

Oncology

Primary amelanotic malignant melanoma of the male urethra with inguinal lymph node metastasis successfully controlled by nivolumab: A case report

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ABSTRACT

We report a rare case of primary amelanotic malignant melanoma of the male urethra. A 65-year-old man with a urethral mass was referred to our hospital. A pathological diagnosis of a biopsy specimen revealed malignant melanoma. Thereafter, the patient underwent partial penectomy. The histopathological diagnosis was amelanotic malignant melanoma of the urethra. The patient had received DAV-Feron in an adjuvant setting; however, PET-CT revealed multiple metastasis. After receiving more than 10 cycles of nivolumab, the accumulation of FDG was no longer observed on PET-CT. The patient is currently free from recurrence at 20 months after nivolumab treatment.

Introduction

Melanoma of the urethra is a rare disease and amelanotic melanoma of the urethra is rarer still.¹ Advanced amelanotic melanoma is associated with an extremely poor prognosis.² There are no satisfactory approaches for the treatment of metastatic or recurrent amelanotic melanoma. We herein report a case of primary amelanotic melanoma of the male urethra with inguinal lymph node metastasis that was successfully controlled by nivolumab.

Case presentation

A 65-year-old man was referred to our hospital for further examination for a located at the urethral meatus mass that had become enlarged over a period of a few months. A physical examination showed left inguinal swelling without pain. The patient had no significant past or family history. A histopathological diagnosis of an incisional biopsy specimen revealed melanoma (Fig. 1a and b). The left inguinal lymph node, which was approximately 20 mm showed the uptake of FDG on PET-CT (Fig. 2a). The clinical diagnosis was primary malignant melanoma of the urethra with left inguinal lymph node metastasis;

(cTxN1M0) stage III. Partial penectomy with amputation of the glans and bilateral inguinal lymphadenectomy was performed. We performed extended lymphadenectomy on the left side according to pre-operation plan. We had planned minimal lymphadenectomy on the right side; however the intraoperative frozen section showed melanocytes. We therefore performed extended lymphadenectomy in addition to right inguinal lymphadenectomy. The final pathological diagnosis was primary amelanotic malignant melanoma of the urethra (Fig. 3) with left inguinal lymph node metastasis; pT4bN3M0, stage IIIc. Adjuvant systemic chemotherapy consisting of DAV-Feron (dacarbazine, nimustine, vincristine, and interferon- β) was administered; however, CT showed multiple liver metastasis, pleural metastasis, and retroperitoneal metastasis. After one course of chemotherapy, PET-CT revealed systemic bone metastasis (Fig. 2b). The patient received more than 10 cycles of nivolumab (an anti-PD-1 antibody); after six months no accumulation of FDG was observed on PET-CT. The patient is currently free from recurrence at 20 months after nivolumab treatment.

Discussion

Primary malignant melanoma of the urethra is generally

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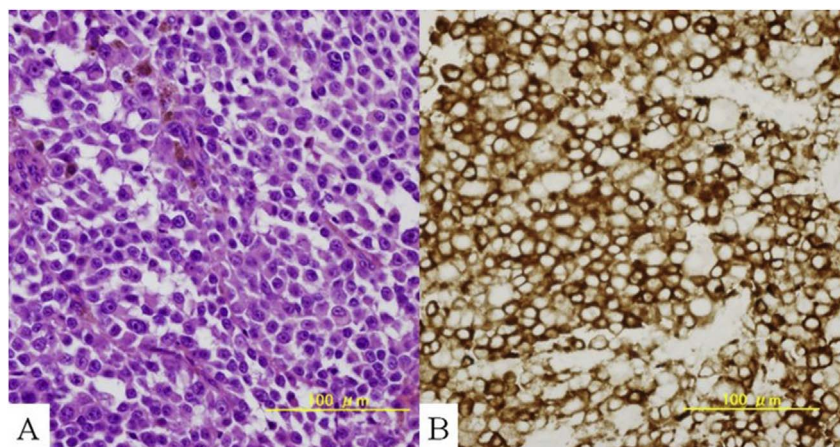


Fig. 1. a) Hematoxylin-eosin staining of the tumor and b) Immunohistochemical staining of HMB-45.

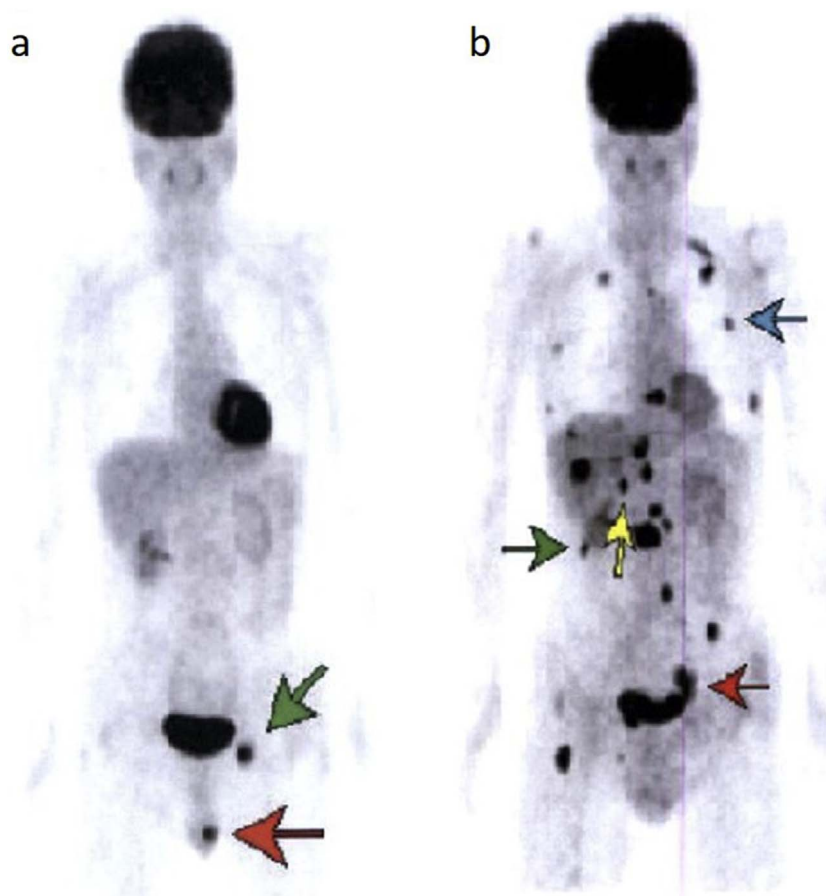


Fig. 2. a) FDG PET-CT image showing left inguinal lymph node metastasis (Green arrow) and b) FDG PET-CT image showing multiple metastasis, including systemic bone metastasis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

uncommon. In male patients with amelanotic melanoma, it is extremely rare. The prevalence of melanoma in men is reported to be one-third of that in women.¹

Radical surgery for metastatic melanoma of the urethra remains controversial due to its extremely poor prognosis.² In our case, the patient was relatively young and PET-CT showed only one metastatic site; thus, we performed partial penectomy and inguinal lymphadenectomy. Bilateral complete inguinal lymphadenectomy is generally thought to be contraindicated because the high invasiveness of the procedure may cause lymphedema, which may interfere with ambulation and cause skin flap necrosis. The final pathological results showed

no malignant cells in the right side lymph node, and macrophages that phagocytized melanin pigment were observed. Alkhatib et al. reported that the intraoperative frozen section analysis of sentinel lymph node biopsy specimens in 133 cases of melanoma yielded no false positives and that it can be an accurate and reliable tool. However, the clinical estimation of melanocytes from intraoperative frozen sections remains controversial.

Some systemic chemotherapy and immunotherapy regimens, including DAV-feron (DTIC, ACNU, VCR and INF-β) and DAC-Tam (DTIC, ACNU, CDDP and tamoxifen), have been used for the treatment of advanced disease; however, none have led to an improvement in overall

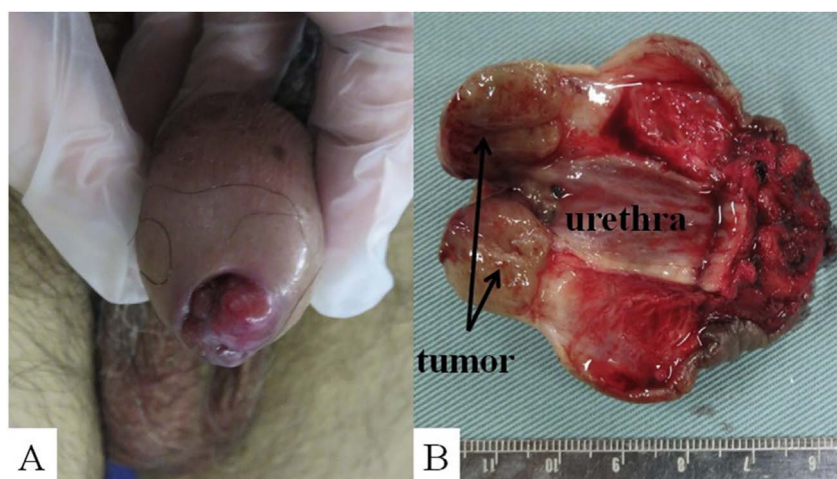


Fig. 3. a) The tumor was observed in the urethral meatus and b) the urethra.

survival. Recently, immune-checkpoint blockade immunotherapy, including cytotoxic T lymphocyte-associated antigen (CTLA-4) and programmed cell death 1 (PD-1) receptor antibody treatment have been showing promising efficacy in the treatment of metastatic melanoma.³ To the best of our knowledge, this is the first case of primary amelanotic melanoma of the urethra to be treated with a novel immunotherapeutic approach using nivolumab (an anti-PD-1 antibody). Penile and urethral melanoma tend to be diagnosed at a late stage in comparison to melanoma at other sites; thus, these patients might benefit from cutting-edge immunotherapy.^{1,4,5}

In conclusion, cases of melanoma of the urethra, especially amelanotic melanoma of the urethra are rarely encountered by the general urologist; however, the possibility of these entities should be considered for appropriate clinical decision-making. Nivolumab might be a new option for the treatment of melanoma of the urethra.

Ethics approval

Ethics approval and consent to participate & Consent for publication. The IRB of Yokohama City University Medical Center approved the present study.

Consent for publication

Written informed consent was obtained from the patients. A copy of the written consent forms is available for review from the Editor-in-Chief of this journal.

Availability of data and material

Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

Conflicts of interest

We declare no conflicts of interest.

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