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Interesting Images

# Dynamic and Static $^{18}\text{F}$ -FDG PET/CT Imaging in SMARCA4-Deficient Non-Small Cell Lung Cancer and Response to Therapy: A Rare Case

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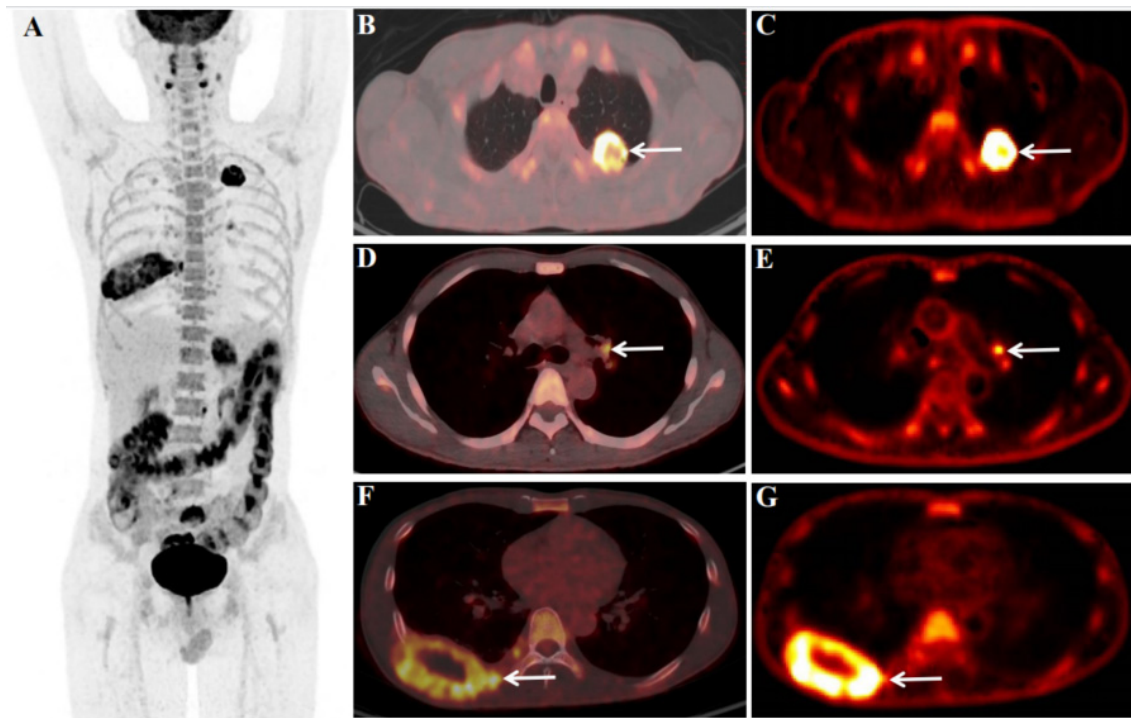
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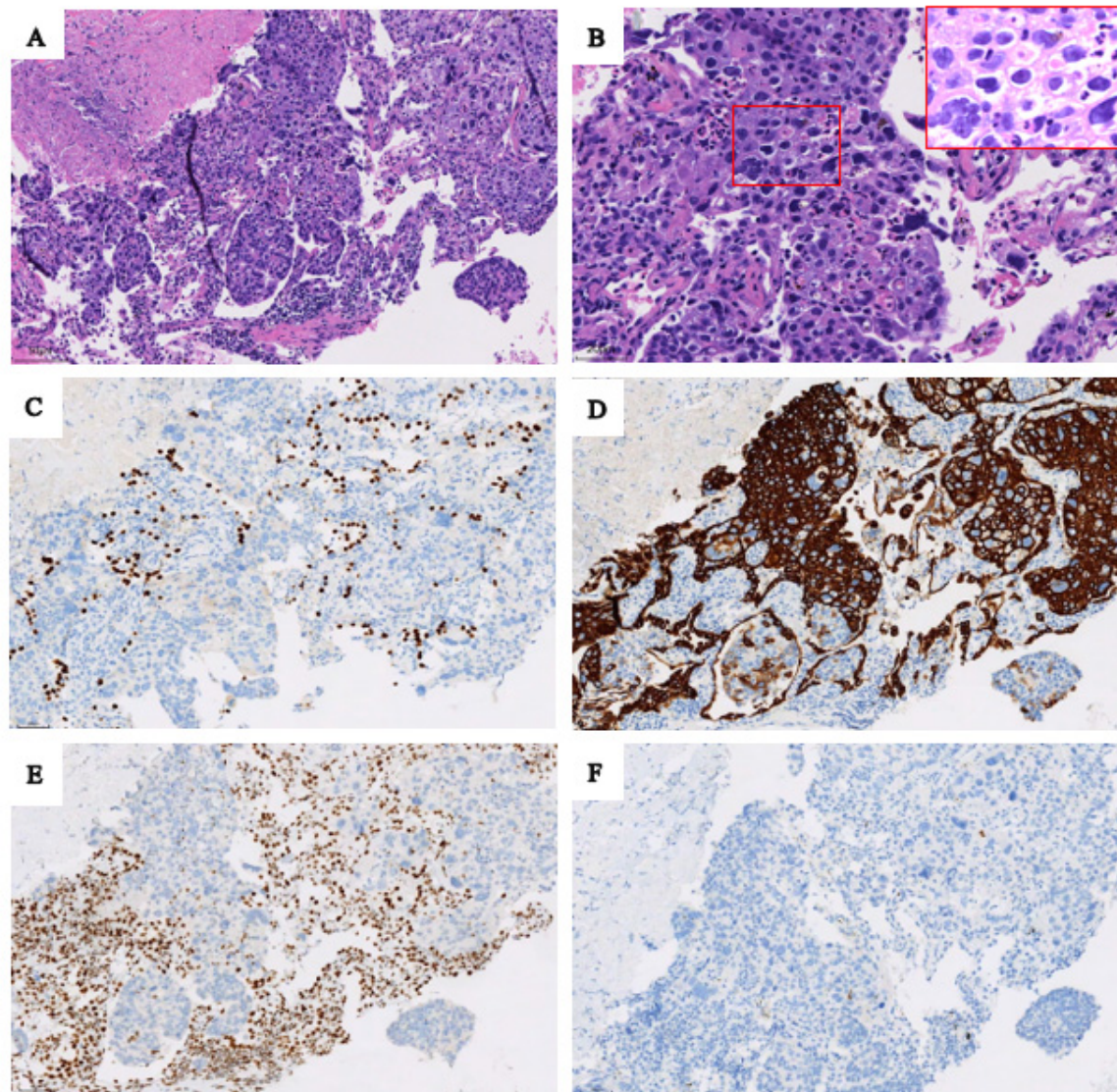
† These authors contributed equally to this work.

**Abstract:** SMARCA4-deficient non-small cell lung cancer (NSCLC) is a more recently recognized subset of NSCLC. We describe the  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) PET/CT findings in a rare case of SMARCA4-deficient NSCLC and response to therapy. A 45-year-old male patient with a history of heavy smoking (10 years) underwent an  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) PET/CT dynamic (chest) + static (whole-body) scan for diagnosis and pre-treatment staging.  $^{18}\text{F}$ -FDG PET/CT showed an FDG-avid mass in the upper lobe of the left lung ( $\text{SUV}_{\text{max}}$  of 22.4) and FDG-avid lymph nodes (LN) in the left pulmonary hilar region ( $\text{SUV}_{\text{max}}$  of 5.7). In addition, there are multiple metastases throughout the body, including distant LNs, adrenal glands, bone, left subcutaneous lumbar region, and brain. Pathological findings confirmed SMARCA-4 deficient NSCLC. After 4 cycles of chemotherapy and immune checkpoint inhibitors (ICI), the patient underwent again an  $^{18}\text{F}$ -FDG PET/CT scan (including dynamic scan) for efficacy evaluation. We report cases that deepen the understanding of the  $^{18}\text{F}$ -FDG PET/CT presentation of SMARCA4-deficient NSCLC as well as dynamic imaging features and parametric characteristics.

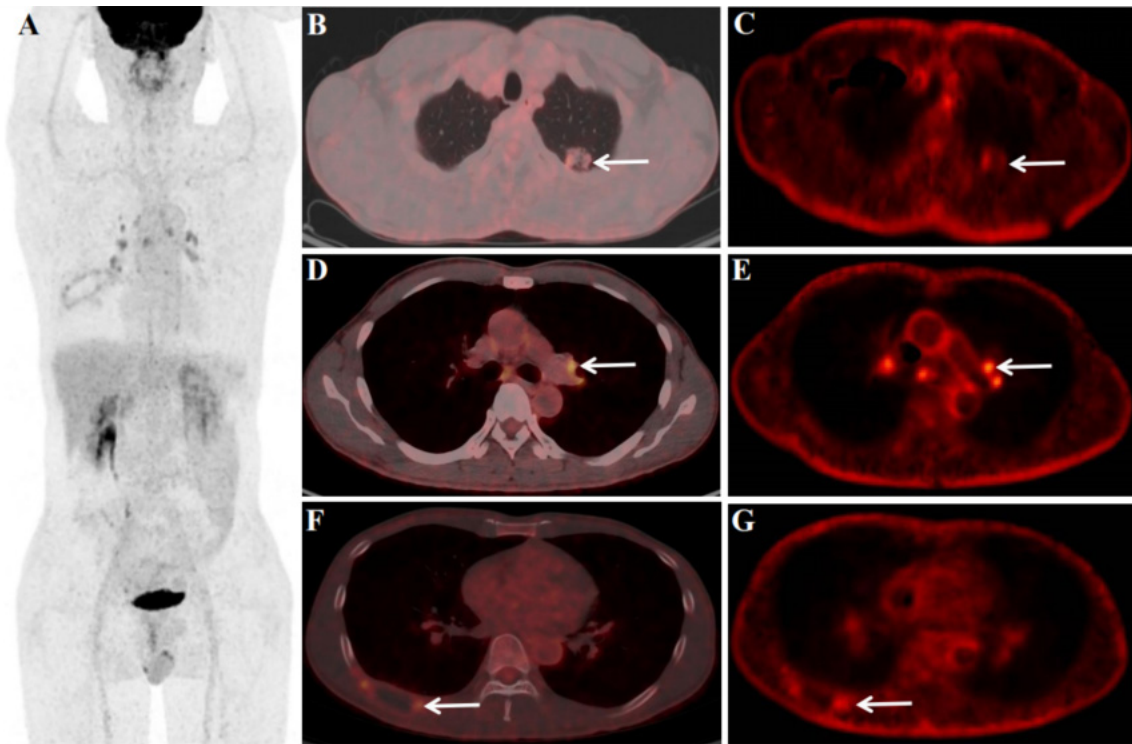
**Keywords:**  $^{18}\text{F}$ -FDG; PET/CT; SMARCA 4; NSCLC; Dynamic imaging; Efficacy evaluation



**Figure 1.** We report the case of a 45-year-old male patient with a history of heavy smoking (10 years, 20 cigarettes/day) underwent an  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) PET/CT dynamic (chest) + static (whole-body) scan for diagnosis and pre-treatment staging. The abnormal serum tumor markers associated with lung cancer before  $^{18}\text{F}$ -FDG PET/CT were CYFRA21-1 18.57 ng/ml ( $<3.3$ ) and CA125 64.60 U/ml ( $<35.0$ ). Before the  $^{18}\text{F}$ -FDG injection, the patient had fasted for at least 6 hours and had a pre-scan glucose level of 4.4mmol/L. According to the body mass index, the chest region PET scans (dynamic) was initiated immediately after the injection of  $^{18}\text{F}$ -FDG (7.07mCi) from an intravenous indwelling needle. The total dynamic scans lasted for 65 minutes. Dynamic scan data were partitioned into 28 frames as follows:  $6 \times 10$  s,  $4 \times 30$  s,  $4 \times 60$  s,  $4 \times 120$  s, and  $10 \times 300$  s. An additional whole-body static PET/CT scan was performed at the end of the dynamic acquisition. Quantitative parameters ( $K_i$ ) was obtained by applying the irreversible two-tissue compartment model using in-house Matlab software.  $^{18}\text{F}$ -FDG PET/CT showed an FDG-avid mass in the upper lobe of the left lung (Fig.1 B and C, white arrow), size of  $3.4 \times 3.0$ cm,  $\text{SUV}_{\text{max}}$  of 22.4 (Fig.1 B),  $K_i$  of 0.0525 ml/g/min (Fig.1 C), FDG-avid LN in the left pulmonary hilar region (Fig.1 D and E, white arrow), size of  $1.1 \times 0.9$ cm,  $\text{SUV}_{\text{max}}$  of 5.7 (Fig.1 D),  $K_i$  of 0.0231 ml/g/min (Fig.1 E), and bone destruction with the mass formation in the right 8th rib (Fig.1 F and G, white arrow), size of  $8.0 \times 4.5$ cm,  $\text{SUV}_{\text{max}}$  of 9.4 (Fig.1 F),  $K_i$  of 0.0214 ml/g/min (Fig.1 G). Multiple metastases throughout the body (Fig.1 A), including retroperitoneal LN (size of  $1.3 \times 1.0$ cm,  $\text{SUV}_{\text{max}}$  of 8.3), left adrenal gland (size of  $3.8 \times 3.5$ cm,  $\text{SUV}_{\text{max}}$  of 8.4), bone of the sacrum (size of  $3.6 \times 3.1$ cm,  $\text{SUV}_{\text{max}}$  of 10.9), left subcutaneous lumbar region (size of  $1.7 \times 1.3$ cm,  $\text{SUV}_{\text{max}}$  of 7.6), and brain (size of  $1.9 \times 1.8$ cm,  $\text{SUV}_{\text{max}}$  of 9.1).



**Figure 2.** Based on the  $^{18}\text{F}$ -FDG PET/CT findings, the patient underwent a puncture biopsy of a mass in the upper lobe of the left lung. Pathological and immunohistochemical findings confirmed SMARCA4-deficient NSCLC. Hematoxylin-eosin staining (original magnifications $\times 200$  [Fig2. A]) showed the tumor cells arranged in sheets and lobules, and (Fig2. B, original magnifications $\times 400$ ) showed sheets of large pleomorphic tumor cells with prominent nucleoli. At immunohistochemistry (original magnification $\times 200$ ), tumor cells were not express TTF1 (Fig2. C) with alveolar epithelial cells as internal positive controls; diffuse expression of cytokeratin 7 (Fig2. D) was seen in tumor cells, and loss of BRG1 protein (Fig2. E) in tumor cells with mesenchymal cells and inflammatory cells serving as internal positive controls, and P63 (Fig2. F) was a negative expression in tumor cells.



**Figure 3.** After 4 cycles of immune checkpoint inhibitors (ICI) and chemotherapy, the patient underwent an  $^{18}\text{F}$ -FDG PET/CT scan (including dynamic scan), the aim is to perform an efficacy evaluation. After treatment,  $^{18}\text{F}$ -FDG PET/CT dynamic + static scan showed a left lung primary foci were smaller than before and FDG uptake was reduced, size of  $2.1 \times 1.2\text{cm}$ ,  $\text{SUV}_{\text{max}}$  of 2.2 (Fig3. B),  $K_i$  of  $0.0070\text{ ml/g/min}$  (Fig3. C),  $\Delta\text{SUV}_{\text{max}}$  (pre-treatment  $\text{SUV}_{\text{max}}$  - treatment  $\text{SUV}_{\text{max}}$ /pre-treatment  $\text{SUV}_{\text{max}}$ ) of 90.18%, and  $\Delta K_i$  (pre-treatment  $K_i$  - treatment  $K_i$ /pre-treatment  $K_i$ ) of 86.67%. For the LNs, most of the LNs in the mediastinal region and pulmonary hilar regions were larger and FDG-avid than before after treatment. Among them, although the left pulmonary hilar LN was larger than before, the FDG uptake and  $K_i$  were reduced than before, size of  $1.2 \times 0.8\text{cm}$ ,  $\text{SUV}_{\text{max}}$  of 4.0 (Fig3 D),  $K_i$  of  $0.0060\text{ ml/g/min}$  (Fig3 E),  $\Delta\text{SUV}_{\text{max}}$  of 29.83%, and  $\Delta K_i$  of 74.03%. The right 8th rib was also significantly smaller than before treatment, and FDG uptake was reduced, size of  $4.5 \times 1.8\text{ cm}$ ,  $\text{SUV}_{\text{max}}$  of 2.8 (Fig3. F),  $K_i$  of  $0.0068\text{ ml/g/min}$  (Fig3. G),  $\Delta\text{SUV}_{\text{max}}$  of 70.21%, and  $\Delta K_i$  of 68.22%. In addition, distant metastases were smaller than before and FDG uptake was reduced, including the retroperitoneal LN (not clearly shown), left adrenal gland (size of  $1.8 \times 1.2\text{cm}$ ,  $\text{SUV}_{\text{max}}$  of 2.1,  $\Delta\text{SUV}_{\text{max}}$  of 75.0%), bone of the sacrum (size of  $3.5 \times 3.0\text{cm}$ ,  $\text{SUV}_{\text{max}}$  of 2.1,  $\Delta\text{SUV}_{\text{max}}$  of 80.73%), left subcutaneous lumbar region (size of  $0.9 \times 0.8\text{cm}$ ,  $\text{SUV}_{\text{max}}$  of 1.4,  $\Delta\text{SUV}_{\text{max}}$  of 81.58%), and brain (size of  $1.0 \times 0.8\text{cm}$ , not uptake seen).

SMARCA4-deficient non-small cell lung cancer (NSCLC) accounts for 3%-6% of all NSCLCs [1]. It is only in recent years has emerged as a distinct NSCLC subset [2]. SMARCA4-deficient NSCLC is prevalent in men aged 40-50 years and shows a strong association with smoking [3]. It is highly aggressive, rapidly progressive, and has a poor prognosis [4-6]. There are very limited descriptions of SMARCA4-deficient NSCLC morphology as well as  $^{18}\text{F}$ -FDG PET/CT features. To our knowledge, we are the first to present a dynamic imaging and metabolic parameter profile for SMARCA4-deficient NSCLC.

Effective treatment for SMARCA4-deficient NSCLC has not been established. Little is known about the efficacy of ICIs in SMARCA4-deficient NSCLC. In 2019, Tomoyuki Naito et al. reported the first case of SMARCA4-deficient NSCLC successfully treated with nivolumab [7]. In the case we reported, the patient also received 4 cycles of ICIs (Tislelizumab).

Dynamic  $^{18}\text{F}$ -FDG PET/CT (dPET/CT) extracts physiological parameters which can better reveal the pathophysiological mechanisms of diseases. However, studies evaluating the efficacy of ICIs in

lung cancer were seldom seen. In this case, the enlarged LNs in the mediastinum and pulmonary hilar region after treatment raised our attention. Therefore, we studied the pre-treatment and post-treatment ratios of static and dynamic parameters for chest lesions (including the upper lobe of the left lung, LN in the left pulmonary hilar region, and the right 8th rib). The results showed that both the primary left lung cancer focus ( $\Delta\text{SUV}_{\text{max}}$  of 90.18%, and  $\Delta\text{K}_i$  of 85.52%) and the right 8th rib ratio were high ( $\Delta\text{SUV}_{\text{max}}$  of 70.21%, and  $\Delta\text{K}_i$  of 68.22%), but the left hilar LN  $\Delta\text{SUV}_{\text{max}}$  was low (29.83%) and  $\Delta\text{K}_i$  was high (74.03%), and the trend of  $\Delta\text{K}_i$  remained consistent with the primary focus. Therefore, whether dynamic metabolic parameters ( $\text{K}_i$ ) can give more metabolic information for the assessment of ICI efficacy deserves further investigation and is something we are studying.

**Author Contributions:** X W and Y L were responsible for writing and guidance. Xx Y provided pathology support and pictures. S J provided internal medicine support and guidance. Yr Z organized the data and figures. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was approved by the ethics committee of Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences (KYLH2022-1).

**Informed Consent Statement:** All patients signed a written informed consent before the  $^{18}\text{F}$ FDG PET/CT imaging with the Declaration of Helsinki.

**Data Availability Statement:** None.

**Conflicts of Interest:** All the authors have participated in the writing and revision of this article and take public responsibility for its content. The present publication is approved by all authors and by the responsible authorities where the work was carried out. All the authors confirm the fact that the article is not under consideration for publication elsewhere and has no conflicts of interest.

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