

Detection of muscle metastases on ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography scan in 13 cases

ABSTRACT

Muscular metastases (MMs) form an infrequent entity, and their physiopathology is still not well-defined. In this study, we estimated the incidence of MMs that were detected by ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography and also specified their metabolic characteristics. This study includes 13 patients with MMs from a remotely located primary tumor. The results of this study showed an incidence of MMs at about 1%, with the most frequently involved muscles being iliopsoas and paraspinal. Lung cancer seems to be the most common tumor that causes MMs. Furthermore, these MMs vary in size and physiological uptake; they seem to be out of the ordinary and easily detected. They are often associated with other extra muscular locations and frequently involve the trunk muscles. Their detection in the course of the evolution of a specific neoplasia testifies to their aggressiveness and portends an unfavorable prognosis. The data in our series confirm that in the literature regarding the underlying primary tumors and anatomical sites involved by MMs.

Keywords: ¹⁸F-fluorodeoxyglucose, iliopsoas, muscular metastases, neoplasia, paraspinal, physiological uptakes, positron emission tomography/computed tomography

INTRODUCTION

Muscular metastases (MMs) are so anecdotal that their physiopathology is still not well-defined. They generally occur during the course of a specific neoplasm, and are often associated with other secondary anatomical sites. Most common involved neoplasms are lung cancer and hematological malignancies. Most of the studies in the last decade report that ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) imaging technique is a turning point in their early detection before any clinical and radiological manifestations. Consequently, this methodology may potentially improve the therapeutic care of such disease.

MATERIALS AND METHODS

Patients

We report here 13 cases of unknown MM-affected patients with the clinical picture and different tumors. Our patients

were selected from a database of 1216 patients referred to Military Hospital Mohammed V, Rabat, Morocco. We have included all patients who underwent ¹⁸F-FDG PET/CT in a period between September 2015 and December 2017. All our patients had more than one single muscle site, and none of them amenable to histological confirmation due to the multiple muscle involvement and association with other remote sites at ganglion, bone, or visceral levels.

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CT morphological images associated with PET images allow, in addition to the attenuation correction and anatomical identification, tissue characterization of structural abnormalities corresponding to hyperactive foci.

Methods

All our patients had ¹⁸F-FDG PET/CT scans after an 8 h of fasting and after checking their fasting blood levels (all patients had a fasting glucose level of <2g/l). The images were acquired using a GE Medical Systems Discovery STE8™ PET/CT camera. Whole-body images were taken 45–60 min after intravenous injection of 3.5–4.5 Mbq/Kg of ¹⁸F-FDG. The duration of each examination was on average 35 min at the order of 8–9 steps of 3 min 30 s each. The reconstruction of the three-dimensional images was performed using an ordered subset expectation maximization-type iterative reconstruction mathematical algorithm (3–5 iterations) and maximum intensity projection images and fusion images in axial, sagittal, and coronal sections were generated. The interpretation of patient images requires a visual analysis of PET and CT images fused together in order to perform a quantification of hypermetabolic foci by using the maximum standardized uptake value (SUVmax) index. This was calculated for all the primary tumor sites and for various muscular hypermetabolic locations. A hypermetabolic muscle focus was considered suspicious for malignancy when its SUVmax was >2.5.

RESULTS

In our series, there were 12 male and one female patient. Their average age was 56 years, with a range of 23 and 67 years. There were six cases of bronchial cancers, all adenocarcinomas, and four cases were lymphomas: one Hodgkin's lymphoma and three non-Hodgkin's large cell lymphoma [Table 1]. ¹⁸FFDG PET/CT was indicative of MMs in seven cases as part of an initial extension assessment, in three patients as part of a therapeutic evaluation report, and in three patients in the context of a recurrence detection report.

The muscles that seem to be the most frequently affected were the iliopsoas muscle (about 19% of cases) and the paravertebral muscles (about 15% of cases) [Table 2]. A single hypermetabolic focus proven by a biopsy as lung cancer MMs was observed in the right popliteal fossa in patient number 4 [Table 3]. The other foci were multiple and very consistent with MMs. A case of myocardial metastasis of the apex complicating a high-grade neuroendocrine tumor (G3) was observed in patient number 2 in Table 1, which was associated with other muscle and bone sites [Figure 1].

Table 1: List of primary tumors causing muscular metastases

Patient ID	Sex/old (years)	Primitive tumour	Indication
1	Female/51	Inflammatory breast cancer	Recurrence
2	Male/67	Neuroendocrine tumour G3	Recurrence
3	Male/60	Diffuse large B-cell lymphoma	Recurrence
4	Male/53	Lung adenocarcinoma	Restaging
5	Male/54	Lung adenocarcinoma	Restaging
6	Male/23	Ewing's sarcoma	Restaging
7	Male/63	Hodgkin's lymphoma	Staging
8	Male/58	Diffuse large B-cell lymphoma	Staging
9	Male/55	Diffuse large B-cell lymphoma	Staging
10	Male/63	Lung adenocarcinoma	Staging
11	Male/61	Lung adenocarcinoma	Staging
12	Male/62	Lung adenocarcinoma	Staging
13	Male/61	Lung adenocarcinoma	Staging

Table 2: Found frequencies of the muscular locations

Muscle site	Number of foci (%)
Iliopsoas	5 (19)
Paravertebral	4 (15)
Intercostal	3 (11)
Gluteal	3 (11)
Thigh muscles	2 (7)
Others	10 (37)

SUVmax indices were measured, including the primary tumors, hyperactive muscle foci, and hyperactive extramuscular foci. The results of these measurements are summarized in Table 3. In the case of lymphomas, the SUVmax for the primary tumor was that of the most active ganglionic focus. SUVmax values ranged from 3.1 to 37.1, with an average of 11.3. On average, the SUVmax values of extramuscular sites, namely lymph nodes, visceral, and bone, were 14.37, 17, and 18.31, respectively.

DISCUSSION

MMs are relatively rare and not very well understood. Their incidence is lower than 1% in published clinical series, which includes recent ones with ¹⁸FFDG PET/CT.^[1,2] There is a higher incidence in men compared to women.^[3] In our study, the incidence was about 1%, and the M/F sex ratio was 12/1.

Physiopathologically, several factors have been put forward to explain the rarity of MMs, including the importance of the vascular supply of skeletal musculature; which alone constitutes 50% of the total body mass.^[4] It is appropriate here to point out the importance of the hematogenous pathway in the dissemination of the neoplastic process in the organs and muscles, as well as the possibility of contiguous involvement of the muscles of the chest wall and the heart by malignant pleuropulmonary processes.^[5] In our series, the

Table 3: Anatomical sites and morphometabolic characteristics of muscular metastases

Patient ID	Muscle sites	MM Size (mm)	MM SUV _{Max}	Primitive SUV _{Max}	Extramuscular active foci
1	Femoris	35	15.1		Lymph nodes, hepatic, cutaneous, pulmonary, and bones
	Trapezius	15	14.3		
	Large dorsal	16	17.7		
	Gluteus medius	30	5.0		
2	Pillar of the diaphragm	10	7.0	14.0	Lymph nodes and sternum bones
	Iliopsoas	28	14.0		
3	Puborectal	38	12.6	22.6	Lymph nodes, adrenal glands, and bones
4	Iliopsoas	32	37.1	11.5	Barety lodge, pulmonary, adrenal glands, and lymph nodes
	Paravertebral	25	32.6		
5	Popliteal hollow	18	23.4	19.0	Lymph nodes, pulmonary, and cutaneous
6	Paravertebral	37	12.1	12.5	Pulmonary and bones
	Iliopsoas	24	9.1		
7	Paravertebral	76	9.1	10.4	Lymph nodes and bones
	Iliopsoas	29	10.9		
8	Gluteal	18	5.0		Lymph nodes and pelvis bones
9	Biceps	16	4.8	14.1	Lymph nodes, splenic, subcutaneous, and bones
	Intercostal	22	3.1		
10	Iliopsoas	60	16.0	22.5	Lymph nodes and bones
	Ilioschial	31	13.8		
	Intercostal	17	8.4		
11	Short tight adductor	28	3.8	8.7	Meningeal, lymph nodes, bones, adrenal glands, and subcutaneous
12	Up spiny	10	4.0	3.4	Lymph nodes, adrenal glands, and bones
	Down spiny	13	4.1		
	Intercostal	9	4.5		
13	Paravertebral	21	5.1	4.3	Lymph nodes, hepatic, cutaneous, and bones
	Abdomen	26	6.3		
	Gluteal	14	7.4		

MM: Muscular metastasis; SUVmax: Maximum standardized uptake value

MMs documented were those from a remote primary tumor. The factors involved in the implantation and development of tumor cells in the muscle tissue, include: (a) the intensity of the contractile activity of the muscle which destroys the microcirculation and induces a too fast and turbulent flow of blood which affects the fixation of the muscle tumor cells on the vascular endothelium, (b) rapid changes in acid pH, (c) temperature and electrical activity changes of the muscle, and (d) the accumulation of enzymedependent protease inhibitors necessary for tumor growth.^[6,7] However, some muscle dysfunctions related to microtrauma contribute to reduce muscle's capacity to produce the lactic acid and to reduce resistance to the migrating cells.^[8] This last factor also enhances the risk of delaying the diagnosis by attributing it to recent trauma.

Clinically, MM data are derived from rare cases published as case reports or limited series. These data are summarized in three points:

1. The common tumors regarding their origin
2. The available imaging techniques in the detection of MMs

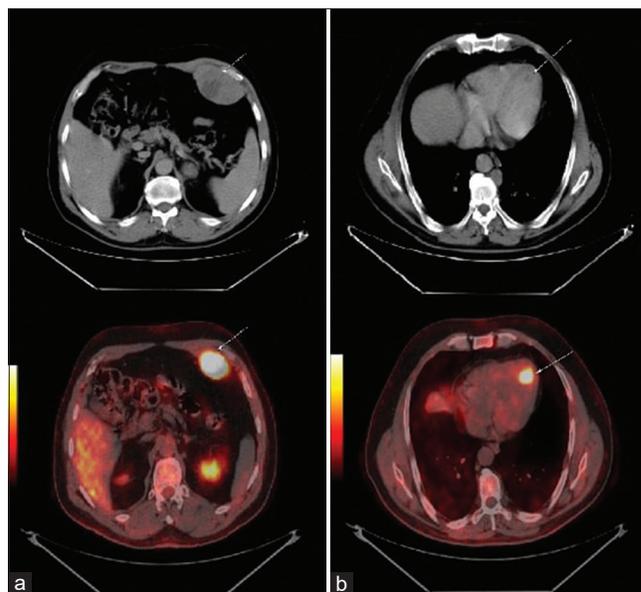


Figure 1: A 67-year-old patient suffered from a high grade of neuroendocrine tumor. Recurrence detection report. (a) Fusion image in axial section shows reached muscle of the left diaphragmatic abutment. (b) Fusion image in axial section shows a secondary localization of the myocardium (localization of the apex proved by a cardiac magnetic resonance imaging)

3. The most affected body muscles by MMs.

Regarding the first point, all authors agree on the high occurrence of MMs associated with lung cancer in male patients. This occurrence is about 30% in male patients in the series of Mathis *et al.*^[9] and about 54% in the series of So *et al.*,^[2] followed by hematological malignancies with an occurrence of about 22%.^[10] On the other side, this time, regarding a female patient, gynecological cancers come in first place with an occurrence of about 36%.^[9] The data in our series are harmonious with ones in the literature, concerning lung cancers and lymphomas in male patients. In the only case of MM in a female patient which was reported in our series, the tumour was initially invasive ductal carcinoma of the recurrent breast after initial treatment. At this point, we should emphasize the metastatic potential of other skeletal muscles and myocardial tumors such as melanomas, differentiated thyroid cancers, and neuroendocrine tumors with frequencies ranging from 1% to 4%.^[9]

Regarding the second point, skeletal muscles most frequently affected by MMs were found each time by the majority of authors. In the Surov *et al.*,^[5] gluteal, iliopsoas and paravertebral muscles were found with respective frequencies of 10.7%, 10.1%, and 10.3%, respectively [Figure 1]. In our series, the same kind of muscles was found with high frequencies: iliopsoas muscles (38%), paravertebral muscles (31%) [Figure 2], and gluteal muscles (23%) [Figure 3b]. Therefore, these muscles seem to be privileged sites for metastatization and the development of secondary tumor foci. In the same line, and in parallel with the data of the literature, we retain the rarity of muscular macrometastases.^[5] This entity was observed in two of our patients with biceps in one patient and localization in the popliteal fossa in the other one [Figure 4].

Particular attention is devoted to the involvement of the heart muscle, also known for its resistance to MMs. This involvement was found in the literature with an occurrence ranging from 1% to 10%, broadly related to lung cancer and melanoma.^[11] More rarely, other solid tumors such as renal cancer, breast cancer, and colon cancer may cause these metastases.^[12,13] Our series includes an infrequent case of MMs of the secondary myocardial apex having a high-grade neuroendocrine tumor as a single similar case reported in the literature in Cornily *et al.*^[14]

The last point that arouses our discussion is the fact that the currently available imaging techniques contribute to the diagnosis and therapeutic evaluation of MMs. In this regard, ultrasound seems to be the simplest and least expensive way to detect MMs. Indeed, it allows the visualization of MMs

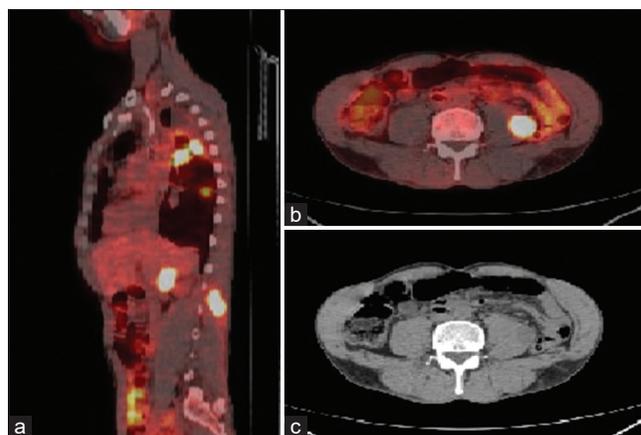


Figure 2: Assessment report after radiochemotherapy for a 53-year-old patient with lung adenocarcinoma. (a) Sagittal sectional fusion image shows involved paravertebral muscle at the height of L1 (maximum standardized uptake value = 32.6). (b and c) Computed tomography and fusion images in axial sections for a metastasis in the left psoas muscle (maximum standardized uptake value = 37.1)

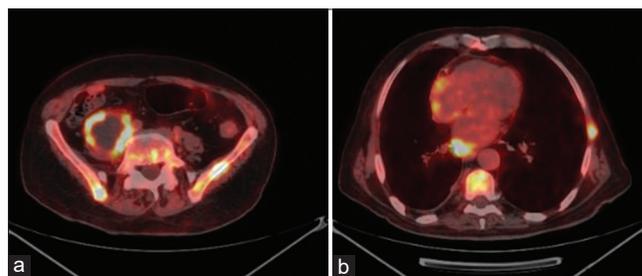


Figure 3: Fusion images in axial sections in a patient with a bronchial adenocarcinoma, showing, in addition to reached iliac bone, two hypermetabolic masses of secondary muscle localizations. (a) Hypermetabolic mass of the right psoas muscle with necrotic ametabolic center. (b) intercostal hypermetabolic focus at the height of K5-K6. Initial extension repon

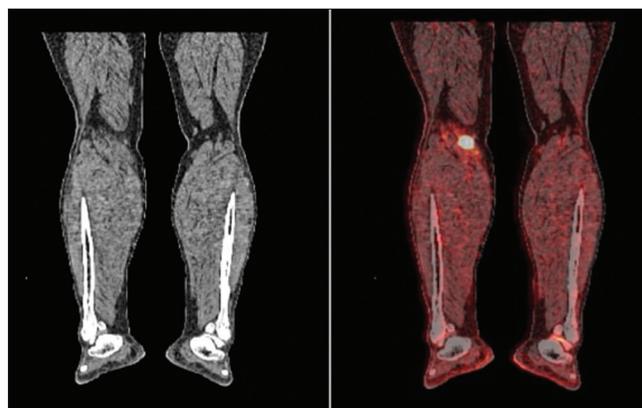


Figure 4: Coronal sectional fusion image showing a reached muscle of the right popliteal fossa (maximum standardized uptake value = 23.4) which corresponds to a mass of tissue tone on the morphological image

in the form of hypoechoic lesion or echoheterogeneous structure or in the form of mass with irregular and poorly defined contours.^[5,15] The weak point in the exploration of the muscle masses lies in its inability to assess the

whole-body and also in the delayed diagnosis imposed on such examination by the late call signs, most often the pain, necessary for its orientation in a particular muscular site.

With regard to CT, which seems to be the most popular examination in routine practice during cancer check-ups and monitoring, it remains crucial in the demonstration of secondary muscle localizations ensuring in the same examination the analysis of cervical structures and upper and lower of trunk diaphragmatic. Its sensitivity remains low in detection around 61%,^[2] hampered by two major factors: the first is intrinsic, is linked to the tomodensitometric image of the tumor tissue, translates into a hypo or isodense aspect, and is difficult to visualize within the muscle mass^[5] and the second is extrinsic and linked to the eye that sees it and the vigilance of the radiologist whose attention is fixed mainly on the regions and organs most affected by metastases, namely the ganglionic areas, lungs, livers, bones, and adrenal glands. As it is false or true so, we thought that many small muscle lesions are unnoticed during CT acquisition. In this kind of radiological imaging, the main differential diagnoses of muscle metastases are abscesses, sarcomas, and hematomas in their initial phase.^[10,16]

As for here, magnetic resonance imaging (MRI) medical imaging technique is the most efficient radiological examination for tumor characterization of muscle metastasis. It provides a superior soft-tissue contrast resolution, and it has a high-resolution imaging capability. However, the visualization of features such as perilesional edema, intralesional hemorrhage, or central necrosis foci is not specific and does not allow to differentiate a metastasis from a muscular sarcoma or an infectious site.^[17] In addition, in the extension and followup assessments of neoplasms, MRI is not routinely requested in total body exploration to allow a fine analysis of the trunk and limb musculature of the limbs and probably also a large part of the body. MMs go unnoticed at infraclinical stages. Its real merit in the diagnosis of MMs is to be able to locate and suspect it by eliminating a benign cause and finally to direct biopsy specimens in nonnecrotic tumor tissue areas.^[18]

The advent of PET/CT, combining in the same examination the morphological and spatial resolution qualities of CT on the one side and the hyperactive character of tumor foci visualized in PET on the other side, contributes to the improvement of the detection sensitivity of MMs, occult reaching in the series of So *et al.* a sensitivity of 100%.^[2] ¹⁸FFDG PET/CT also draws its power from the total fetal lesion mapping that it allows, added to that, its great negative predictive value that eliminates the diagnosis of MMs when

suspicious muscle damage on conventional imaging does evince pathological hypermetabolism. Conversely, intense focused hypermetabolism +/-nonfixating centre is highly suspect [Figure 3a] and imposes its confrontation with diagnostic CT [Figure 4]. The most common false positives in these situations are mainly related to bursitis, tendonitis, and muscle contractures.^[19] ¹⁸FFDG PET/CT can detect unmasked MMs without call signs,^[20,21] which was the case of 12 patients from 13 of our series.

The identification of MMs by ¹⁸FFDG PET/CT was almost always made in the presence of secondary extramuscular locations and thus without any impact on the staging of the disease. However, sometimes, MMs were identified in the isolated state, contributed to change in the staging of the disease, and then, ensure a better cure. This change in staging was observed in 50% of cases in the series.^[22] In our series, all of the muscular foci were associated with other secondary localizations showing an advanced stage of the disease and an unfavorable prognosis. It should be noted here that the average SUVmax value of muscular foci was not the highest value regarding other affected anatomical sites. Consequently, it does not represent the most aggressive one at all. PET in these cases allows a better estimation of their sizes and intensities of fixation by visual analysis and semi-quantitative indices. The latter facilitates their monitoring on consecutive examinations.^[23,24]

The use of the SUVmax index reinforces and also supports the diagnosis of metastasis when its value exceeds 2.5.^[25] In the current literature, the mean value of SUVmax measured at the metastatic foci was 8 ± 5 in Savas *et al.* study^[25] and 8.0 ± 4.4 in Surov *et al.* study^[16] and SUVmax values were between 1.5 and 34 in Roman and Hovsepien's review.^[26] In our selected patients, this value is averagely 11.3, with extremes of 3.1 and 37.1. As for the size of muscle foci, CT showed MMs of variable size, with an average of 44.9 mm over 260 MMs analyzed by Surov *et al.*,^[5] In contrast, the ¹⁸FFDG PET/CT was able to highlight MM sizes, respectively, of 16 ± 6.25 mm and 25.1 ± 14.5 mm in the series of Savas *et al.*^[25] and in ours showing superiority of PETCT over CT in early detection MMs at stages in which their size is still smaller than 40 mm.

In PET, studies of MMs have so far been very limited to small series, including ours, confirming the superiority, in terms of sensitivity, of ¹⁸FFDG PET/CT compared to ones of CT and MRI.^[2,5,15,24,25,27] Larger series studies would undoubtedly provide adequate conclusions about the exact place of ¹⁸FFDG PET/CT in the diagnosis, staging, and monitoring of MMs.

The most appropriate cure for these specific lesions remains controversial. Surgical therapy from the start allows both symptomatic and oncologic treatments.^[28] The place of radiotherapy should also be discussed for analgesic purposes and local control after surgical excision. For the majority of the teams, adapted chemotherapy remains the proper indication when these metastases are multiple and asymptomatic.^[29]

CONCLUSION

MMs are so infrequent. The knowledge of their existence constitutes a factor of a bad prognosis. Their care varies from one patient to another. Primary studies in ¹⁸F-FDG PET/CT have shown, its superiority over other medical imaging techniques in the detection of these infrequent infraclinical lesions. To emphasize this conclusion, we suggest that more extensive future studies must be undertaken.

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Conflicts of interest

There are no conflicts of interest.

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