Letter to the Editor

Focal myocardial ^{18}F-fluorodeoxyglucose (^{18}F-FDG) uptake occasionally revealed by whole-body positron emission tomography/computed tomography (PET/CT) imaging in a patient suspected to have a lung tumor indicated myocardial ischemia caused by severe coronary artery disease

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Introduction

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) imaging is widely used in the diagnosis, staging, and evaluation of therapeutic responses in malignant tumors (1). Previous studies (2,3) have reported that some tumor patients exhibit distinct abnormal uptake patterns in the left ventricle during whole-body ^{18}F-FDG PET/CT imaging. When myocardial ischemia occurs, there is a shift in myocardial energy substrate utilization from free fatty acids to glucose, resulting in the increased uptake and use of glucose (4,5). After myocardial ischemia-reperfusion, there is a prolonged persistence of myocardial metabolic abnormalities, characterized by delayed recovery, which is a hallmark of myocardial ischemia known as "ischemic memory" (5-7). ^{18}F-FDG PET/CT whole-body imaging can simultaneously provide information on abnormal cardiac imaging while evaluating tumors. The careful identification of myocardial ^{18}F-FDG uptake patterns during image analysis may aid in the identification of potential cardiovascular diseases, thereby providing additional valuable information for patient clinical diagnosis, treatment, and decision-making management.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 70-year-old man was admitted to the Third Affiliated Hospital of Soochow University as "pulmonary nodules had been found on physical examination for one year". A nodule had been detected in his upper left lung one year ago during a chest examination. A subsequent CT scan of the chest 10 days before his admission revealed an enlargement of the nodule (measuring approximately 1.3 cm in diameter) in the upper left lung. An ^{18}F-FDG

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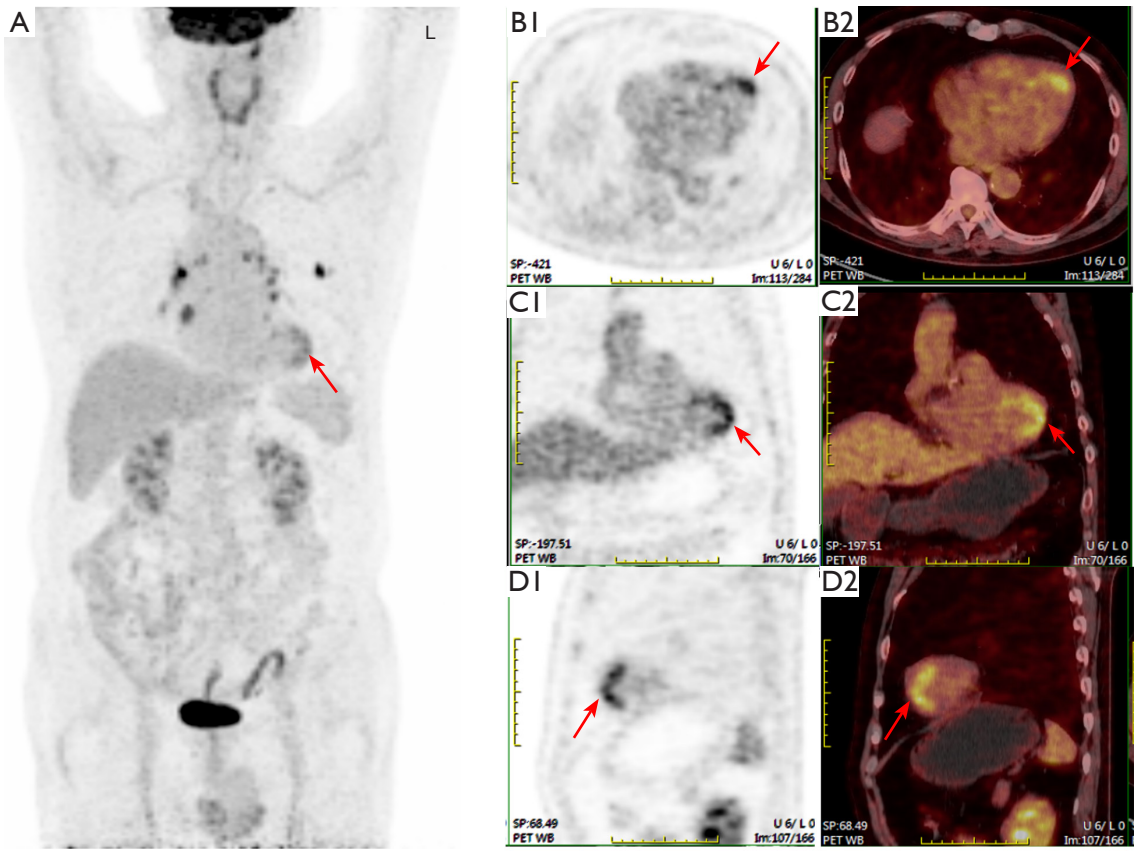

Figure 1 ^{18}F-FDG PET/CT image of the patient. (A) The whole-body PET maximum intensity projection showed focal abnormal uptake in the left ventricular myocardium (as indicated by the red arrow). PET images (B1-D1) and PET/CT fusion images (B2-D2) displayed in the transverse, coronal, and sagittal planes exhibited focal abnormal uptake in the apical anterior, apical, apical septal, and apical inferior of the left ventricular myocardium (as indicated by the red arrows). ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; PET/CT, positron emission tomography/computed tomography.

PET/CT whole-body examination was performed to evaluate if the pulmonary nodule was benign or malignant. The patient had experienced no apparent symptoms of chest pain, palpitations, shortness of breath, coughing, sputum production, or hemoptysis. For the past 10 years, the patient had been regularly taking amlodipine besylate tablets orally to manage hypertension. His blood pressure had been maintained at approximately 125–130/90–95 mmHg. In addition to treatment for hypertension, the patient had been taking statins for over five years to manage hyperlipidemia. He also had a history of smoking for more than 40 years, consuming approximately 20 cigarettes per day.

The laboratory tests revealed no significant abnormalities in the routine blood tests, urine analysis, stool analysis, or liver and kidney function. His serum tumor markers were within normal limits, including carcinoembryonic antigen, neuron-specific enolase, and squamous cell carcinoma-associated antigen. Cardiac markers, such as high-sensitivity troponin I, creatine kinase, and creatine kinase isoenzyme, were also within normal ranges. The electrocardiogram showed a sinus rhythm. Echocardiography did not reveal any significant abnormalities, and his left ventricular ejection fraction was measured at 55%.

Following a fasting period of more than six hours, the patient was intravenously administered ^{18}F-FDG (purchased from Nanjing JYAMS Electronic Research & Development Co., Ltd., Nanjing, China) at a dosage of 8 millicurie (mCi). Subsequently, a PET/CT whole-body scan was performed after a quiet rest period of 60 minutes. In addition to the pulmonary nodules, mediastinal and bilateral hilar lymph nodes, we accidentally observed focal abnormal uptake in the myocardium of the apical anterior,

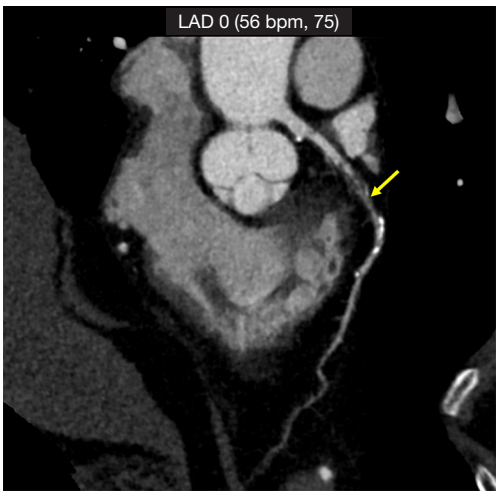

Figure 2 CCTA image of the patient. This CCTA image showed multiple calcified and non-calcified plaques in the LAD artery, with evident stenosis observed in the proximal and middle segments of the lumen. The narrowest point was approximately 68% (as indicated by the yellow arrow). CCTA, coronary computed tomography angiography; LAD, left anterior descending.

apical, apical septal, and apical inferior regions of the left ventricle, with a maximum standard uptake value of 5.0 on the ^{18}F-FDG PET/CT imaging (*Figure 1*). The focal uptake in the myocardium of the left ventricle was observed in the region dominated by the left anterior descending (LAD) artery, raising suspicion of accompanying coronary artery disease (CAD). Subsequently, we recommended the patient undergo a coronary computed tomography angiography (CCTA) examination. The CCTA examination revealed coronary arteriosclerosis characterized by multiple calcified and non-calcified plaques in the LAD artery, with significant luminal stenosis, reaching approximately 68% at its narrowest point (*Figure 2*). Additionally, calcified and mixed plaques were observed on the wall of the second diagonal branch, resulting in apparent luminal stenosis. Multiple calcifications were present on the left circumflex (LCX) artery, although the lumen did not exhibit significant narrowing. Mixed plaques were identified in the proximal and middle segments of the right coronary artery (RCA), with calcified, non-calcified, and mixed plaque compositions but no notable luminal stenosis.

Further inquiry into the patient's medical history revealed that for the past two years, he had experienced recurring chest discomfort following exercise. The discomfort was localized to the precordial region and was not accompanied by chest pain, palpitations, or dizziness. His symptoms typically subsided after a few minutes of rest without any intervention. However, the patient did not pay much attention to his symptoms.

Next, exercise and rest ^{99m}Tc methoxy-isobutyl-isonitrile (^{99m}Tc-MIBI) single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) were performed, and revealed severe reversible myocardial ischemia in the apical anterior, apical, apical septal, and apical inferior regions of the left ventricle (LAD artery blood supply area) (*Figure 3*). Subsequent coronary angiography (CAG) indicated no evident stenosis in the left main artery but revealed 90% stenosis in the proximal and middle segments of the LAD artery (*Figure 4*) with thrombolysis in myocardial infarction (TIMI) grade 0–1 distal flow. Additionally, there were findings of 30% proximal stenosis and 50% distal stenosis on the LCX branch with plaque infiltration, and plaque infiltration throughout the RCA with 50% stenosis in the proximal and middle segments. Based on these examination results, severe LAD artery stenosis resulting in myocardial ischemia was clinically considered, leading to the diagnosis of CAD.

The CAG of this patient revealed severe stenosis in the proximal and middle segments of the LAD artery. Both the MPI and ^{18}F-FDG PET imaging indicated myocardial ischemia in the region supplied by the LAD artery. Consequently, percutaneous coronary intervention (PCI) was successfully performed, and a stent was inserted into the LAD artery. Secondary prevention and treatment of CAD, health education, and regular follow-up were conducted after the procedure. The patient experienced significant improvement in chest discomfort after PCI, and no cardiovascular adverse events were observed during the three-year follow-up period.

Discussion and conclusions

^{18}F-FDG PET myocardial metabolic imaging is now routinely employed in clinical practice to assess myocardial viability and inflammation (8,9). The assessment of myocardial viability necessitates a glucose-insulin load beforehand to optimize ^{18}F-FDG uptake of viable myocardium, improve image quality, and facilitate accurate diagnosis (9). In the evaluation of suspected cardiac inflammation (such as sarcoidosis), ^{18}F-FDG PET/CT scans are typically conducted in a fasting state, and are achieved by administering heparin and adopting a high-fat diet to increase serum levels of free fatty acids, thereby suppressing

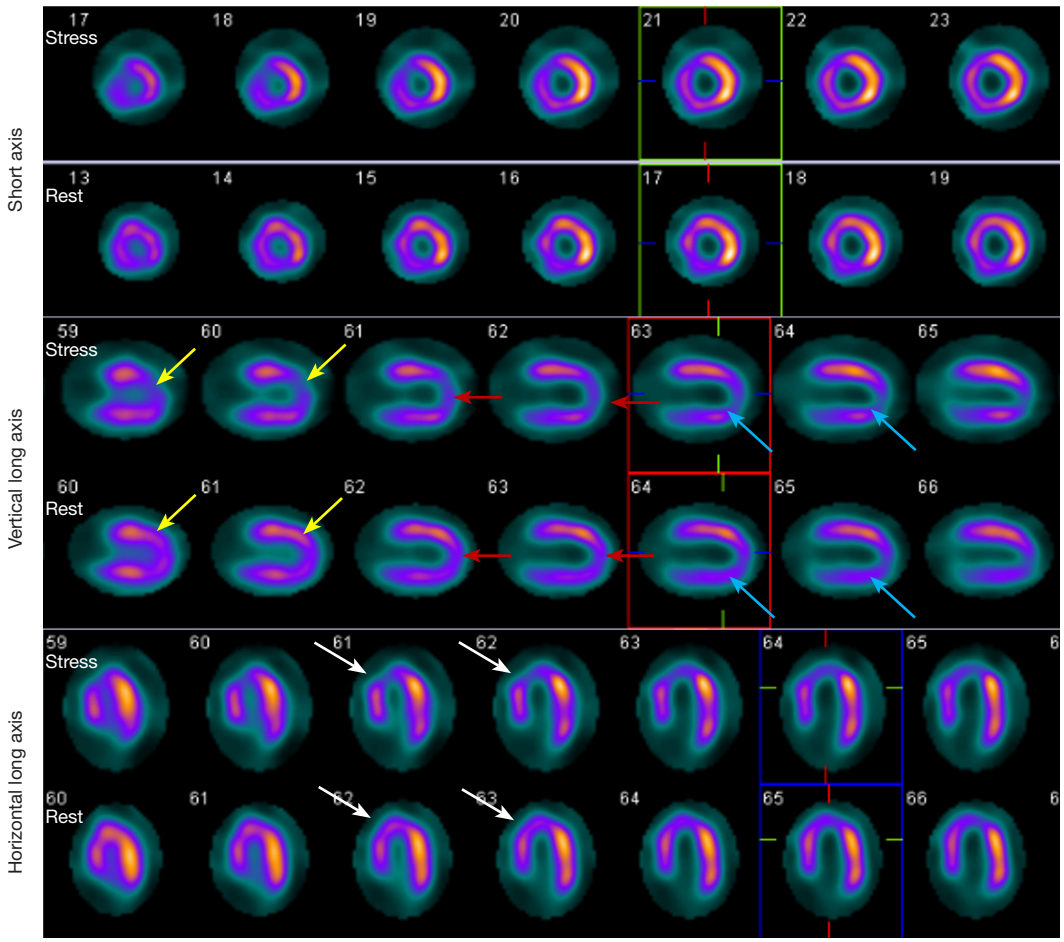

Figure 3 Stress-rest ^{99m}Tc-MIBI MPI image of the patient. This image revealed the reversible perfusion defects or sparsity in the apical anterior (as indicated by the yellow arrow), apex (as indicated by the red arrow), apical inferior (as indicated by the blue arrow), and apical septal of the left ventricular (as indicated by the white arrow), suggesting severe reversible myocardial ischemia corresponding to the territory supplied by the LAD artery. ^{99m}Tc-MIBI, ^{99m}Tc methoxy-isobutyl-isonitrile; MPI, myocardial perfusion imaging; LAD, left anterior descending.

the physiological uptake of ^{18}F-FDG by myocardial cells (9). Therefore, using ^{18}F-FDG PET/CT whole-body imaging of the tumor to assess myocardial viability and inflammation is not feasible.

According to the characteristics of myocardial "ischemic memory", ^{18}F-FDG PET/CT whole-body imaging may assist in the diagnosis of asymptomatic myocardial ischemia that has occurred in a patient's daily life. It is well known that there is a significant degree of regional variability in ^{18}F-FDG uptake by the left ventricular myocardium under fasting conditions (10). A prolonged fasting period helps suppress glucose uptake by the normal myocardium, thereby maximizing the difference in glucose uptake between non-ischemic and ischemic myocardium, allowing only the ischemic myocardium to be visualized (5). Hence, almost all published studies have reported that the patients were required to fast for at least 12 hours (or perhaps longer, if possible) to reduce plasma insulin levels, and thus physiological glucose uptake into normal cardiomyocytes (11). However, patients are only required to fast for more than six hours before undergoing ^{18}F-FDG PET/CT imaging of tumors. As the fasting period is relatively short, a certain proportion of patients may present diffuse uptake in the left ventricular myocardium (3), which may reduce the diagnostic sensitivity of the examination. Therefore, adequate preparation before the examination

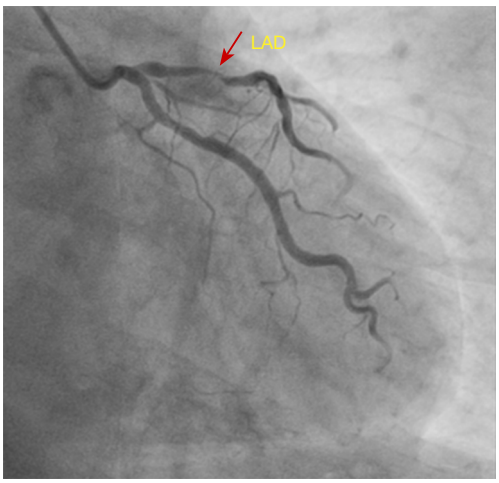

Figure 4 CAG image of this patient. The CAG image showed 90% stenosis in the proximal and middle segments of the LAD artery (as indicated by the red arrow), with distal blood flow graded as TIMI 0–1. CAG, coronary angiography; LAD, left anterior descending; TIMI, thrombolysis in myocardial infarction.

and the reasonable interpretation of images for such patients are very important.

Myocardial glucose uptake is influenced by various factors (12). During whole-body ^{18}F-FDG PET/CT examinations conducted under regular fasting conditions to assess non-cardiac diseases, regional ^{18}F-FDG uptake in the heart is occasionally observed. Common causes include CAD, pulmonary hypertension, and atrial fibrillation. The left ventricle is the most frequent site of abnormal uptake, and myocardial ischemia is one of the factors contributing to abnormal myocardial uptake in the left ventricle. Several studies (13,14) have shown that ^{18}F-FDG uptake remains increased for up to 48 hours following a myocardial ischemic event in patients with stable CAD. Dou *et al.* (15) reported that 86% of patients with unstable angina pectoris exhibited "focal" or "focal on diffuse" uptake, while only 8% of patients without unstable angina pectoris demonstrated such uptake. In patients with a well-established history of previous myocardial infarction, regional high uptake of ^{18}F-FDG indicates an ischemic but viable myocardium (hibernating myocardium) at the site of the infarction. However, in patients lacking a history of myocardial infarction or related evidence, the abnormal focal uptake of ^{18}F-FDG may signify persistent or recurrent myocardial ischemia (stunned myocardium) (2).

According to previous studies (15,16), myocardial ^{18}F-FDG uptake can be categorized into four patterns as follows: Pattern 1, "no uptake"; Pattern 2, "diffuse uptake"; Pattern 3, "focal uptake"; and Pattern 4, "focal on diffuse uptake". Abnormal uptake (which is indicative of myocardial ischemia) is defined as the presence of pattern 3 (focal uptake) or pattern 4 (focal on diffuse uptake). While focal uptake in the left ventricular basal segment (including the papillary muscles) is considered normal. There may be variations in physiological ^{18}F-FDG uptake in the myocardium; however, knowledge of the common uptake patterns of ^{18}F-FDG in the myocardium could aid in the identification of additional underlying diseases and facilitate patient management.

Aikawa *et al.* (17) reported a case in which a ^{18}F-FDG PET/CT examination of a female with malignant melanoma on the left calf revealed focal uptake in the anterior wall of the left ventricle. CAG confirmed the presence of severe stenosis in the LAD artery, indicating asymptomatic CAD with myocardial ischemia. The focal uptake in the left ventricular myocardium disappeared five months after successful PCI during follow-up. Minamimoto *et al.* (18) observed that incidental myocardial focal uptake in ^{18}F-FDG PET/CT tumor imaging was closely associated with a high risk of CAD. Another study (3) demonstrated that the abnormal ^{18}F-FDG uptake pattern in PET/CT was strongly correlated with abnormalities in MPI, including myocardial ischemia, myocardial scarring, and cardiac function impairment. Based on the mechanism of myocardial "ischemic memory", the focal uptake of ^{18}F-FDG is more likely to indicate myocardial ischemia if it corresponds to the distribution area of the coronary artery.

The patient in the present case frequently experienced chest tightness and discomfort, particularly after physical activity, along with hypertension, and hyperlipidemia, and also had smoking risk factors for CAD. Noninvasive imaging evaluation can provide additional valuable information for clinical diagnosis and treatment. Subsequently, CCTA revealed multiple calcifications in three vessels of the coronary artery. A previous study (19) confirmed that the presence of coronary artery calcification is a risk factor for acute coronary events. Moreover, the higher the coronary artery calcification score, the greater the risk of CAD (20). Therefore, in this case, the presence of multiple coronary artery calcifications suggested a high likelihood of CAD. The detection of coronary artery calcification on ^{18}F-FDG PET/CT imaging can also help to identify individuals at risk of acute coronary events, warranting further cardiac screening. Further, due to the

interference of coronary artery calcification artifacts, CCTA may not accurately estimate the degree of coronary artery stenosis, particularly when evaluating severe calcification, and thus has certain limitations. Consequently, in this case, the most severe stenosis in the LAD artery measured by CCTA software was only 68%.

Radionuclide stress-rest MPI is a noninvasive imaging technique commonly used to assess myocardial ischemia in clinical settings, and has high sensitivity and specificity (21). The results of the stress-rest MPI for this patient confirmed myocardial ischemia corresponding to the focal uptake of ^{18}F-FDG in the left ventricular myocardium observed on whole-body PET/CT imaging, further supporting the notion that ^{18}F-FDG focal uptake in the myocardium in this patient indicated myocardial ischemia in CAD. This confirms that patients with abnormal regional ^{18}F-FDG uptake in left ventricular myocardium on tumors whole-body PET/CT will benefit from further cardiovascular risk assessment. Therefore, further screening for cardiovascular disease and inquiries about past medical history is necessary when incidental myocardial focal uptake is observed during ^{18}F-FDG PET/CT tumor imaging. This additional evaluation can provide valuable information for clinical diagnosis and treatment.

As a physician specializing in nuclear medicine, it is imperative to thoroughly understand the pathological and physiological uptake patterns of ^{18}F-FDG in cardiomyopathy. Mastering the interpretation criteria for the abnormal uptake of ^{18}F-FDG in the left ventricular myocardium is essential, as is vigilance about abnormal cardiac uptake during tumor screening in clinical practice. We can accurately distinguish between normal and abnormal uptake patterns through these measures, thereby providing vital clues and evidence for clinical diagnosis and treatment.

In summary, ^{18}F-FDG PET/CT imaging not only provides insights into tumor evaluation, it also provides valuable information on cardiac abnormalities. It aids in the identification of potential cardiovascular diseases, and thus plays a pivotal role in the clinical diagnosis, treatment, and decision-making management of such patients.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-743/coif). F.Z. reports that she received funding from the Postgraduate Research and Practice Innovation Program of Jiangsu Province (Yangzhou University) (No. SJCX23_2021) and the Top Talent of Changzhou "The 14th Five-Year Plan" High-Level Health Talents Training Project (No. 2022-260). Y.W. reports that this work was supported by funding from the Key Research and Development Program of Jiangsu Province (Social Development) (No. BE2021638), the National Natural Science Foundation of China (No. 82272031), the Changzhou Clinical Medical Center (Nuclear Medicine) (No. CZZX202204), and the Clinical Medical Science and Technology High-end Platform and Transformation Base Construction Project of Soochow University (Characteristic Discipline) – Nuclear Medicine and Outstanding Talent of Changzhou "The 14th Five-Year Plan" High-Level Health Talents Training Project (No. 2022-260). The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying

images. A copy of the written consent is available for review by the editorial office of this journal.

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