Case Report

Upfront Skeletal Muscle Metastases from Non-small Cell Lung Carcinoma: Report of an Extremely Rare Occurrence Detected by 18F-Fluorodeoxyglucose Positron Emission Computed Tomography Scan

Abstract

Adenocarcinoma lung with upfront metastases to skeletal muscle is rarely encountered in clinical practice since skeletal muscles are highly resistant to dissemination from solid organs. Moreover, these muscle metastatic lesions generally present with pain and palpable mass to get detected clinically. However, silent skeletal muscle metastases without any symptoms or signs getting detected by functional imaging with whole body 18F-fluorodeoxyglucose positron emission/computed tomography (18FDG-PET/CT) scan have been scarcely described in literature, while we present such an interesting case in a 45-year-old female. She was diagnosed as a case of biopsy-proven metastatic adenocarcinoma lung after evaluation by 18FDG-PET/CT. Despite treatment with palliative chemoradiotherapy, her disease progressed, and she finally succumbed to her illness. This case is discussed to highlight an unusual scenario we encountered, the clinical course of the disease with its management and overall poor prognosis.

Keywords: *18-F-fluorodeoxyglucose positron emission tomography scan, adenocarcinoma, metastases, nonsmall cell lung carcinoma, skeletal muscle*

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Introduction

Skeletal muscle metastases (SMM) from non-small cell lung carcinoma (NSCLC) though documented is extremely rare[1] with an incidence of 0.0%–0.8%.[2] Gastrointestinal and genitourinary tract malignancies are the most common primaries[3] with an overall incidence of 0.8%–1%.[4] SMM presents most commonly with pain or palpable mass,[4,5] but an asymptomatic lesion detected by 18F-fluorodeoxyglucose positron emission/computed tomography (18FDG-PET/CT) has been seldom reported. 18FDG-PET/CT scan is the imaging modality of choice for detecting SMM.[6] Histopathology (HPR) remains the gold standard of differentiation from soft-tissue sarcomas (STS)[2,7] and initiation of appropriate therapeutic modality, though no definitive measure does exist due to its rarity.[5,8]

Case Report

A 45-year-old female with no known comorbidities presented with acute onset breathlessness, face and neck swelling for which chest roentgenogram showed a right lung mass. CT scan chest showed a mass lesion right upper and middle lobe (RUL/RML) causing superior vena cava obstruction. Image-guided biopsy from the lung mass revealed adenocarcinoma with immunohistochemistry (IHC) positive for thyroid transcription factor-1 (TTF-1) and CK7 [Figure 1]. She was treated with radiotherapy to mediastinum to a dose of 20 Gy in 5 fractions which resulted in the resolution of symptoms. Magnetic resonance imaging (MRI) brain was normal, while whole-body 18FDG-PET/CT (WB-18FDG-PET/CT) showed FDG avid RUL/RML irregular marginated mass lesion with standard uptake value (SUV) of 7.36 [Figure 2] and FDG avid soft-tissue lesion left gluteus muscle with a SUV of 9.83 [Figures 3 and 4], biopsy from which revealed metastatic deposit from adenocarcinoma lung with IHC staining positive for TTF-1 [Figure 5] and negative for desmin, thus ruling out STS. She was started on palliative chemotherapy with cisplatin and pemetrexed, but after 3 cycles, she presented with severe lower back and pelvic pain. WB-18FDG-PET/

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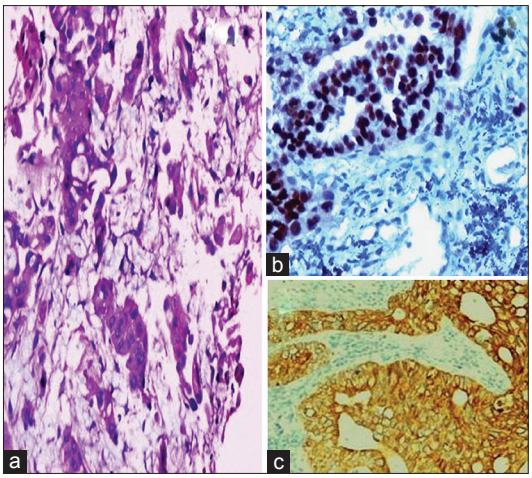

Figure 1: Image-guided biopsy from the lung mass showing (a) adenocarcinoma pattern (H and E, ×100); (b) Immunohistochemistry of lung mass staining positive for thyroid transcription factor-1 (×100) (c) immunohistochemistry staining positive for CK-7 (×50)

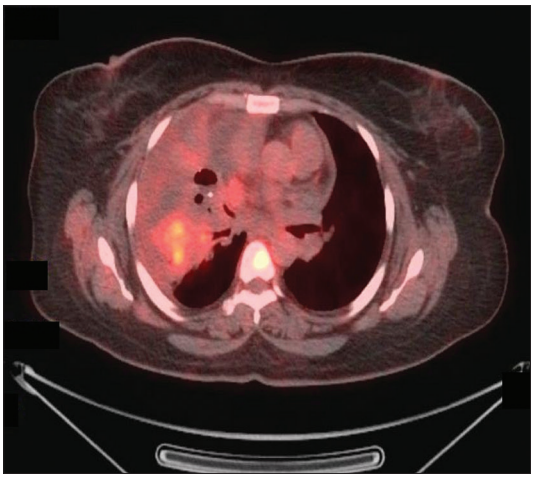

Figure 2: Whole body 18F-fluorodeoxyglucose positron emission/computed tomography scan fused image showing fluorodeoxyglucose avid irregular marginated mass lesion right lung

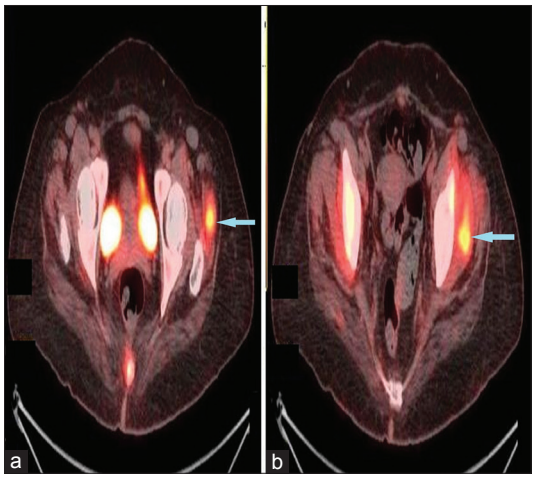

Figure 3: Whole body 18F-fluorodeoxyglucose positron emission/computed tomography scan fused image axial section showing fluorodeoxyglucose avid soft-tissue mass lesion left gluteus muscles (yellow pointer)

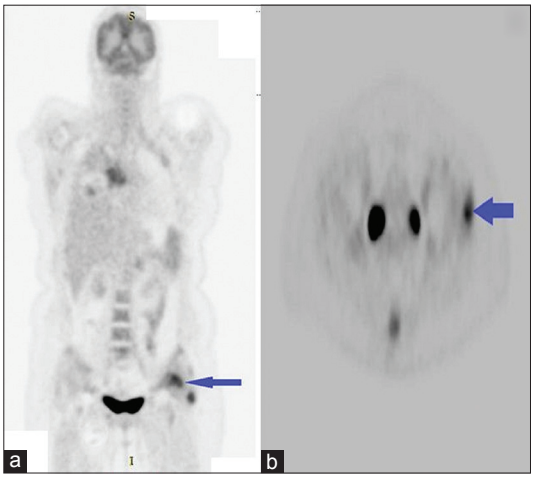

Figure 4: Whole body 18F-fluorodeoxyglucose positron emission/computed tomography scan maximum intensity projection image (a) coronal section; (b) axial section showing fluorodeoxyglucose avid soft-tissue mass lesion left gluteus muscles (blue pointer)

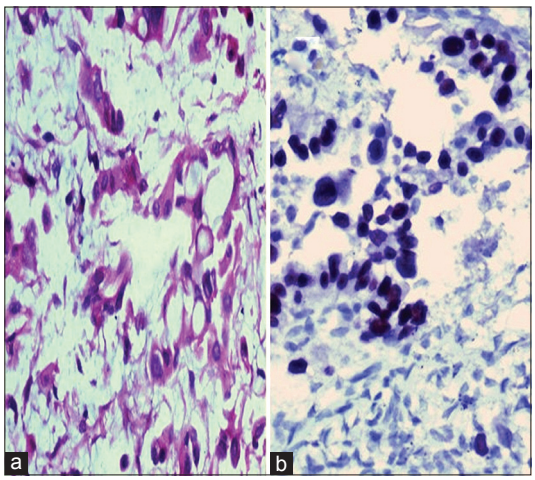

Figure 5: Biopsy from left gluteus muscle mass showing (a) metastases from adenocarcinoma lung (×200); (b) Immunohistochemistry positive for thyroid transcription factor-1 (×100)

CT showed new FDG avid metastases to bilateral supraspinatus [Figure 6], psoas muscles, pelvis, and lumbar vertebrae suggestive of disease progression [Figure 7]. She was treated with lower hemi-body radiation to dose of 8 Gy in 2 fractions. However, despite pain relief, her condition kept on deteriorating and she finally succumbed to her illness within a span of 3 months from diagnosis.

Discussion

Skeletal muscle, especially striated muscle, is highly resistant to primary as well as metastatic lesions.[5] Several hypotheses do exist regarding muscle resistance like acidic pH due to lactic acid, muscle contractibility, tissue pressure, variable blood flow, oxygen free-radical production, cellular and humoral immunity, and hypersensitivity reactions.[5-7] The most common primaries with SMM are from gastrointestinal and genitourinary tract

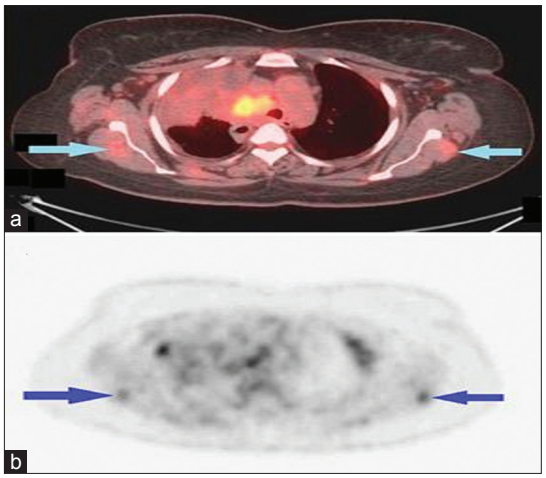

Figure 6: Whole body 18F-fluorodeoxyglucose positron emission/computed tomography scan post 3 cycles of chemotherapy showing new findings of fluorodeoxyglucose avid soft-tissue metastases to bilateral supraspinatus muscles (blue arrow) (a) fused image; (b) maximum intensity projection image

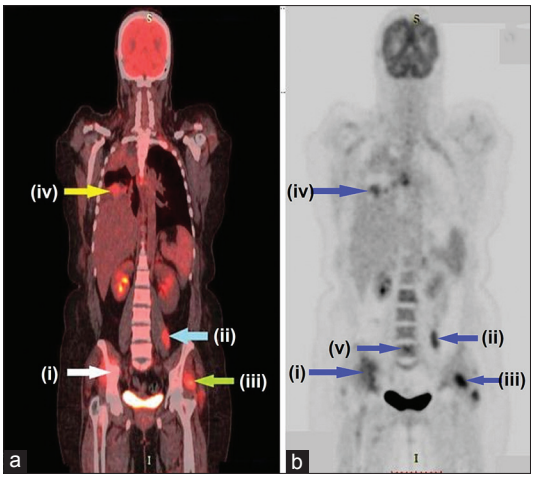

Figure 7: Whole body 18F-fluorodeoxyglucose positron emission/computed tomography scan after 3 cycles of chemotherapy: (a) Fused image showing (i) new fluorodeoxyglucose avid skeletal metastases to pelvis; (ii) new metastases to psoas muscle (iii) persistent left gluteus muscle metastases; (iv) progressive primary lung mass. (b) Maximum intensity projection image showing corresponding lesions described above along with (v) lumbar vertebral metastases visualized more clearly

malignancies,[3] with an incidence of 0.8%–1% SMM.[4] Wittich in 1854 reported the first incidence of SMM, while Willis first reported SMM from lung.[5] NSCLC most commonly metastasizes through hematogenous route to distant organs such as brain (10%), bones (7%), liver (5%), and adrenal gland (3%), while SMM accounts for a mere 0.0%–0.8%,[2] which depicts the rarity of such occurrence. Most information regarding this rare phenomenon has been described in case reports and few case series with maximum 16 cases of lung SMM reported by Pop *et al*.[5] Adenocarcinoma has been described to be more aggressive with poor prognosis[9] than squamous cell carcinoma to cause SMM[5,8,9] with a mean survival of 5.6 months.[5]

SMM occurs more commonly in males compared to females with smoking as the principal predisposing factor.[5,8,10] For SMM, pain is the most common symptom followed by palpable mass[2-10] whether SMM gets detected before or synchronously within 6 months or metachronously after 6 months of diagnosis of primary.[5] A painful mass has often been associated with SMM in contrast to STS,[8] while a silent SMM like our case has been scarcely reported.[7] Although SMM can be found in any muscle group, lower extremity, especially calf and thigh,[8] is the most common location as compared to upper extremities[5,7,8] with a solitary SMM having a better prognosis than multisite lesions.[8,10] Regarding the detection of SMM, CT scan shows rim-enhancing mass with central hypoattenuation but can be confused with an intramuscular abscess.[5] MRI with gadolinium contrast shows peritumoral enhancement suggestive of central necrosis and vascularity but are not specific for SMM,[8] though few consider it as the imaging of choice.[7] 18FDG-PET/CT identifies regions of active proliferation within the primary tumor and SMM. FDG is a surrogate marker of tumor cell metabolism and proliferation and increases the diagnostic specificity[6] as compared to CT and MRI, thus making it the imaging modality of choice for metastatic workup. The possible differentials for focal and diffuse muscle uptake of FDG along with their imaging characteristics are given below [Table 1].

Although 18FDG-PET/CT can identify silent metastatic lesions, the definite diagnosis of origin is identified by HPR supported by IHC.[2,7] The most common differential diagnosis of SMM is STS and notwithstanding the various clinical criteria, HPR do differentiate between the two which becomes more relevant in case of silent metastases[7] as was seen in our case. Tissue biopsy from both primary lung lesion and SMM showed adenocarcinoma with IHC positivity for TTF-1 and SMM staining negative for desmin, a muscle-specific protein. Due to rarity of lung SMM, no definite or optimal management protocol exists,[5,8] and all therapeutic approaches are palliative only.[10] Surgery and/or RT has been used in localized disease without any dissemination with the primary lung carcinoma under control to alleviate pain or mass effect. However, the use of local therapy in a systemic disease has not shown any survival benefit and palliative chemotherapy has been considered the cornerstone of treatment in case of extensive disease.[5,8,10]

Conclusion

NSCLC with a silent SMM do pose a diagnostic and therapeutic dilemma for treating oncologists. WB-18FDG-PET/CT is of immense benefit in detecting such occurrence and if not done, the metastatic lesions may remain hidden, thus altering the therapeutic approach. As 50% NSCLC is metastatic at the time of diagnosis,[5] 18FDG-PET/CT is of utmost importance complimented with tissue biopsy to give the final diagnosis. Unfortunately, SMM from primary lung without previous dissemination

Table 1: Differentials for focal and diffuse muscle uptake of FDG along with their imaging characteristics

Differentials	Imaging characteristics	Remarks
Normal uptake in skeletal muscle	Mild and homogeneous	
Patient on insulin	"Muscle scan" tumor uptake can be faint (false negative)	Insulin-dependent GLUT-4 translocation to plasma membrane
Postprandial scan	Diffuse increase uptake in skeletal muscle and heart	Insulin induced
Stress-induced muscle tension	Mostly seen in trapezius and paraspinal muscle (can be reduced by benzodiazepine)	Physiological uptake is mostly linear, mild to moderate, frequently symmetric
Hyperventilation	Diaphragm (linear uptake)	
Activities such as talking, chewing, etc.,	Uptake limited to muscles involved	
Improper positioning during imaging	Asymmetric uptake of the side involved	
Acute hemiparesis	Reduced muscle uptake on the involved side	Likely due to denervation and altered muscle energetics
Postoperative/biopsy site	Increased uptake in surrounding muscles	Surgery-induced inflammatory change
Soft-tissue sarcoma	Can be intense, asymmetric, heterogeneous uptake	FDG helpful in staging, restaging and response assessment due to SUV and total lesion glycolysis
Metastatic tumor	Solitary or multiple foci	Generally rare involvement
	Maybe no corresponding morphological abnormality on CT	Most common: gastrointestinal and genitourinary tract
		Adenocarcinoma >SqCC
Lymphoma	Gluteal and pelvic muscle most commonly affected	Generally unusual involvement (extranodal)
	Skeletal muscle involvement in NHL are generally iso-intense in CT (FDG uptake is helpful in showing involvement)	Either contiguous involvement from nearby involved LNs or by haematogenous/lymphatic spread
Multiple myeloma	Focal, intramuscular masses	Usually a component of extramedullary disease
	Most frequently paraspinal, thigh, iliopsoas, and calf muscle	PET helps in differentiating local infiltration from adjacent bone lesion and exclusive intra muscular involvement
	Very rarely generalized myopathy	

CT: Computed tomography, FDG: Fluorodeoxyglucose, SUV: Standard uptakes value, SQCC: Squamous cell carcinoma, NHL: Non-Hodgkin's lymphomas, PET: Positron emission tomography

to other anatomically predictable locations suggests an aggressive disease with dismal prognosis. However, proper interpretation of the molecular and pathophysiological mechanisms of SMM may help to device novel therapeutic approaches to counter this disease process.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name, and initial will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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