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Case Report

Utility of different positron emission tomography/computed tomography tracers in the evaluation of incidentally detected dual malignancies: An experience from a tertiary care center

ABSTRACT

Multiple primary malignancies in a cancer patient are not a rare occurrence. The most common presentation of multiple primary malignancies is dual malignancies. The usefulness of different positron emission tomography (PET)/computed tomography (CT) tracers in the evaluation of dual synchronous primary malignancies is not well documented. Here, we present a case series, where two patients, referred for PET/CT, after being diagnosed with one primary malignancy were found to be having a second primary malignancy, diagnosed incidentally in PET/CT, further validated by PET/CT with another tracer.

Keywords: Dual malignancies, fluorodeoxyglucose positron emission tomography/computed tomography, positron emission tomography/computed tomography tracers, prostate-specific membrane antigen positron emission tomography/computed tomography

INTRODUCTION

Multiple synchronous or metachronous malignancies in a single cancer patient are not a rare occurrence. Although ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is the workhorse of positron emission tomography (PET) imaging, the main disadvantage of ^{18}F-FDG is its limited utility in few malignancies such as prostate cancer, hepatocellular carcinoma (HCC), neuroendocrine tumors (NETs), and renal cell carcinoma, due to varying tumor biology mechanisms. In this case series, we have demonstrated the utility of other PET tracers such as ^{68}Ga-labeled prostate-specific membrane antigen (PSMA) in complementing the role of ^{18}F-labeled FDG in diagnosis of dual malignancies in patients.

CASE REPORTS

Case no. 1

A 73-year-old patient, a recently diagnosed case of carcinoma prostate, was referred for ^{68}Ga PSMA PET/computed tomography (CT) scan for staging. MIP ^{68}Ga PSMA PET/CT scan [Figure 1b] revealed ^{68}Ga PSMA avid lesions in the prostate gland, corresponding to the known carcinoma prostate [white arrow in Figure 1B1] with multiple non-PSMA avid lesions in the liver, multiple osteolytic skeletal lesions with multiple non-PSMA avid cervical, mediastinal, and abdominal lymph nodes [Figure 1B3-1B4], and suspicious of tuberculosis or synchronous malignancy. In view of suspicion

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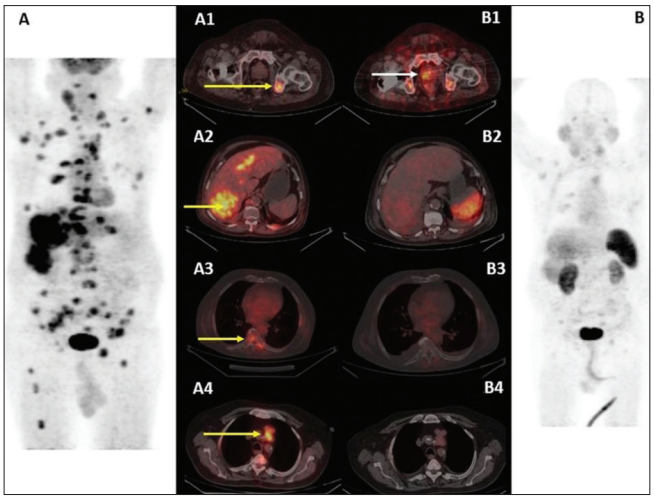

Figure 1: MIP image of whole-body ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan (A). MIP image of whole-body ^{68}Ga prostate-specific membrane antigen positron emission tomography/computed tomography scan (B). The axial fused ^{68}Ga prostate-specific membrane antigen positron emission tomography/computed tomography (B1) image showing prostatomegaly with focally increased prostate-specific membrane antigen uptake and multiple nonprostate-specific membrane antigen avid lymph nodes and hypodense coalescent lesions (B2-B4) in liver and multiple intraosseous and osteolytic skeletal lesions. The axial fused ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography images showed multiple FDG avid lesions involving liver, skeletal lesions, and mediastinal lymph nodes [Figure 2A1-A4]

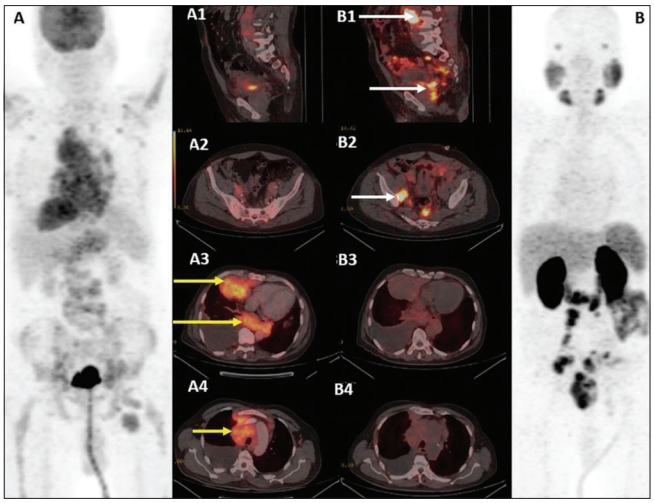

Figure 2: MIP image of whole-body ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan (A). MIP image of whole-body ^{68}Ga prostate-specific membrane antigen positron emission tomography/computed tomography scan (B). The axial fused ^{68}Ga prostate-specific membrane antigen positron emission tomography/computed tomography (B1 and B2) images showing prostatomegaly with multiple ^{68}Ga prostate-specific membrane antigen avid lesions in the prostate with multiple prostate-specific membrane antigen avid iliac lymph nodes and multiple nonprostate-specific membrane antigen avid mediastinal and parasternal lymph nodes (B3 and B4). The axial fused ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography images (A3 and A4) showed multiple FDG avid mediastinal and parasternal lymph nodes (A3 and A4). The axial fused ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography images (A1 and A2) also showed mild ^{18}F-fluorodeoxyglucose uptake in the prostate gland lesions and iliac lymph nodes

of synchronous malignancy or tuberculosis, the patient underwent an ^{18}F-FDG PET/CT scan. The MIP ^{18}F-FDG PET/CT scan [Figure 1a] showed ^{18}F-FDG uptake in discrete and coalescent lesions in the liver, multiple osteolytic skeletal lesions, and multiple cervical, mediastinal, and abdominal lymph nodes [Figures 1A1-1A4]. The ^{18}F-FDG PET/CT scan showed no significant ^{18}F-FDG uptake in the lesions in the prostate gland. Thus, the ^{18}F-FDG PET/CT increased the chances of dual pathologies in the patient. Histopathology from the liver lesions and mediastinal lymph nodes demonstrated features of mantle cell lymphoma, confirming the diagnosis of synchronous malignancy in the patient.

Case no, 2

A 73-year-old patient, a recently diagnosed case of carcinoma prostate, was referred for ^{68}Ga PSMA PET/CT scan for staging. ^{68}Ga PSMA PET/CT scan [Figure 2b] revealed prostatomegaly with multiple ^{68}Ga PSMA avid lesions in the prostate with extension to urinary bladder and bilateral seminal vesicles with multiple PSMA avid iliac lymph nodes [Figure 2B1 and B2], with non-PSMA avid mediastinal and parasternal lymph nodes with mass formation [Figure 2B3 and B4], and suspicious of tuberculosis or synchronous malignancy. In view of suspicion of synchronous malignancy or tuberculosis, the patient underwent an ^{18}F-FDG PET/CT scan. The ^{18}F-FDG PET/CT scan [Figure 2a] showed intensely ^{18}F-FDG avid mediastinal and parasternal lymph nodes with mass formation [Figure 2A3 and A4]. The ^{18}F-FDG PET/CT scan showed mild ^{18}F-FDG uptake in the lesions in the prostate gland [Figure 2A1] and iliac lymph nodes [Figure 2A2]. Thus, the ^{18}F FDG PET/CT increased the chances of dual pathologies in the patient. Histopathology from the mediastinal lymph nodal mass formation demonstrated features of diffuse large B cell lymphoma, confirming the diagnosis of synchronous malignancy in the patient.

DISCUSSION

Multiple primary malignancies in a cancer patient are not a rare occurrence. The diagnosis of a second or a third primary is not easy to arrive at due to the possibility of recurrent or secondary lesions from the known existing primary malignancy.[1] Timely diagnosis and appropriate management can alter the overall prognosis and survival in multiple primary malignancies. The first case of multiple primary malignancies was described by Billroth in 1889.[2] The most common presentation of multiple primary malignancies is dual malignancies.[3] Multiple primary malignancies can be divided into synchronous or metachronous on the basis of the time interval between the diagnosis of the two

primaries. Synchronous or "simultaneous" malignancies are those primary tumors that occur in the same patient within 6 months of each other, whereas metachronous or "interval" malignancies are those that occur in the same patient separated by a period of more than 6 months.[4] PET/CT is a technological advancement having a significant impact in oncology. Currently, ^{18}F-FDG represents the workhorse in oncological PET/CT imaging. The basis for using FDG in oncology was demonstrated by Warburg, who observed an increase in glycolytic activity in cancer cells under both aerobic and anaerobic conditions.[5] The main disadvantage of ^{18}F-FDG is that it is not a specific oncological tracer, as several malignancies (i.e., prostate cancer, HCC, NETs, renal cell carcinoma) cannot be adequately assessed by ^{18}F-FDG PET. Therefore, other new radiopharmaceuticals have been developed that are capable of giving more specific information, leading to better sensitivity and specificity or just complementing ^{18}F-FDG PET results.[6]

The most important characteristic of NETs is the expression of somatostatin receptors (SSTR) on their cell membrane, namely SSTR1–5. The SSTR2, SSTR3, and SSTR5 subtypes are particularly overexpressed on the cell membranes of NETs in most of the cases.[7] Various ^{68}Ga-DOTA-peptides show affinity to SSTR2, SSTR3, and SSTR5 and are excellent candidates for imaging and staging patients with NETs, including the localization of primary tumors in patients with known NET metastasis (carcinoma of unknown primary origin with sensitivity and specificity ranging from 97% to 100% and 96% to 100% in various series).[8,9] Since NETs are heterogeneous group of neoplasm and tumor heterogeneity cannot be completely assessed by tumor biopsy becasue limited tissue in some cases may not give accurate Ki-67 index value. The Ki-67 index value may vary in primary and metastatic lesions, or it may vary over time in the same patient in response to treatment and progression of the disease. Thus, dual-tracer imaging with Ga-68 DOTANOC and FDG PET/CT scan may reflect different aspects of tumor biology, SSTR expression, and glucose metabolism. However, dual-tracer imaging is helpful in patients with Ki-67 index >10%.

PSMA is a cell surface protein expressed abundantly in prostate carcinoma cells.[10] While choline metabolism has not increased in a large number of cases, PSMA is overexpressed in most prostate carcinoma.[11] ^{68}Ga-labeled PSMA ligands can detect prostate cancer relapses and metastases with high sensitivity.[12,13] Liver metastases are the third most common site for systemic spread in prostate cancer after bone and lung. ^{68}Ga PSMA PET/CT scan can produce false-negative liver metastases in advanced metastatic castration-resistant prostate cancer as they lose PSMA expression. A possible explanation for the same could be the diversity of phenotypes in metastases. In prostate cancer, liver metastases are frequently associated with neuroendocrine differentiation characteristics. In our cases, the non-PSMA avid liver lesions were initially suspected to be prostate cancer metastases; however, since there were many other non-PSMA avid lesions, FDG PET/CT scan was advised and this scan demonstrated multiple FDG avid and later biopsy confirmed diagnosis of lymphoma also. The usefulness of dual-tracer PET/CT in evaluating dual synchronous primary malignancies is not well documented.

Our two cases were carcinoma prostate and lymphoma; thus, ^{18}F-FDG and PSMA PET tracers helped in reaching the diagnosis. In these patients, the second PET/CT was advised to look for the most appropriate site of biopsy to characterize nontracer avid lesions in the first PET/CT scan and in case of second malignancy to stage the other malignancy. After review of literature, we came across only one case report describing role of dual PET/CT tracer in the evaluation of dual malignancies.[14] Rest of the case reports described role of dual PET/CT tracer imaging in the evaluation of single malignancy.[15,16].Here, we report an interesting case series about the use of dual-tracer PET/CT in the evaluation of in dual primary malignancies.

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Conflicts of interest

There are no conflicts of interest.

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