^{177}Lu-PSMA Therapy for Metastatic Testicular Mixed Germ Cell Tumor

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Abstract: Prostate-specific membrane antigen (PSMA) overexpression in various tumors are demonstrated in both in vitro and in vivo studies. Prostate-specific membrane antigen–directed radionuclide therapies are generally used in prostate cancer and could be also useful in PSMA-avid other malignancies. Herein, we present a case of a 46-year-old male patient who had progressive metastatic testicular mixed germ cell tumor, despite repeated operations and treatments. ^{68}Ga-PSMA PET/CT was performed to assess eligibility for ^{177}Lu-PSMA therapy. Patient had intense PSMA uptake in metastatic lesions, and ^{177}Lu-PSMA has been given to control of disease. However, α-fetoprotein level progressed, and mixed therapy response was detected in ^{68}Ga-PSMA PET/CT.

Key Words: ^{68}Ga-PSMA, ^{177}Lu-PSMA, mixed germ cell tumor, testis cancer

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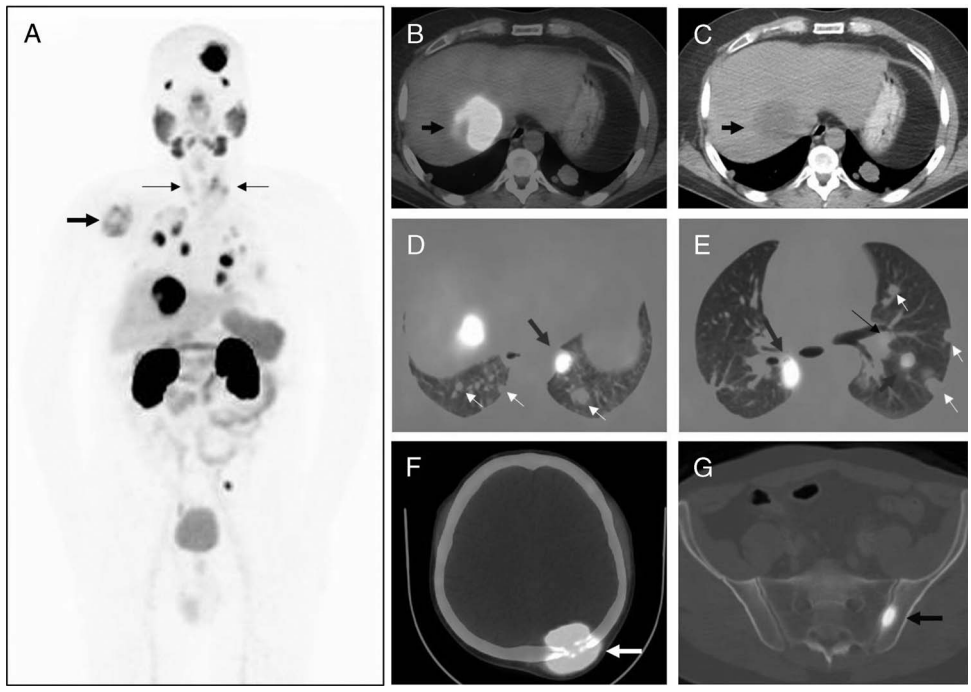


FIGURE 1. A 46-year-old man who had progressive metastatic testicular mixed germ cell tumor consisting of immature teratoma and yolk sac carcinoma was referred to our clinic for prostate-specific membrane antigen (PSMA)–directed radionuclide therapy. Patient had received several treatments for metastatic disease including different chemotherapy protocols, local radiotherapies, mediastinal/retroperitoneal lymph node dissections, and autologous bone marrow transplantation repeated twice due to the refractory disease within 16 years. After failure of all treatments, the patient underwent ^{68}Ga-PSMA PET/CT to determine eligibility for radionuclide treatment with ^{177}Lu-PSMA as a theranostic approach. Bone (**A**–**G**: black arrows, **F**: white arrow) and liver (**B**, **C**: black arrows) metastases had intense uptake, whereas lymph node metastases on the neck (**A**: black thin arrows) and mediastinum (**E**: black thin arrow) had moderate uptake and lung metastases (**D**, **E**) had mild to intense uptake (black arrows) or no PSMA avidity (white arrows) on ^{68}Ga-PSMA PET/CT. ^{177}Lu-PSMA was planned to control progressive disease.

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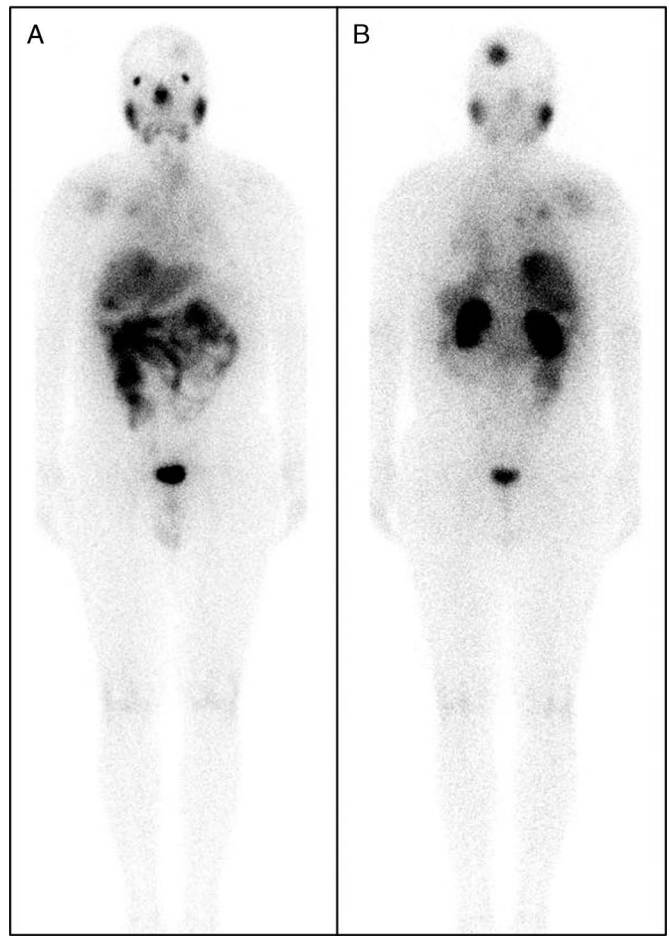


FIGURE 2. ^{177}Lu-PSMA 7.5 GBq was given to the patient (α-fetoprotein: 38,669 ng/mL), and posttherapy imaging was performed 48 hours after the intravenous administration of ^{177}Lu-PSMA. Adequate uptakes were detected in metastatic lesions on whole-body posttherapy images (**A**, **B**) similar to pretreatment ^{68}Ga-PSMA PET/CT. The patient well tolerated the treatment without any adverse effects. However, in follow-up at month 1, α-fetoprotein level progressed to 62,600 ng/mL, and ^{68}Ga-PSMA PET/CT was planned.

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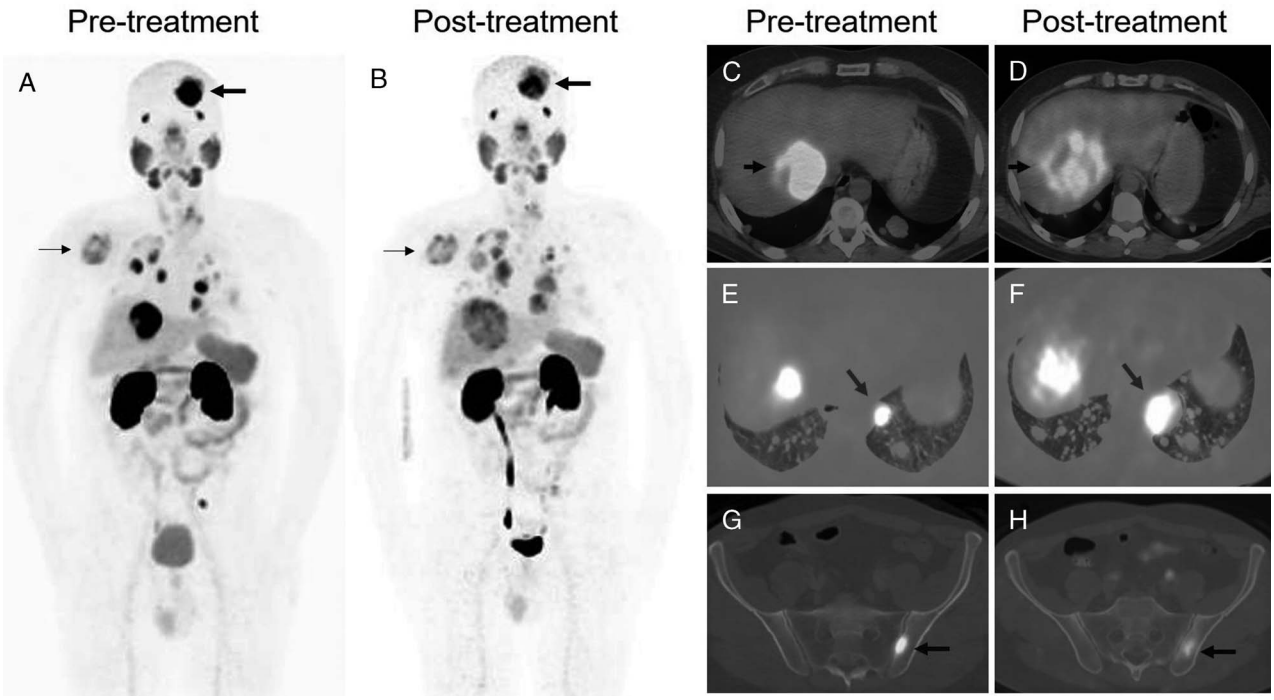


FIGURE 3. Posttreatment ^{68}Ga-PSMA PET/CT (**B**, **D**, **F**, **H**) showed anatomic progression, mostly in the liver (**C**, **D**: black arrows), lung (**E**, **F**: black arrows), and bone metastases (**A**, **B**, **G**, **H**: black arrows) compared with pretreatment ^{68}Ga-PSMA PET/CT (**A**, **C**, **E**, **G**), despite the PSMA uptake of metastatic lesions with intense PSMA uptake regressed after therapy. Moreover, new PSMA-negative lung lesions (**F**) were detected. Because of the anatomic progression and increased α-fetoprotein level, a second cycle of ^{177}Lu-PSMA was not considered, and the patient was referred to medical oncology department for palliative therapies. Testicular neoplasms containing nonseminoma features show worse prognosis than pure seminoma.[1] Most testicular germ cell tumors have been successfully treated in last decades; 10% to 20% of patients with metastatic disease cannot reach a complete and durable remission because of the incomplete response and/or a tumor relapse.[2] Increased PSMA uptake is demonstrated in various tumors on ^{68}Ga-PSMA PET/CT because of the PSMA overexpression and/or neovasculature of malignant neoplasms.[3–5] Metastatic mixed germ cell tumor is also one of the PSMA-overexpressing tumors reported in *in vitro* studies.[6,7] ^{177}Lu-PSMA treatment for nonprostatic malignancies has been demonstrated in selective patients as a safe theranostic approach in literature.[8–10] Based on these encouraging results, we applied ^{177}Lu-PSMA therapy to the patient for control of progressive metastatic mixed germ cell tumor. Despite the adequate PSMA uptake of tumors, α-fetoprotein level and tumor sizes progressed within 1 month both after 1 cycle of ^{177}Lu-PSMA, even if the PSMA uptake of lesions mostly regressed on PET/CT. In conclusion, ^{68}Ga-PSMA PET/CT seems to be useful for detection of testicular mixed germ cell tumors, whereas the effectiveness of ^{177}Lu-PSMA treatment is not evident for these patients with highly aggressive tumor biology.

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