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CASE REPORT

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Pitfalls of 18F-FDG-avid PET-CT in the vocal cord: variation in the glucose metabolic patterns

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Abstract

Background Integrated positron emission tomography/computed tomography (PET/CT) using 2-[18F]fluoro-2-deoxy-D-glucose (18F-FDG PET/CT) is an invaluable tool for assessing glucose metabolism and providing detailed anatomical imaging in oncologic evaluations. However, interpreting 18F-FDG PET/CT remains challenging, especially because FDG has non-specific uptake in both benign conditions and malignancies.

Aim of the work This report highlights the importance of understanding the mechanisms behind FDG accumulation in the vocal cords. We present three clinical cases where tumours, inflammatory processes, and normal tissue environments are often indistinguishable.

Case presentation Case 1: 42-year-old man with 2 weeks of hoarseness and a left upper-lobe FDG-avid lung mass (T3N2M0). CT showed an atrophic left vocal cord; PET demonstrated compensatory increased FDG uptake in the right vocal cord (SUVmax 5.01). Case 2: 63-year-old diabetic woman with weight loss and nocturnal fever; chest CT suggested chronic changes consistent with secondary tuberculosis. PET/CT showed FDG-avid pulmonary lesions and bilateral vocal cord thickening with pericardial fat stranding consistent with glottitis (vocal cord SUVmax 6.78). Case 3: 60-year-old ex-smoker with 6 months of hoarseness of voice and stridor; CT revealed a left vocal cord nodule with local fat invasion, and PET showed an FDG-avid lesion (SUVmax 4.95) with multiple low FDG-avid cervical nodes. Laryngoscopy and biopsy confirmed moderately differentiated squamous cell carcinoma.

Conclusions Understanding these variations in FDG uptake is essential, particularly for inexperienced PET/CT readers. This knowledge helps avoid misinterpretation and ensures accurate diagnosis and patient care.

Keywords Vocal cord, 18F-FDG PET, Laryngeal cancer, Recurrent laryngeal nerve, Hypertrophy

Background

The 18F-FDG PET/CT is a crucial tool for evaluating glucose metabolism. It also provides detailed anatomic imaging in oncologic practice. 18F-FDG PET/CT has been utilized for diagnosis, staging, assessment of early treatment response, evaluation of metastatic disease, and prognostication [1]. Besides its oncologic uses, 18F-FDG PET/CT also helps image infections and inflammatory processes, as high glucose uptake often corresponds to active inflammation [2].

However, interpreting 18F-FDG PET/CT is challenging because benign conditions, such as inflammation, infection, and muscular activity, can influence the non-specific uptake of FDG. Among these challenges, FDG avidity in the vocal cords is especially problematic.

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Regular laryngeal FDG activity is symmetric and low grade, with a reported mean SUV in resting vocal cords of 1.77. Symmetrical increases occur if the patient vocalizes before the 18F-FDG injection, which is attributable to muscle contraction [3]. Its variable uptake patterns can mimic malignancy, causing false positives. Incidental primary glottic tumours and non-malignant findings are commonly encountered on 18F-FDG PET-CT scans [4]. Nevertheless, the reported 18F-FDG metabolic pattern distinguishing all the cellular reprogramming remains scarce [5].

Distinguishing between benign and malignant vocal cord uptake with 18F-FDG PET/CT is crucial for guiding proper clinical management.

Benign conditions such as Reinke's oedema or chronic irritation from persistent coughing, especially in cases of underlying lung infection, may result in unilateral or bilateral FDG uptake. This uptake is often diffuse and associated with cord thickening on CT imaging [6]. In contrast, primary laryngeal carcinoma or metastatic disease typically exhibits focal and intense FDG uptake, often corresponding to a tumour mass with possible infiltration into adjacent structures [7].

This study aims to analyse and document distinct patterns of FDG avidity in the vocal cords across different clinical scenarios to improve interpretative accuracy and minimize diagnostic pitfalls. Misinterpretation of 18F-FDG PET/CT images can occur due to false-positive hypermetabolic lesions, often leading to unnecessary investigations or inappropriate clinical interventions. By understanding the imaging pitfalls and the underlying physiological and pathological mechanisms of FDG uptake, clinicians and radiologists can reduce the risk of misdiagnosis in 18F-FDG PET/CT studies [8], ultimately improving patient care and management outcomes.

Aim of the work

This report highlights the need to understand the mechanisms of FDG accumulation in the vocal cords, as tumour, inflammation, and normal tissue uptake can appear indistinguishable in three clinical cases.

Case presentation

Case 1

A 42-year-old male with hoarseness of voice for 2 weeks. The patient was referred for a laryngoscopy, with no significant abnormality noted. The PET/CT scan showed a left upper lobe FDG-avid lung mass with mediastinal and left bronchopulmonary FDG-avid lymph node metastasis—stage T3N2M0. On the correlated CT scan, there is an atrophied, irregular, hypodense left vocal cord leaflet, suggesting fatty infiltration with an adjoining standard right vocal cord calibre. 18F-FDG PET scan revealed a compensatory FDG-avid right vocal cord—SUVmax 5.01. There are also reactive non-FDG-avid cervical lymph nodes seen (Fig. 1).

Case 2

A 63-year-old female with known NIDDM presented with progressive weight loss, associated with nocturnal fever. The patient had bronchial breath sounds in both lungs. In contrast, the CT scan reveals extensive, enhancing, hypodense lesions in both the lung parenchyma and pleural surfaces, with varied features that conform to consolidative lesions, cavities, tree-in-bud appearances, and reticulo-nodular patterns. These changes are in favour of secondary tuberculosis infection. On the 18F-FDG PET-CT, these pulmonary lesions exhibited FDG avidity with an SUVmax of 6.78. In addition, there is irregular thickening of the bilateral vocal cords with fat stranding surrounding, suggesting glottitis. An 18F-FDG PET scan showed a focal FDG-avid area in the vocal cords bilaterally with a SUVmax of 6.78. There are multiple cervical lymph node with minimal FDG uptake (Fig. 2).

Case 3

A 60-year-old gentleman has had hoarseness of voice, stridor, and cough for the past 6 months. The CT scan examination showed a homogeneously enhancing nodule arising from the left vocal cord with erosion and local invasion through fat tissue behind the nodule. On the correlated PET-CT scan, a left vocal cord lesion with an FDG avidity (SUVmax, 4.95) is observed, accompanied by multiple FDG-avid cervical lymph nodes (Fig. 3). Laryngoscopy revealed a left vocal cord mass with bilaterally moving vocal cords, accompanied by a histological finding of moderately differentiated squamous cell carcinoma.

Discussion

In these three cases with differing clinical backgrounds, the FDG avidity of the vocal cords varied according to the underlying pathology (Table 1). Asymmetric FDG uptake is more pronounced with inflammation or vocal cord paralysis. Reported normal-to-paralysed peak SUV ratios are commonly 3.4 or 2.4, whereas chronic post-surgical cases may show a lower ratio of 1.5. With regard to the nerve palsy cases, peak SUV in the compensatory (normal) vocal cord has been recorded to be elevated (8.9 and 6.0) with paralysed peak SUV ratios of 3.4 and 2.4,

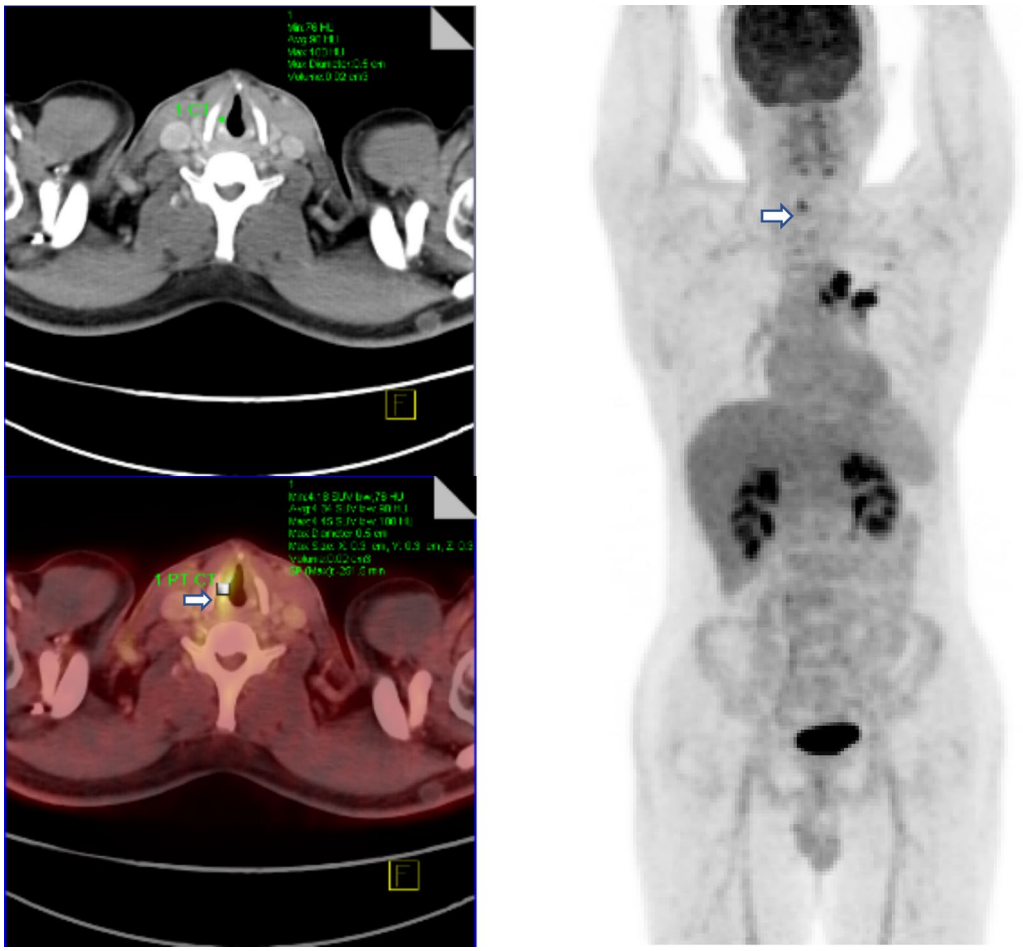

Fig. 1 Compensatory hyperfunction in vocal cord paralysis: Axial PET/CT: intense right vocal cord FDG uptake with nonavid, fatty left cord (HU – 22), indicating compensatory hyperfunction from left recurrent laryngeal nerve palsy due to infiltrative NSCLC

respectively. In the post-surgical case, a lower ratio of 1.5 was observed. In distinguishing laryngitis and tumours, the published SUVmax cut-off values after initial and delayed imaging were 3.6 and 6.1, respectively [9, 10]).

Physiological hyperfunctioning

In Case 1, there was increased FDG uptake in the right vocal cord, attributed to compensatory hyperfunction resulting from paralysis of the left vocal cord leaflet. The deranged glucose metabolism in the hyperfunctioning right cord is a result of cellular hypertrophy, which demands higher utilization via glycolysis [11]. The paralysed left vocal cord demonstrated no FDG avidity, which was further substantiated by fatty infiltration observed on CT imaging, characterized by low-density fat on the correlated CT, consistent with muscle atrophy. The physiological increased FDG uptake in the vocal cords occurs at the initiation of the vocalization following the FDG injection because of muscle contraction which is related to phonation and the SUVmean could be 1.77. In this patient, the squamous cell carcinoma of the lung had infiltrated the left recurrent laryngeal nerve (which innervates the left vocal cord leaflet) at the ligamentum arteriosum [12, 13]. The FDG uptake in the laryngeal muscles, particularly the vocal cords, can be observed symmetrically or asymmetrically in conditions such as malignancy, vocal cord paralysis, and Reinke's oedema [14]. The distinction between vocal cord paresis and a vocal cord neoplasm may not be discriminatory on the 18F-FDG PET. The peak SUV in normal vocal cords in the literature attributed to nerve palsy has been reported to be elevated at 8.9 and 6.2, respectively. Therefore, the SUV quantification is non-specific in comparing tumour from vocal cord paresis. Laryngoscopy and biopsy remain the gold standard for further complementary [9].

Inflammatory mechanism

In Case 2, bilateral FDG avidity of the vocal cords was noted, indicating glottitis, persistent coughing, and

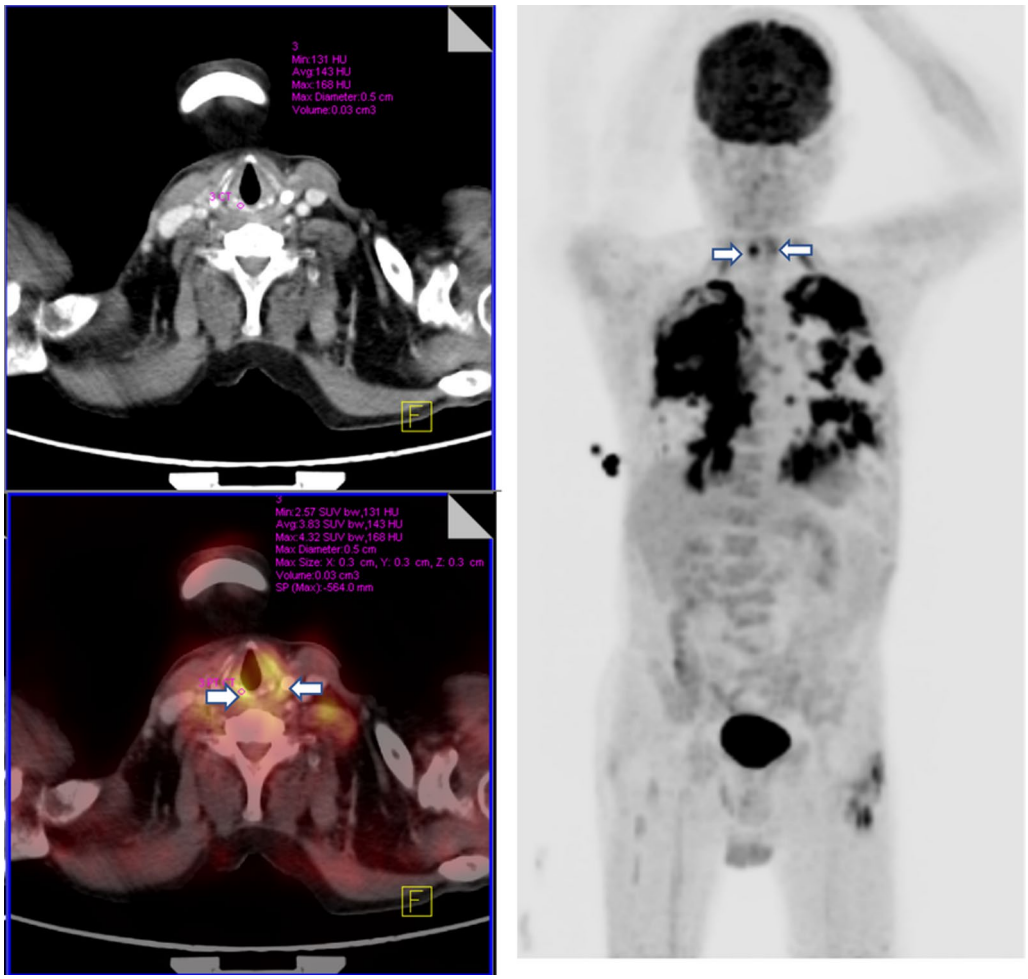

Fig. 2 Axial PET/CT demonstrates bilateral increased FDG uptake of the vocal cords (arrows) with thickened cords and pericordal fat stranding on CT, most compatible with chronic inflammatory reaction from prolonged coughing and active pulmonary tuberculosis

superimposed infection. The patient had active pulmonary tuberculosis, which led to repeated irritation of the vocal cords on chronic coughing. CT imaging revealed thickening of both vocal cords with surrounding fat stranding, indicative of an inflammatory process. The FDG avidity in such cases arises from increased glucose metabolism by inflammatory cells, notably macrophages, neutrophils, and lymphocytes, that accumulate at sites of infection and inflammation [15–17].

Malignant changes

In Case 3, the patient had laryngeal carcinoma, presenting with focal FDG avidity in a posterior left vocal cord lesion. CT imaging demonstrated a hypodense mass with infiltration into surrounding fat planes, consistent with a malignant tumour. The increased FDG uptake in this case reflects the Warburg effect, where tumour cells prefer to utilize glucose via aerobic glycolysis to sustain rapid proliferation [18, 19].

The differentiation between each cellular reprogramming in the pathophysiology of the vocal cord has a rather varied FDG accumulation pattern. Therefore, the FDG uptake signal is not specific. However, it has high sensitivity in localizing abnormal pathology far beyond the capabilities of structural imaging, i.e. the standalone CT and MRI characterization of the FDG uptake pattern in a living cell requires accurate clinical familiarity with the PET FDG pattern to avert false-positive results [20].

Conclusion

These cases highlight the clinical significance of evaluating FDG avidity patterns on PET/CT imaging for accurate differentiation between various vocal cord pathologies. Recognizing these patterns, whether resulting from compensatory hyperfunction, inflammatory response, or malignant infiltration, is crucial in avoiding false-positive interpretations, especially among

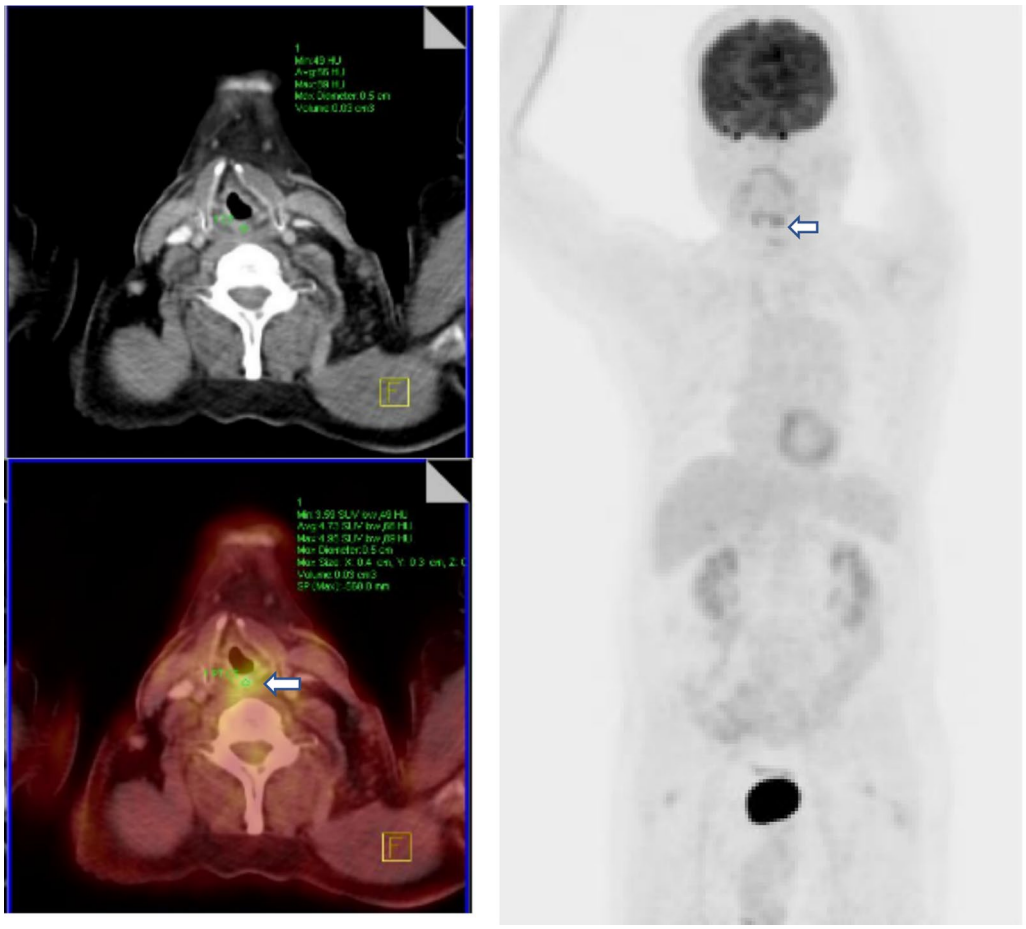

Fig. 3 Axial PET/CT: focal intense FDG uptake in a hypodense posterior left vocal cord (arrow) mass with adjacent fat-plane infiltration, consistent with primary laryngeal carcinoma (Warburg effect). Courtesy: centre for diagnostic nuclear imaging

Table 1 Mechanism of deranged glycolysis driven by vocal cord hypertrophy, inflammation and malignancy for cases 1–3

Cases	Clinical symptoms and diagnosis	FDG uptake pattern	CT changes	Variation of the glucose metabolic pattern
1	Hoarseness of voice Left vocal cord paralysis due to NSCLC infiltration of the left recurrent laryngeal nerve	Unilateral FDG avidity of the hyperfunctioning cord	Hypertrophy of the hyperfunctioning cord and fat infiltration of the atrophied cord	Physiological FDG uptake as a result of more ATP-upregulation in the mitochondria in the KREB's cycle that deranges the glucose metabolism rate
2	TB-infection with weight loss	Bilateral FDG intensity of both vocal cords	Thickened and fat stranding of both cords and at the peripheries	Macrophages-laden vocal cord inflammation causing deranged glucose metabolism
3	Hoarseness of voice and left vocal cord tumour	Intense left FDG-avid vocal cord nodule	Enhancing nodular lesion in the left vocal cord	Warburg's effect that reprogrammed the tumour lesion in the left vocal cord

less experienced readers. Awareness of these variations enhances diagnostic accuracy and aids in informed clinical decision-making, as these FDG uptake patterns in the vocal cords are non-specific and should be clinically considered; the CT/MRI and biopsy are warranted.

Abbreviations

18F-FDG	2-[18F] fluoro-2-deoxy-D-glucose
18F	Fluorine -18
PET-CT	Positron emission tomography-computed tomography
TB	Tuberculosis
SUV	Standardized uptake value

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Author contributions
All authors have approved the submitted version and agree to be personally accountable for authors' own contributions. Conceptualization, F.F.A.S., S.L.G.Y.T., S.S.P, R.M.S Validation, F.F.A.S., S.P., Resources, F.F.A.S., S.L.G.Y.T., S.S.P, R.M.S, R.F.R., review editing, F.F.A.S. All authors have read and approved the manuscript and ensure that this is the case.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board [or Ethics Committee] of Ethics Committee for Research involving Human Subjects, Universiti Putra Malaysia [JKEUPM-2019-339; 21st January 2020].

Informed consent
Informed consent was obtained from all subjects involved in the study.

Competing interest
The authors declare no competing interests.

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