



# Pseudoprogression Shown on <sup>18</sup>F-FDG PET/CT After Pembrolizumab Treatment in a Case of Metastatic Bladder Cancer

Metastatik Mesane Kanseri Bir Olguda Pembrolizumab Tedavisi Sonrası <sup>18</sup>F-FDG PET/BT'de Gösterilen Psödoprogresyon

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## Abstract

A 57-year-old man diagnosed with a metastatic bladder tumor was initiated on pembrolizumab treatment. <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) positron emission tomography/computed tomography (PET/CT) imaging performed to evaluate treatment response showed numerical-dimensional and metabolic increase in the metastatic lesions. In the <sup>18</sup>F-FDG PET/CT imaging performed 8 weeks later due to suspicion of pseudoprogression, a significant regression of the lesions was observed, and the patient was diagnosed with pseudoprogression. Pseudoprogression should be kept in mind when <sup>18</sup>F-FDG PET/CT is performed after the use of immunotherapy, and evaluation with follow-up PET/CT is recommended to confirm that the patient has hyperprogression or pseudoprogression.

**Keywords:** Immunotherapy, pseudoprogression, bladder cancer, pembrolizumab, PET/CT

## Öz

Metastatik mesane tümörü tanılı 57 yaşında erkek hastaya pembrolizumab tedavisi başlandı. Tedavi yanıtının değerlendirilmesi için yapılan <sup>18</sup>F-florodeoksiglukoz (<sup>18</sup>F-FDG) pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/BT) görüntülemesinde, metastatik lezyonlarda sayısal-boyutsal ve metabolik artış izlendi. Psödoprogresyon şüphesi nedeniyle 8 hafta sonra yapılan <sup>18</sup>F-FDG PET/BT görüntülemesinde, lezyonların belirgin gerilediği görüldü ve psödoprogresyon tanısı konuldu. İmmünoterapi kullanımı sonrası yapılan <sup>18</sup>F-FDG PET/BT'de psödoprogresyon akılda tutulup hastanın hiper veya psödoprogrese olduğunu göstermek için takip PET/BT ile değerlendirme önerilir.

**Anahtar kelimeler:** İmmünoterapi, psödoprogresyon, mesane kanseri, pembrolizumab, PET/BT

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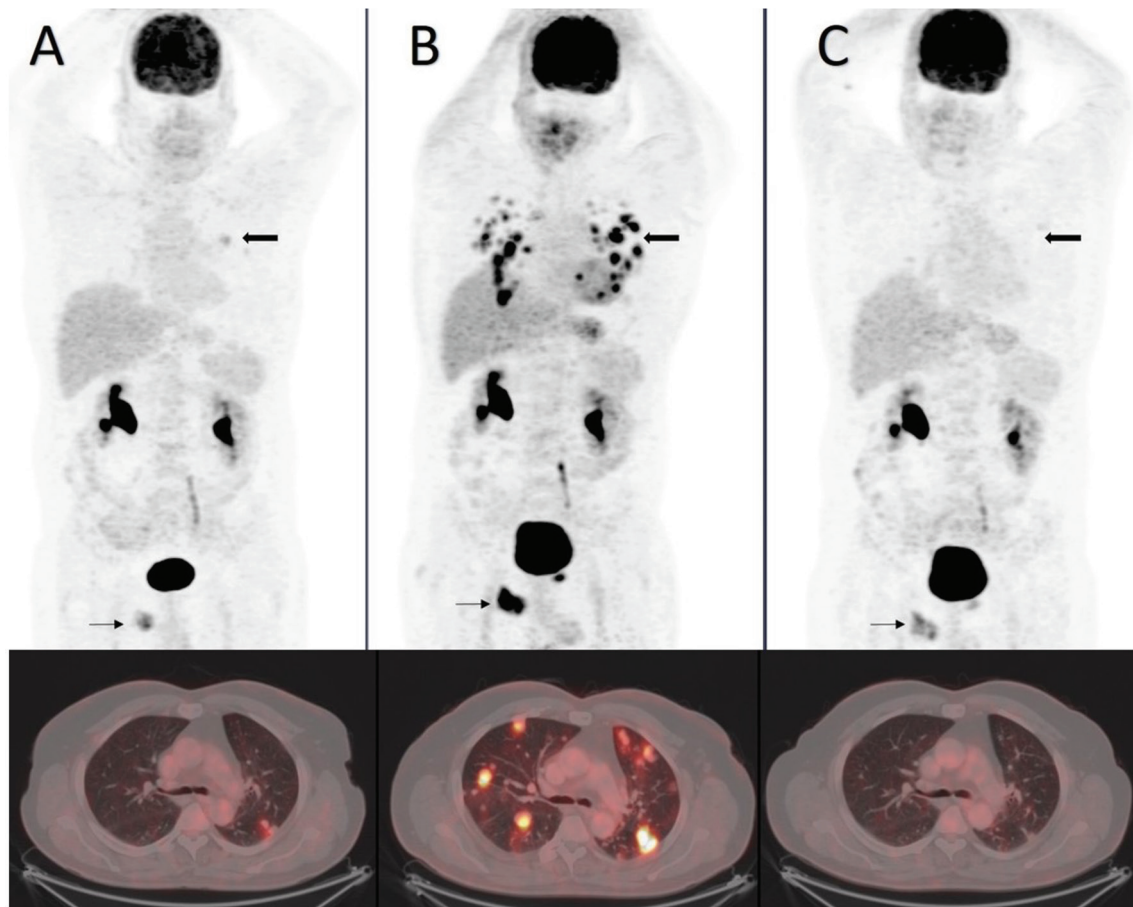
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**Figure 1.** A 57-year-old man with high-grade papillary urothelial carcinoma who underwent transurethral resection of the bladder received gemtastatin, cisplatin, and zoledronic acid due to lung and bone metastases in the initial staging.  $^{18}\text{F}$ -Fluorine-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) positron emission tomography/computed tomography (PET/CT) imaging [A: maximum intensity projection (MIP) and axial fusion] performed to evaluate treatment response showed increased  $^{18}\text{F}$ -FDG uptake in multiple nodular lesions (thick arrows) [maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ): 4.4], the largest of which was 11x8 mm in both lungs and lytic lesion (thin arrow) ( $\text{SUV}_{\text{max}}$ : 8.2) in the right ischium. Because there was a numerical progression in lung metastases compared with the previous PET/CT imaging (not shown), pembrolizumab treatment was initiated as second-line treatment. After 4 cycles of pembrolizumab treatment (after 3 months), PET/CT imaging (B: MIP and axial fusion) showed markedly increased intense  $^{18}\text{F}$ -FDG uptake in multiple nodular lesions (thick arrows) ( $\text{SUV}_{\text{max}}$ : 15.4), the largest of which was 23x23 mm in both lungs and lytic-sclerotic lesions (thin arrow) ( $\text{SUV}_{\text{max}}$ : 15.6) in the left pubic-right ischial bones. In the multidisciplinary oncology council, the patient was considered pseudoprogession, and pembrolizumab treatment was continued. PET/CT imaging 8 weeks later (C: MIP and axial fusion) showed significant numerical and metabolic regression of nodular lesions (thick arrows) in both lungs, the largest of which regressed to 11x11 mm in size, and low  $^{18}\text{F}$ -FDG uptake was observed in the nodules ( $\text{SUV}_{\text{max}}$ : 2.2). Reduced  $^{18}\text{F}$ -FDG uptake was observed in the right ischial and left pubic bones (thin arrow) ( $\text{SUV}_{\text{max}}$ : 7) compared with the previous study. The patient was diagnosed with pseudoprogession, and treatment was continued. Immune checkpoint inhibitors have a wide range of indications, and their frequency of use is increasing (1). Overexpression of programmed cell death protein-1 (PD-1)/programed cell death ligand 1 (PD-L1) in muscle invasive bladder cancer (MIBC) tissue was found to be associated with high  $^{18}\text{F}$ -FDG uptake in the tumor (2). A recent study prospectively investigated the value of  $^{18}\text{F}$ -FDG PET/CT for predicting lymph node metastasis (LNM) in MIBC patients receiving neoadjuvant pembrolizumab. PET/CT results were compared with histopathological findings, and the sensitivity to detect LNM was found to be 27% and 37.5%, and the specificities were 97% and 98% for  $^{18}\text{F}$ -FDG PET/CT before and after pembrolizumab, respectively (3). Pseudoprogession describes the phenomenon of marked disease progression (increase in size and  $^{18}\text{F}$ -FDG-affinity of lesions) on  $^{18}\text{F}$ -FDG PET scan within 12 weeks of the start of immunotherapy, with a reduction in tumor burden if immunotherapy is continued (4). The incidence of pseudoprogession in urothelial cancer ranges from 1.5% to 17% (5). A new category of unconfirmed progression (iUPD) has been created in the immune-based therapeutics Response Evaluation Criteria in Solid Tumors and requires confirmation of progression (increase in size or number of lesions) on follow-up imaging. This treatment is usually recommended after 4-8 weeks following an initial study showing significant disease progression (6). The role of pseudoprogession on  $^{18}\text{F}$ -FDG PET/CT in patients with MIBC treated with immunotherapy requires further investigation.

## Ethics

**Informed Consent:** Informed consent was obtained from the patient.

## Authorship Contributions

Concept: H.K., C.G., Design: H.K., C.G., İ.H.D., Data Collection or Processing: F.K., V.Ş., İ.H.D., Literature Search: F.K., C.G., V.Ş., Writing: F.K., C.G.

**Conflict of Interest:** No conflicts of interest were declared by the authors.

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