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^{18}F-FDG PET/CT imaging features of Cardiac Arrhythmia - induced by Panitumumab

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Abstract:

Panitumumab is a new humanized anti-epidermal growth factor receptor (EGFR) monoclonal antibody (mAb) approved for the treatment of advanced colorectal cancer. There is an increase in the use of this drug due to a good response rate and possible secondary resection in advance colorectal cancer. Here we present ^{18}F-FDG PET/CT imaging findings of cardiac arrhythmia in a patient receiving Panitumumab for the treatment of metastatic infiltrating rectal adenocarcinoma. Cardiotoxicity is a known adverse effect associated with Panitumumab. By far to our knowledge, no documented imaging findings for the same are available in the literature.

Clinical History:

A 68 years old non-smoker male presented with intermittent hematochezia of 6 months duration. He underwent colonoscopy examination, which showed a large fungating, ulcerated, and non-obstructing mass in the rectum. Biopsy from the lesion revealed infiltrating adenocarcinoma of the rectum. The carcinoembryonic antigen (CEA) level was high and KRAS/NRAS/BRAF wild type was positive. The patient underwent ^{18}F-FDG PET/CT scan for staging which showed FDG avid right lobe hepatic lesion in addition to FDG avid rectal wall thickening and perirectal lymph nodes. The myocardium demonstrated diffuse blood-pool tracer activity without any distinct abnormal focal tracer uptake (Figure-1). Biopsy from the liver lesion was positive for adenocarcinoma metastasis. The patient was staged as advanced colorectal adenocarcinoma(Stage IV) and was started on the FOLFOX regimen(folinic acid, fluorouracil, and oxaliplatin) with Panitumumab. There was interim microwave thermal ablation of the hepatic lesion. Post 8 cycles of combination chemotherapy, a follow-up ^{18}F-FDG PET/CT scan was performed 9 months after the prior imaging. It demonstrated reduction in metabolic activity of primary rectal mass lesion and resolution of FDG avidity in metastatic hepatic lesion. There was an incidental finding of intense FDG uptake in bilateral atrial walls, more intense in the left atrium, with maximum metabolic activity (SUV_{max}) of 9.2 (Figure-2). The patient underwent cardiac evaluation with electrocardiography which showed irregular rhythm with changes of left axis deviation, atrial fibrillation, and rapid ventricular response (Figure-3). Echocardiography showed normal systolic function with an ejection fraction of 55 % and no evidence of thrombus. Comprehensive metabolic

panel including electrolytes were within normal range. A clinical diagnosis of cardiac arrhythmia secondary to cardiotoxicity of EGFR inhibitor Panitumumab was postulated. The patient was put off panitumumab and treated with diltiazem and a future plan for abdomino-perineal resection of rectal tumor mass was considered.

Discussion:

Colorectal cancer is one of the most common cancers worldwide. Median survival in metastatic colorectal cancer has improved due to combined use of chemotherapy and targeted agents *(1)* such as anti-vascular endothelial growth factor and anti–EGFR therapies. Panitumumab is a human immunoglobulin G2 monoclonal antibody against EGFR. It binds with the EGFR and reduces cell proliferation and induces apoptosis *(2)*. There are adverse effects associated with Panitumumab, like skin-related toxicities and cardiac arrhythmias. Pre-existing cardiac disease and hypertension are assumed to increase the risk of developing cardiac arrhythmia *(3)*. Wei-Xiang Qi et al reported an overall increase of 8.4 % incidence of cardiac events in Panitumumab combination therapy as compared to 6.8% in chemotherapy alone *(3)*. ^{18}F-FDG PET/CT usually demonstrates variable tracer uptake in the myocardium, which is presumed to be due to shifting of metabolism between glucose and fatty acids *(4)*. However, in cases of cardiac arrhythmia, there may be distinctly abnormal increased myocardial FDG uptake *(5)*. According to a study published by Mathieu Sinigaglia et al. *(6)*, diffuse increased FDG uptake in the atrium was seen in one-third of the patients with atrial fibrillation, and intensity of FDG uptake was associated with underlying heart rhythm. The article also suggested an increased risk of stroke association with detectable abnormal atrial FDG

uptake. Though FDG uptake in the myocardium is considered non-specific on FDG PET scans performed for oncology purposes, for the above-mentioned reason, the reading physician should be aware of certain patterns of tracer uptake indicative of the underlying disease process. As seen in this case, the patient treated with Panitumumab had new atrial fibrillation with increased atrial wall FDG activity, findings were attributed to possible cardiotoxicity, known to be associated with anti-EGFR immunotherapy.

Conclusion:

Incidental findings in whole-body ^{18}F-FDG PET/CT scans performed on oncology patients may point towards underlying metabolic abnormalities. Although cardiac uptake on whole-body FDG PET scan is nonspecific, occasional abnormal myocardial FDG uptake pattern may warrant further evaluation. Cardiotoxicity associated with Panitumumab may present as an abnormal finding on FDG PET scan, as demonstrated in this presented case. Knowledge about such patterns of tracer uptake may improve diagnostic efficiency and contribute to holistic patient care.

References:

1. Cremini C, Schirripa M, Antoniotti C, et al. First-line chemotherapy for mCRC—a review and evidence-based algorithm. *Nat Rev ClinOncol*. 2015; 12(10):607-619.

2. Anandappa G, Cunningham D. Panitumumab Alone for Maintenance Treatment in Advanced Colorectal Cancer. *JAMA Oncol*. 2019; 5(9):1262–1264.

3. Wei-xiang Qi, Shengguang Zhao, JiayiChen.Risk factors for developing cardiac toxicities in cancer patients treated with panitumumab combination therapy. *Future Oncology*. 2020; 16(19): 1359-1370.

4. Fujii H, Ide M, Yasuda S, Takahashi W, Shohtsu A, Kubo A. Increased FDG uptake in the wall of the right atrium in people who participated in a cancer screening program with whole-body PET.*Ann Nucl Med*. 1999 Feb;13(1):55-9.

5. Gupta K, Jadhav R, Prasad R, Virmani S. Cardiac uptake patterns in routine 18F-FDG PET-CT scans: A pictorial review. *J NuclCardiol*. 2020 Aug; 27(4):1296-1305.

6. Sinigaglia M, Mahida B, Piekarski E, Chequer R, Mikail N, Benali K, Hyafil F, Le Guludec D, Rouzet F. FDG atrial uptake is associated with an increased prevalence of stroke in patients with atrial fibrillation. *Eur J Nucl Med Mol Imaging*. 2019 Jun; 46(6):1268-1275.

Figures and Legends:

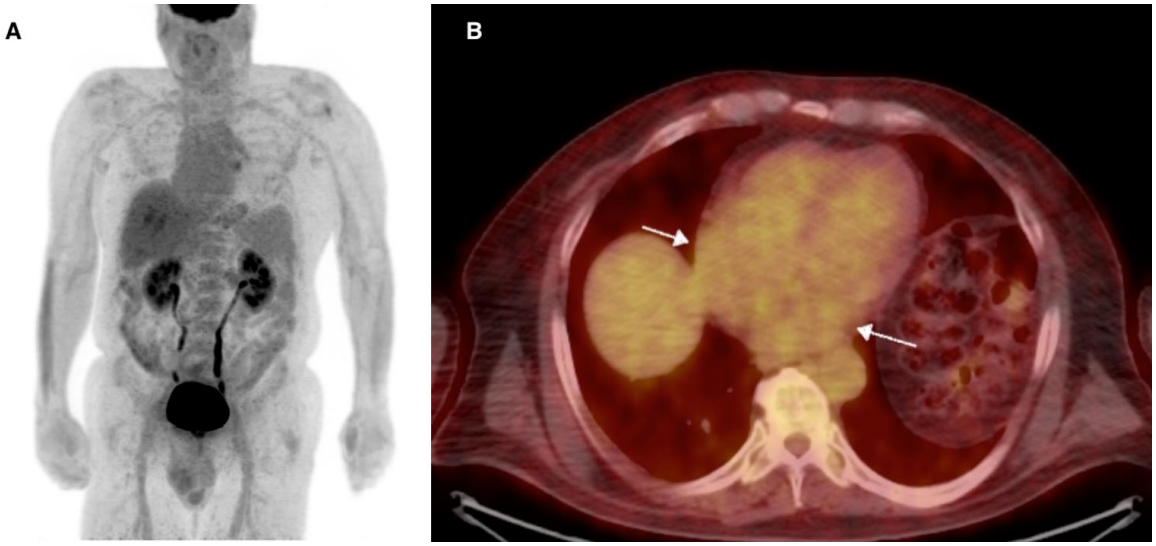

Figure 1: (A) MIP (Maximum Intensity Projection) image of whole-body ^{18}F-FDG PET/CT pre-therapy staging scan in a patient with colorectal cancer, acquired 62 minutes after IV injection of 9.8 mCi of ^{18}F-FDG. (B) Trans-axial fused ^{18}F-FDG PET/CT image demonstrating diffuse blood-pool FDG activity in the myocardium (white arrows) SUV_{max} 3.3 and SUV_{min} 1.8.

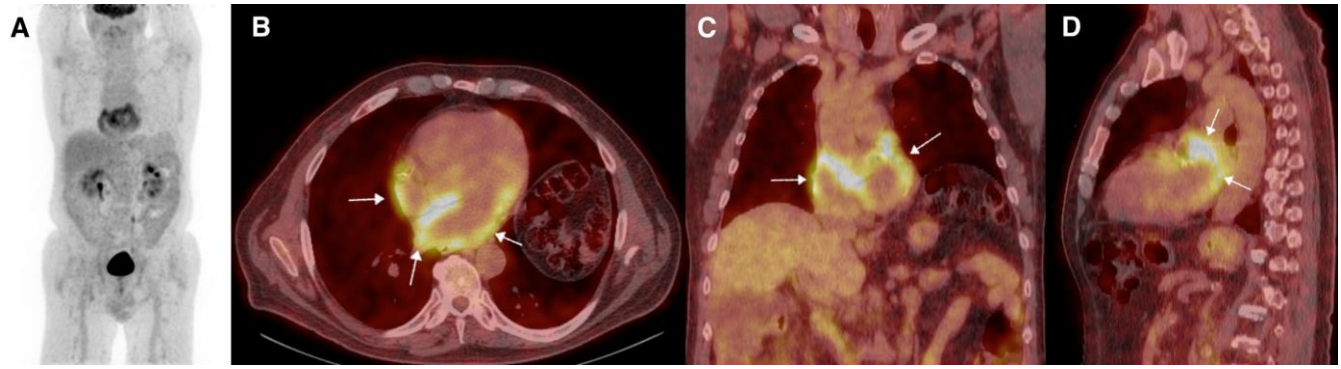

Figure 2: (A) MIP image of whole-body ^{18}F-FDG PET/CT scan in the patient post combination therapy (Folfox regimen + Panitumumab) for colorectal cancer, acquired 66 minutes after IV injection of 11.8 mCi of ^{18}F-FDG. Trans-axial (B), coronal (C), and sagittal (D) fused ^{18}F-FDG PET/CT images demonstrating intense FDG uptake in the myocardial wall in bilateral atria (white arrows), more intense in the left atrium with SUV_{max} 9.2 and SUV_{min} 5.9.

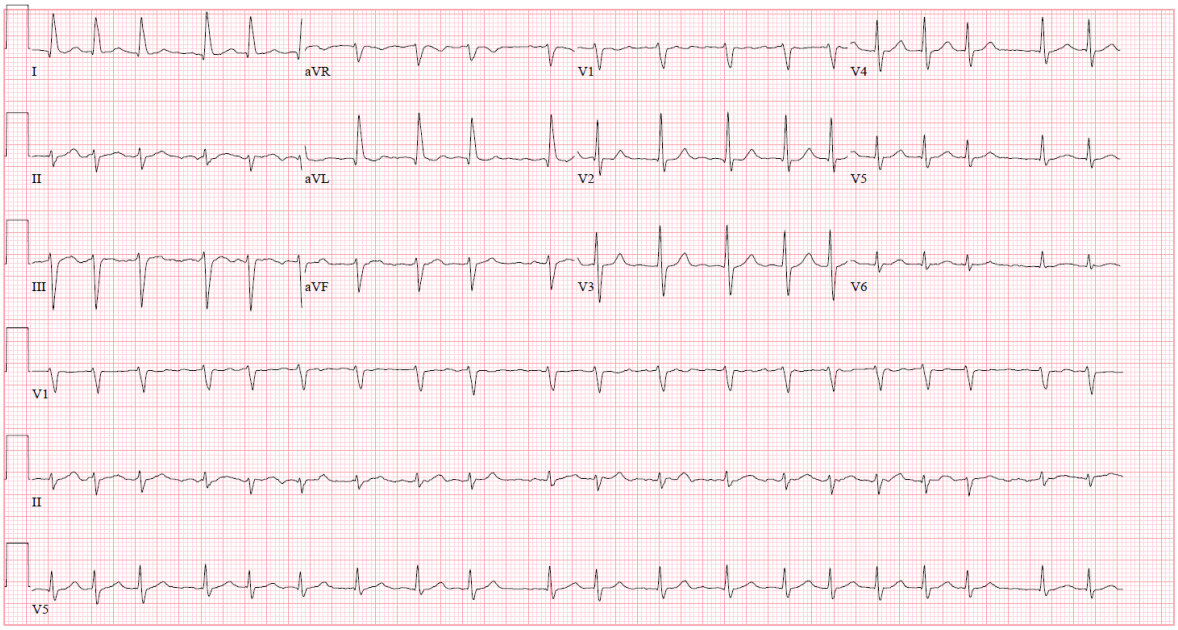

Figure 3: Electrocardiography demonstrating irregular rhythm with changes of left axis deviation, atrial fibrillation and rapid ventricular response.