can arise in any tissues, most cases of MM arise in skin where numerous melanocytes are present. Rarely, MM arise in retina, esophagus and rectum.[2–4] Melanoma arising in urethra is very rare; a Pubmed search revealed only 84 cases of MM occurring in urethra.[5,6] The distribution of melanocytes in urethra is unclear, but it seems that proximal urethra is free of melanocytes while distal urethra contains melanocytes.

2. CASE REPORT

An 84-year-old woman presented dysuria. Physical and endoscopic examination revealed a polypoid tumor (circa 2 cm) in proximal urethra, and endoscopic tumorectomy was performed. The tumor could not be seen in outer genitalia. Grossly, the tumor is brownish soft tumor measuring 15 mm × 26 mm × 23 mm. Multiple sections were made and immunohistochemical procedures were performed. Microscopically, malignant epithelioid cells with brown pigment were seen to proliferate and invade under the urothelium of

*Correspondence: Tadashi Terada, M.D., Ph.D.; Email: piyo0111jp@yahoo.co.jp; Address: Departments of Pathology, Shizuoka General Hospital, No. 4-27-1, Kita-Ando, Aoi-ku, Shizuoka, 420-8527, Japan.

proximal urethra (see Figure 1A). The urothelium lacked melanocytes. The size of tumor was circa 13 mm × 21 mm × 18 mm. The depth of invasion was 10 mm (pT4), but it was not clear whether or not the margins were positive for tumor cells. Lymphovascular permeation seen, yet no obvious vascular invasion was noted. Necrotic foci were scattered (see Figure 1A). The tumor cells were apparently malignant and showed epithelioid appearances (see Figure 1B). Masson-Fontana argentaffin stain yielded black color products (see Figure 1C), which means the brown pigment was melanin. An immunohistochemical study was carried out with the use of Envision method. The study showed that tumor cells were positive for vimentin, S100 protein (see Figure 1D), HMB45 (see Figure 1E), Melan A, p53, and Ki67 (labeling index = 85%) (see Figure 1F), KIT and PDGFRA, while they were negative for cytokeratins (clones AE1/3 and CAM5.2). Nuclear DNA was extracted from the paraffin embedded tissues, and it was subjected to a genetic analysis of KIT and PDGFRA genes (both encode receptor tyrosine kinases), using PCR-direct sequencing of hot exons (KIT, exons 9, 11, 13 and 17. PDGFRA, exons 12 and 18), as previously reported.[7,8] The analysis showed no mutations in the exons of KIT and PDGFRA genes. No apparent metastatic lesions were seen after the diagnosis. The outcome of the patient is unknown because the patient was referred to a large hospital specializing in cancer treatment.

3. Discussion

The diagnosis of MM is easy in skin MM, but is relatively difficult in MM of non-skin tissues. It was particularly difficult in MM not producing melanin (amelanotic MM). In such cases, immunohistochemical procedures and electron microscopic demonstration of melanosomes can provide definite diagnosis MM. MM should always be considered when pathologists encounter tumors with pigment and tumor showing intermediate histology between carcinoma and sarcoma. Even in ordinary melanotic MM, immunohistochemical demonstration of S100 protein and HMB45 or Melans are mandatory. Melanin can be identified by Masson-Fontana stains. The present case fulfilled these histological and immunohistochemical criteria of melanotic MM.

The present tumor was located in female proximal urethra. Microscopically, obvious urothelium (transitional epithelium) were seen over the MM nests, thus confirming that the tumor is located in proximal urethra. The overlying urothelium in this location lacked melanocytes. Therefore, the origin of the present MM is unclear as with the case of MM in non-melanocytic locations such as esophageal and rectal MM.

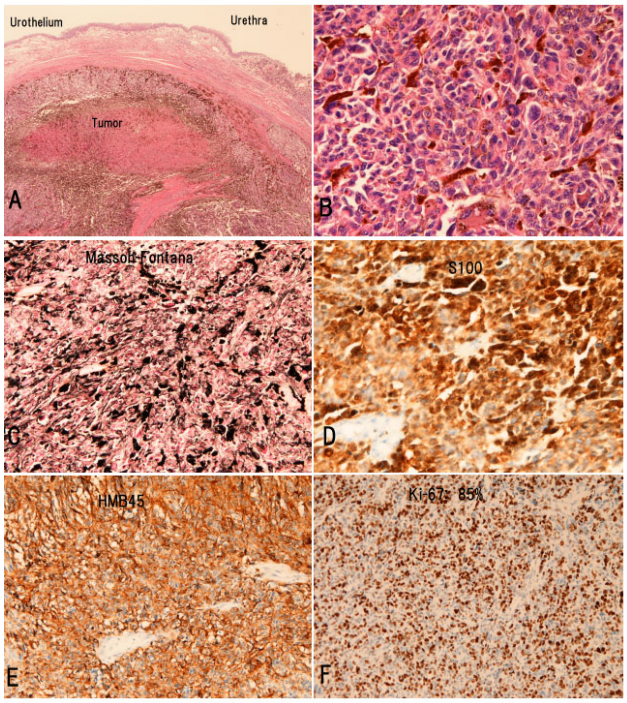

Figure 1. Histological (A, B), histochemical (C), and immunohistochemical (D-F) features of the urethral tumor
A: Low power view shows tumor with necrosis and overlying urothelial epithelium. HE, ×20. B: High power view shows that the tumor is composed of epithelioid malignant cells with brown pigment. HE, ×300. C: The pigment is proved to be melanin. Masson-Fontana stain, ×200. D-F: Immunohistochemitry. The tumor cells are positive for S100 protein (D), HMB45 (E), and Ki67 (labeling index = 85%). D,E: ×150. F: ×100.

No mutations were found in the hot exons of KIT and PDGFRA genes in the present tumor. It is known that rate of these mutations in KIT and PDGFRA is low in Japan (about 10%) compared to those in Caucasians. It is well known that BRAF mutations are often noted in MM, and BRAF (V600E) immunohistochemistry can help to detect the BRAF mutations.[9,10] Therefore, future works will include BRAF mutational profiling of MM.

4. Conclusions

The author presented a very rare case of MM of the proximal urethra. The MM showed typical histochemical and immunohistochemical features. No mutations of KIT and PDGFRA were seen.

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