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HEMATOLOGIC TOXICITY OR TUMOR BIOLOGY TRANSLATIONAL PITFALLS OF ^{177}LU-PSMA IN ADVANCED PROSTATE CANCER

Gabriela Araujo Moreira [a],
Nadia Sclearuc de Siqueira [a],
Laisy Beatris Dolfini Celim [a],
Elba C.S.C. Etchebehere [b]

[a] *Hospital de Clínicas da Universidade Estadual de Campinas, Campinas, SP, Brazil*
[b] *Faculdade de Ciências Médicas da Universidade Estadual de Campinas, Campinas, SP, Brazil*

Background: Prostate-specific membrane antigen (PSMA) – based theranostics has reshaped the treatment landscape of metastatic castration-resistant prostate cancer (mCRPC) by integrating molecular imaging with targeted radionuclide therapy. Lutetium-177–PSMA (177Lu-PSMA) has demonstrated meaningful clinical benefit in selected patients; however, important translational challenges persist. These include optimal patient selection, prediction of hematologic toxicity, and differentiation between treatment-related adverse effects and manifestations of aggressive tumor biology, particularly in patients with extensive skeletal disease. **Objective:** To describe a case of mCRPC treated with 177Lu-PSMA complicated by severe pancytopenia, highlighting the translational challenges in distinguishing radionuclide-induced myelotoxicity from bone marrow infiltration by metastatic prostate cancer. **Case Report:** A 63-year-old man presented with a clinical and radiologic profile highly suggestive of metastatic prostate cancer, with markedly elevated PSA levels (1749 ng/mL) and widespread bone and nodal disease. Cross-sectional imaging revealed diffuse osteoblastic and osteolytic lesions involving the axial and appendicular skeleton, multiple pathologic fractures, and retroperitoneal and pelvic lymphadenopathy. PSMA PET demonstrated intense radiotracer uptake across multiple skeletal sites, consistent with high-volume PSMA-avid disease. Histologic confirmation of the primary tumor was not feasible due to a concomitant low rectal tubulovillous adenoma with high-grade dysplasia, which precluded transrectal biopsy. Following surgical castration and subsequent biochemical progression, the patient was classified as having mCRPC. Given the extensive PSMA expression and lack of alternative systemic options due to limited performance status, 177Lu-PSMA therapy was initiated. After the first cycle, the patient developed progressive anemia, neutropenia, and thrombocytopenia, complicated by febrile neutropenia. Further radionuclide therapy was withheld due to concern for severe hematologic toxicity. Bone marrow evaluation was pursued to clarify the underlying mechanism of cytopenias in the setting of extensive skeletal disease. Bone marrow biopsy revealed morphologic and immunohistochemical features consistent with metastatic prostatic adenocarcinoma involving the marrow, supporting tumor infiltration as a contributing factor to the observed cytopenias. **Conclusion:** This case shows how difficult it can be to distinguish hematologic toxicity from 177Lu-PSMA therapy from bone marrow involvement caused by high-volume disease. Imaging-based selection alone may be insufficient to predict hematologic risk. Integrative translational strategies incorporating molecular imaging, baseline marrow assessment, and predictive biomarkers are essential to optimize patient selection and safely expand the clinical impact of theranostics in advanced prostate cancer.

Keywords: Prostatic neoplasms, Castration-resistant prostate cancer, Theranostics, Prostate-specific membrane antigen, Lutetium Lu 177.

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INTEGRATION OF NUTRITIONAL, CACHEXIA, AND INFLAMMATORY ASSESSMENT IN GASTRIC CANCER: A CASE REPORT

Larissa Ariel Oliveira Carrilho,
Renata Erbert Contriciani, Leo Victor Kim,
Fabíola Furtuoso Zarpelão,
Sandra Regina Branbilla, Barbara Cipriano,
Ligia M Antunes Correa,
Maria Emilia Seren Takahashi, Jun Takahashi,
Luiz Roberto Lopes, Nelson Adami Andreollo,
Celso Dario Ramos, Elba C.S.C. Etchebehere,
Maria Carolina Santos Mendes,
José Barreto Campello Carvalheira

Universidade Estadual de Campinas, Campinas, SP, Brazil

Introduction: Patients with gastric cancer are at high nutritional risk and frequently develop cancer cachexia, a condition associated with systemic inflammation and poorer treatment response and prognosis. Even in the absence of metastatic disease on standard imaging, metabolic and inflammatory alterations may already reflect the interaction between tumor biology and host response. **Case Report:** A 70-year-old female patient was diagnosed on October 11, 2023, with gastric cancer located in the antrum, pathological stage as IV (T3N2M1), ECOG 0. She underwent exclusive surgical treatment with partial gastrectomy on April 16, 2024, at the Hospital de Clínicas of UNICAMP. The PET-CT scan showed FDG uptake in the thickened gastric wall, but without signs of metastases. However, surgery identified metastasis in adipose tissue of the greater curvature/omentum. Preoperative

nutritional assessment revealed severe weight loss (18.44% over 6 months), low Body Mass Index (19.9 kg/m^2) and a low hand grip strength (10 kg). The patient was classified with severe malnutrition by the Patient-Generated Subjective Global Assessment (PG-SGA). Cachexia was diagnosed according to both Global Leadership Initiative on Malnutrition – GLIM criteria (weight loss, low BMI, low muscle mass, reduced food intake, and systemic inflammation evidenced by a neutrophil-to-lymphocyte ratio [NLR] of 11.5) and Fearon criteria (weight loss, low BMI, low muscularity, and inflammation). Body composition assessment by computed tomography at the level of the third lumbar vertebra demonstrated low muscle mass (Skeletal Muscle Index -SMI of 34.6 cm^2/m^2). Preoperative plasma analysis using multiplex technology revealed elevated levels of GDF-15 (1825.76 pg/mL), associated with an altered inflammatory and metabolic profile, including IL-6 of 4.51 pg/mL, TNF-a of 2.64 pg/mL, interferon-? of 2.54 pg/mL, and insulin of 265.48. During follow-up, the patient experienced disease progression and died of sepsis, with an overall survival of 9 months. The study was approved by the local Ethics Committee (CAAE:76237023.0.0000.5404). **Discussion:** Although the patient underwent standard imaging procedures during initial staging, no radiological evidence of metastatic disease was identified. However, she already exhibited a preoperative phenotype characterized by systemic inflammation, low skeletal muscle mass, severe malnutrition, and established cachexia, conditions consistently associated with poorer prognosis in gastric cancer. The integration of imaging findings with body composition analysis, inflammatory biomarkers, and comprehensive nutritional assessment tools enabled the early identification of a high-risk clinical and nutritional profile that was not captured by anatomical staging alone. Elevated GDF-15 levels further support its role as a mediator of anorexia, muscle wasting, and adverse clinical outcomes, reinforcing its potential value as a prognostic biomarker. **Conclusion:** This case highlights the importance of integrating nutritional status, body composition, and inflammatory and metabolic biomarkers into the initial assessment of patients with gastric cancer. The presence of cancer cachexia may indicate occult metastatic disease, particularly peritoneal carcinomatosis not detected by conventional imaging, allowing earlier identification of patients at higher prognostic risk and supporting more individualized clinical decision-making.

Keywords: Cachexia, Body composition, Stomach neoplasms, Nutrition assessment, Inflammation mediators.

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18F-PSMA PET/CT IN THE MULTIMODAL ASSESSMENT OF METASTATIC GASTRIC ADENOCARCINOMA: A CASE REPORT

Renata Erbert Contriciani,
Fabíola Furtuoso Zarpelão,
Larissa Ariel Oliveira Carrilho,
Barbara Cipriano, Leo Victor Kim,
Sandra Regina Branbilla,
Caroline Torricelli Corrêa,
Natália Tobar Toledo Prudente da Silva,
Luiz Roberto Lopes, Nelson Adami Andreollo,
Maria Carolina Santos Mendes,
Elba C.S.C. Etchebehere,
José Barreto Campello Carvalheira

Universidade Estadual de Campinas, Campinas, SP, Brazil

Introduction: The expression of Prostate Specific Membrane Antigen (PSMA) in the neovascular endothelium of non-prostatic tumors has presented new diagnostic perspectives. This report describes a young female patient with metastasis from gastric adenocarcinoma who underwent 18F-PSMA PET/CT during staging. **Case Report:** A 42-year-old female with no prior oncologic history was diagnosed with metastatic gastric adenocarcinoma (cT4bN3M1). As part of an institutional clinical trial, she underwent 18F-FDG and 18F-PSMA PET/CT before treatment initiation. Imaging revealed central nervous system (CNS) involvement, non-regional lymphadenopathy, bone metastasis and muscle implants. In the primary tumor, 18F-FDG uptake was higher than 18F-PSMA (SUVmax 23.5 vs. 6.4). A 1.5 cm brain metastasis in the left frontal lobe showed substantial uptake in both studies (SUV max 9.1 for PSMA vs. 15.4 for FDG). Notably, 18F-PSMA exclusively identified additional focal areas in the right frontal and temporal lobes (SUV max 9.2), further imaging studies are pending. Additionally, a T6 vertebral lesion (SUVmax 4.8) was present in the PSMA study and was occult on 18F-FDG PET/CT. The patient was referred for CNS radiotherapy and initiated palliative chemotherapy with capecitabine and oxaliplatin. **Discussion:** The clinical utility of PSMA PET/CT in gastric cancer remains poorly explored in the literature. In this case, PSMA PET/CT demonstrated significant uptake in CNS and bone lesions, suggesting sensitivity for detecting specific metastatic sites through tumor neovasculature imaging. **Conclusion:** 18F-PSMA PET/CT represents a promising diagnostic tool in non-prostate malignancies and may provide incremental diagnostic value when used in conjunction with 18F-FDG PET/CT. Further clinical trials investigating the role of PSMA-targeting tracers in gastrointestinal cancers are warranted.

Keywords: Metastatic gastric cancer, 18F-PSMA PET/CT, 18F-FDG PET/CT, Multimodal imaging.

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